I.M.A.G.S.B. NEWS BULLETIN

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GUJARAT MEDICAL JOURNAL

INDIAN MEDICAL ASSOCIATION, GUJARAT STATE BRANCH

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GMJ

STATE PRESIDENT AND HON. STATE SECRETARY'S MESSAGE

Dear Members,

Our best wishes are always there for you & your family members. This is the month of festivals. We have Raxabandhan, Independence Day, Janmashtami, Paryushan, Ganesh Utsav & this all will be followed by world's longest dance festival Navratri, Dashera & Diwali , followed by New Year. There is series of festivals & we all are celebrating eachone of them in a unique way with fun, joy & enthusiasm. This is possible because in this country we are free to express our emotions & views in public. But my dear friends, I would like to reiterate that any kind of freedom comes with its own responsibilities too. I am very much sorry to mention that in today's era, most of us are not fulfilling our duties towards our beloved Nation. We all are very much aware about our rights.

Whenever there is some common issue, we believe that someone else will do it. Then who someone else? Freedom without duties is always harmful to the nation in long run. We expect our leaders to perform in extraordinary way. To my views, nation will develop through each one of us's small & unique effort. Not by anyone's huge effort.

The similar thing is applicable to our own IMA too. As we are at Ahmedabad, this year organising IMA NATCON-2014 in the month of December, we also expect all of yours small contribution in away by becoming delegate for this grand event which we are hosting after a huge span of 25 years. That will certainly boost our morale & enthusiasm. We also invite your active participation in other modes too which inspires you. Friends, don't wait till last date & register by today only.

We request our leaders at different zones & branches to make active efforts to persue the information & feeling to every members of our state. We don't need to say too much as we all are wise enough to get our duties for our IMA.

This month we are publishing journal to keep our members update not limited to heir branch but as a whole, because we have to satisfy our patients by resolving their basic queries related to almost all fields. We do accept your suggestion to improve the quality of our publication ongoingly.

We strongly believe that " WORKING TOGETHER WORKS." See you next month. Till then enjoy life fully, fulfilling your duties simultaneously too.

Thanking you

DR. BIPIN M. PATEL
President, IMA GSB.

DR. JITENDRA N. PATEL
Hon State Secretary, IMA GSB.

FROM THE DESK OF EDITORS



Dear friends,

While putting the second issue of Gujarat Medical Journal in your hands in this year, we regret that, the issue is published a month late, instead of July, in August.

As per the article published in Lancet (May 2014), according to a study done by researchers of the University of Washington, about 29% of world is overweight, it means 2.1 million people are either overweight or obese in 2013! The prevalence of overweight and obese population rose by 27.5% for adults and 47.1% for children between 1980 and 2013. In 1980, 857 million people were overweight or obese. The study was carried out in 183 countries. It revealed that today 36.9% of world's men and 38% of women are overweight or obese. Nearly two out of three obese live in developing countries. According the study, U.S. stands first and China is the second, while India is third with 40.4 millions in the list of overweight people. Ahmedabad Medical Association carried out a survey of about 8500 school children in 2013 and results shown that about 20% or more children were overweight or obese! This is alarming.

In last five years of time many new medical collages have started in our state and that will create many new doctors to serve the country and the society. At the same time a demand for new academic minded medical teachers is also increasing. Our hospitals and expertise are world class and that pushes the medical tourism in Gujarat far ahead. Our hospitals and institutes are well equipped with world class equipments and infrastructures.

People from developed and underdeveloped countries come here for treatment and we provide them world best treatment at a cheaper rates then that is available in developed countries. Also we get large number of patients from our own domestic population and this provides ample of opportunities for our colleagues working in hospitals, medical collages and research institutes for research. GMJ provides them a platform.

You all know our GMJ is an INDEXED JOURNAL. For last few years, indeed, we get more research articles for publication. Without making any compromise in our laid down standards and policy, it has always remained our effort to make GMJ more informative, more interesting and more popular so that large number of our colleagues read it and utilize the knowledge and information provided in it. For this, we welcome your suggestions and comments also.

Our sincere thanks to GSB president Dr. Bipin Patel and hon. secretary Dr. Jitendra N. Patel for encouragement and suggestions. We are grateful to Dr. Kirtibhai Patel and Dr. Mahendrabhai Desai for their guidance and help. Our particular thanks to GMJ ex. editor Dr. Amitbhai Shah for all sorts of help and guidance that he has provided us time to time.

Promising you the best reading,

With regards,

DR. K. R. SANGHAVI
Editor-IMA-GSB-GMJ

DR. B. I. PATEL
Hon. Secretary -IMA-GSB-GMJ

DR. HARSHAD C. PATEL
Jt. Editor-IMA-GSB-GMJ

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CASE REPORT

REVIEW ARTICLE

PHOTOPHARESIS : Modality Of Therapeutic Apharesis

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KEY WORDS : Extracorporeal Photochemotheray (ECP), Theerapeutic Apharesis, Photoactivation

ABSTRACT

Graft-versus-host disease (GvHD) is the major cause of mortality and suffering following allogeneic hematopoietic stem-cell transplantation. Conventional treatments are associated with multiple side effects and are often ineffective. New therapeutic approaches for the control of GvHD is developed called Photopharesis or Extracorporeal Photochemotherapy. Extracorporeal photochemotherapy (ECP) was developed in the 1970s for the treatment of cutaneous T-cell lymphoma . ECP has also proved an effective therapy for immune-related conditions, particularly GvHD, even in patients refractory to conventional therapies. The treatment involves the mechanical separation of circulating white cells, which are exposed to psoralen and UVA light and then returned to the patient. ECP is extremely well tolerated with minimal side effects. Thus, ECP appears to offer selective immune modulation without generalized immunosuppression, but its mechanism of action remains poorly understood. This review discusses the historical aspect of ECP, its use in the treatment of GvHD, and other indications , its principle and method of usage as well as current hypothesis of its mechanism of action along with adverse reactions.

HISTORICAL ASPECT OF APHARESIS

In twentieth century separating blood components was recognized as a therapy called Apheresis. Abel experimentally performed Apheresis for the first time in 1914 on dog. In the 1950s discontinuous-flow manual procedure was performed to carry out Apharesis. In the 1960s, continuous-flow hemapheresis machines were introduced. In May 1981, one of the most important educational and scientific contributions to the apheresis practice,was by establishing the American Society for Apheresis (ASFA) whose guidelines to perform aparesis are very useful . [1,7,9]

Apharesis dealt with separating components of the blood and then returning the blood back to the donor. However as the time passed Apharesis was also employed for Therapeutic purposes Broadly TYPES OF APHERESIS employed with the advent of modernization were as under :

BASED ON COMPONENT THAT IS SEPARATED :

Plasma (plasmapheresis)
Platelets (plateletpheresis)
Red Blood Cells(Erythrocytapheresis)
Leukocytes (leukapheresis)
Stem cell harvesting - circulating bone marrow cells are harvested
BASED ON PURPOSE :
For Donation and Therapeutic Apharesis

INTRODUCTION

The word “apheresis” literally means “to separate” or “to take away ” , derived from a Greek word, as is done by the blood sucking worm called leech. The process of apheresis involves removal of whole blood from a patient or donor. Apharesis instrument is essentially designed as a centrifuge, the components of whole blood are separated. One of the separated portions is then withdrawn and the remaining components are retransfused into the patient or donor. [1,6,8] Photopharesis is a modality of apharesis used for therapeutic purpose. It follows the principle of apharesis . Here Extracorporeal photopheresis (ECP) is performed using the UVAR XTS Photopheresis System developed by Therakos, Inc (Exton, Pa). The process is performed through one intravenous access port and has 3 basic stages: (1) leukapheresis, (2) photoactivation, and (3) reinfusion. [2,5,7] The process takes 3-4 hours to complete.

THERAPEUTIC INDICATIONS OF PHOTOPHARESIS:: [2,3,4,5,6]

patients with Cutaneous T Cell Lymphoma (CTCL)

Graft versus host disease (GVHD).

The efficacy of Extracorporeal Photopharesis is also found in the treatement of

Type 1 Diabetes Mellitus,

Pemphigus Vulgaris ,

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Bullosa acquisita,

Atopic dermatitis

Inflammatory bowel disease..

Systemic Lupus Erythematosus

Scleromyxedema.

Nephrogenic systemic sclerosis

Nephrogenic fibrosing dermopathy.

MECHANISM AND PRINCIPLE OF PHOTOPHARESIS

The combination of 8-MOP and UVA radiation causes apoptosis of the treated T cells and may cause preferential apoptosis of activated or abnormal T cells, thus targeting the pathogenic cells of cutaneous T-cell lymphoma (CTCL) or graft versus host disease (GVHD).

However, given that only a small percentage of the body's lymphocytes are treated, this seems unlikely to be the only mechanism of action causing apoptosis of activated or abnormal T cells. (Fig. 1.)

Other evidence suggests that extracorporeal photopheresis also induces monocytes to differentiate into dendritic cells capable of phagocytosing and processing the apoptotic T-cell antigens. When these activated dendritic cells are reinfused into the systemic circulation, they may cause a systemic cytotoxic $CD8^+$ T-lymphocyte–mediated immune response to the processed apoptotic T-cell antigens. Finally, evidence from animal models also indicates that photopheresis may induce antigen-specific regulatory T cells, which may lead to suppression of allograft rejection or GVHD. [6,7,9]

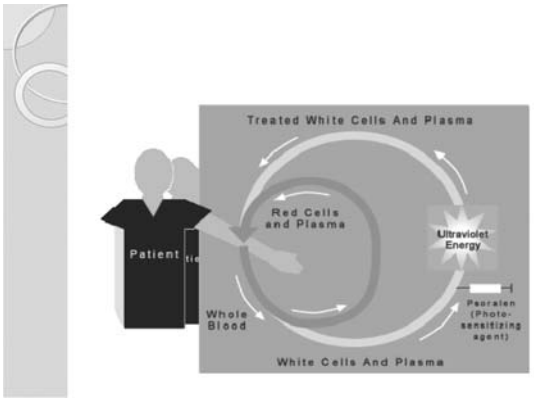

Fig 1. Mechanism and Principle of Photopharesis

PROCEDURE FOR PHOTOPHARESIS : (Fig.2)

Extracorporeal photopheresis (ECP)is performed using the UVAR XTS Photopheresis System developed by Therakos, Inc (Exton, Pa). The process is performed through one intravenous access port and has 3 basic stages: (1) leukapheresis, (2) photoactivation, and (3) reinfusion. (2,5)

The process takes 3-4 hours to complete.

- One 16-gauge peripheral intravenous line or central venous access is established in the patient.
- Blood (225 mL) is passed through 3 cycles of leukapheresis, or 125 mL of blood is passed through 6 cycles, depending on the patient's hematocrit value and body size. At the end of each leukapheresis cycle, the red blood cells and plasma are returned to the patient.
- The collected WBCs (including approximately 5% of the peripheral blood mononuclear cells) are mixed with heparin, saline, and 8-methoxypsoralen (8-MOP), which intercalates into the DNA of the lymphocytes upon exposure to UVA light and makes them more susceptible to apoptosis when exposed to UVA radiation.
- The mixture is passed as a 1-mm film through a sterile cassette surrounded by UVA bulbs for 180 minutes, resulting in an average UVA exposure of 2 J/cm2 per lymphocyte.
- The treated WBC mixture is returned to the patient.

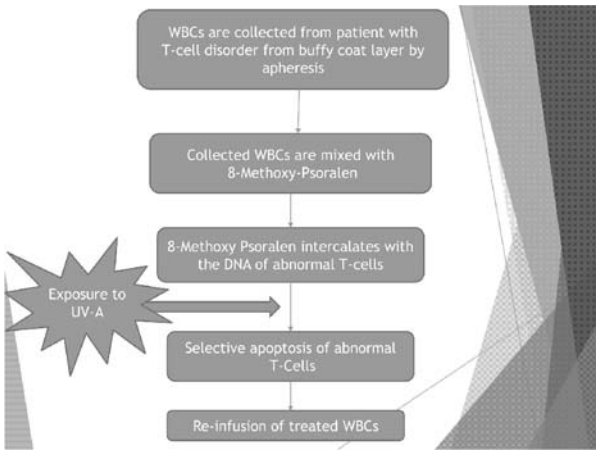

Fig. 2 : Procedure For Photopharesis

ADVERSE REACTIONS DURING PHOTOPHARESIS

Extracorporeal photopheresis (ECP) is a very well-tolerated procedure.

*Transient hypotension may occur in some patients during the collection phase of the treatment, but this is asymptomatic in most and usually resolves with reinfusion of the blood products. Occasionally, saline must be given during extracorporeal photopheresis to maintain blood pressure, and patients taking antihypertensives are asked to withhold these medications until after the procedure.

*Two to 12 hours after extracorporeal photopheresis, some patients experience low-grade fevers, likely due to the release of cytokines. Over the same time course,

some patients with cutaneous T-cell lymphoma (CTCL) may experience an increase in pruritus or redness.

*Finally, although patients with hypertriglyceridemia do not experience any further adverse events during extracorporeal photopheresis, they may have a less efficacious treatment because of the inability of the UVAR machine to separate the WBCs from the lipid-rich blood. Because of this, patients should have triglyceride levels of less than 300 mg/dL and should fast (except for fluid intake) before the procedure.

*In all of the various patient groups treated, no immunosuppression, opportunistic infections, or neoplasia has been associated with extracorporeal photopheresis. [8,9]

*Although 8-MOP is rapidly cleared from the blood, levels in the eyes have not been measured. The risk of cataract formation is minimal if the patient protects the eyes using UVA-blocking sunglasses the day of the procedure.

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REVIEW ARTICLE

Management of Cancer Pain

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KEY WORDS : Cancer pain, opioids, NSAIDS

ABSTRACT

Advances in the diagnosis and treatment of cancer, coupled with advances in understanding the anatomy, physiology, pharmacology, and psychology of pain perception, have led to improved care of the patient with pain of malignant origin. The goal of pain therapy for patients receiving active treatment is to provide them with sufficient relief to tolerate the diagnostic and therapeutic approaches required to treat their cancer. For patients with advanced disease, pain control should be sufficient to allow them to function at a level they choose and to die relatively free of pain.

INTRODUCTION

There are 19 million new cases of cancer diagnosed worldwide each year and more than 7 million cancer deaths.[1] Existing studies based on numerous national and international surveys and WHO estimates suggest that moderate to severe pain is experienced by one-third of cancer patients who receive active therapy and by 60% to 90% of patients with advanced disease. Bone pain is the most common type, with tumor infiltration of nerve and hollow viscus as the second and third most common pain sources. Cancer therapy causes pain in 15% to 25% of patients receiving chemotherapy, surgery, or radiation therapy. Chronic pain is also prevalent in cancer survivors, with prevalence rates ranging from 5% to 40% of patients and varying by tumor type and cancer treatment.[2,3]

Definition of Pain

The definition of pain proposed by the International Association for the Study of Pain is “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.[4]

Types of Pain

Three types of pain have been described from activation and sensitization of nociceptors and mechanoreceptors in the periphery by either mechanical stimuli (e.g., tumor compression or infiltration) or chemical stimuli (e.g. epinephrine, serotonin, bradykinin,).

Somatic Pain - When nociceptors are activated in cutaneous or deep tissues, somatic pain results, typically characterized by a dull or aching but well-localized pain. Metastatic bone pain, postsurgical incisional pain, and myofascial and musculoskeletal pain are common examples of somatic pain.

Visceral Pain - Visceral pain results from activation of nociceptors from infiltration, compression, extension, or stretching of the thoracic, abdominal, or pelvic viscera. This type of pain is poorly localized; is often described as deep, squeezing, and pressurelike; and when acute is often associated with significant autonomic dysfunction, including nausea, vomiting, and diaphoresis. Increasing data have demonstrated the role of kappa-opioid receptors in modulating visceral pain.[5]

Neuropathic Pain - Neuropathic pain results from injury to the peripheral or central nervous system as a consequence of tumor compression or infiltration of peripheral nerves or the spinal cord or from chemical injury to the peripheral nerve or spinal cord caused by surgery, radiation therapy, or chemotherapy. Pain from nerve injury is often severe and is described as burning or dysesthetic, with a viselike quality. The pain is typically most common in the site of sensory loss and may be associated with hypersensitivity to nonnoxious (allodynia) and noxious stimuli.

Temporal Aspects of Pain

Acute Pain - Acute pain is characterized by a well-defined temporal pattern of pain onset, generally associated with subjective and objective physical signs and with hyperactivity of the autonomic nervous system. All of the pain in this category of acute pain have associated autonomic hyperactivity.

Chronic Pain - Chronic pain is pain that persists for more than 3 months, with a less well-defined temporal onset. The autonomic nervous system adapts, and chronic pain

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patients lack the objective signs common to those with acute pain. Chronic pain leads to significant changes in personality, lifestyle, and functional ability.

Baseline pain is the average pain intensity experienced for 12 or more hours during a 24-hour period. *Breakthrough pain* is a transient increase in pain to greater than moderate intensity that occurs on a baseline pain of moderate intensity or less.

Intensity of Pain

Specific categoric scales of pain intensity is used in which patients are asked to describe their pain as mild, moderate, severe, or excruciating. Visual analog scales (VASs) have also been used. These are often a 10-cm line anchored on either end by two points, signifying *no pain* and *worst possible pain*. Numeric scales are also commonly used, and patients are asked to rate their pain between 1 (no pain) and 10 (worst possible pain).

Measurement of Pain

Multidimensional pain assessment is the recommended approach to the study of pain prevalence and pain intervention. Several validated instruments for pain measurement attempt to look at it in a multidimensional way.

Brief Pain Inventory - The Wisconsin Brief Pain Inventory (BPI) is a self-administered, easily understood, brief method to assess pain.[6]. Patients are asked to rate their pain at its worst, their usual pain, and their pain at the time they are completing the questionnaire. Patients are asked to report the treatments they receive for pain, the percentage relief that these medications or treatment provide, their belief about the cause of their pain and how much the pain interferes with their mood, and functional ability

McGill Pain Questionnaire - The McGill Pain Questionnaire (MPQ) is an extensively used pain assessment instrument that produces scores on four empirically derived dimensions, as well as several summary scores.[7] The instrument consists of 78 adjectives that cluster in 20 categories. Within each category, the adjectives are arranged in order of intensity from low to high. The categories are divided into four dimensions: sensory, affective, evaluative, and miscellaneous.

Memorial Pain Assessment Card - The Memorial Pain Assessment Card (MPAC) is used to assess the relative potency of new and standard analgesic drugs. The MPAC consists of three VASs that measure pain intensity, pain relief, and mood and a set of pain severity descriptors adapted from the Tursky rating scale.

Memorial Symptom Assessment Scale -The Memorial Symptom Assessment Scale (MSAS) is a validated, patient-rated measure that provides multidimensional information about a diverse group of common symptoms.[8] Thirty-two physical and psychological symptoms are characterized in terms of intensity, frequency, and distress. The MSAS provides a Global Distress Index (MSAS-GDI), a ten-item subscale that reflects global symptom distress and separate subscales that measure physical (MSAS-Phys) and psychological (MSAS-Psych) symptom distress.

European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30 and Edmonton Symptom Assessment Scale These scales has been validated in cancer patients and correlated closely with the MSAS and BPI measurement tools.[9]

Clinical Assessment of Pain

Certain general principles should be followed in evaluating cancer patients who complain of pain.[10] The general principles are the following:

- Believe the patient's complaint of pain.
- Take a careful history of the patient's pain complaint.
- Evaluate the patient's psychological state.
- Perform a careful medical and neurologic examinations.
- Order the appropriate diagnostic studies and personally review the results.
- Treat the pain to facilitate the appropriate workup.
- Reassess the patient's response to therapy.

Perform Careful Medical and Neurologic Examinations

Medical and neurologic examinations help provide the necessary data to substantiate the history. They also provide a direct assessment of the cognitive status of the patient. Defining the degree of motor or sensory changes can help identify the specific site in the nervous system that may be involved. Similarly, in patients with sensory loss, the presence of allodynia and hyperesthesia can further identify the nature of the sensory problem and define a neuropathic pain syndrome.

Management of Cancer Pain

The basic approach employs three categories of agents: opioid analgesics, nonopioid analgesics, and adjuvant therapies. The foundation of this approach is an individualized combination of opioid and nonopioid drugs; to this foundation is added tailored care that selects from a broad array of adjuvant interventions to achieve maximum comfort for the individual patient.

Pharmacologic Management of Cancer Pain

Analgesic Drug Therapy: the Mainstay of Cancer Pain Management

Cancer pain management combines treatment of the primary disease with (1) analgesic drug therapy and (2) specific approaches that may include anesthetic, neurosurgical, rehabilitative, psychological (cognitive-behavioral), psychiatric, or complementary and alternative methods.

The World Health Organization Cancer Pain Guidelines

The WHO guidelines on cancer pain continue to provide a framework approach for pharmacologic management of cancer pain management. Field testing of these guidelines, as well as clinical experience, has shown that 70% to 90% of cancer patients' pain can be controlled using a simple and inexpensive method described as the *three-step analgesic ladder*.[11,12]

Step 1 of the WHO ladder focuses on analgesic drug therapy for patients with mild to moderate cancer pain. Such patients should be treated with a nonopioid analgesic that may or may not be combined with an adjuvant drug, depending on the specific pain pathophysiology.

Step 2 of the WHO ladder focuses on patients with moderate pain who do not experience adequate pain relief from a nonopioid analgesic. These patients are candidates for a combination of a nonopioid, such as aspirin, acetaminophen, other NSAIDs, and low doses of opioid analgesics. These patients often require adjuvant drugs, depending on the pain pathophysiology.

Step 3 pertains to patients who report either severe pain (often gauged as greater than 7 to 10 on a 0 to 10 scale) or moderate pain that is inadequately managed after appropriate administration of drugs at the second step of the WHO ladder. For these patients, nonopioids are often used in combination with more potent doses of opioids to mitigate the opioid effect, and adjuvants are administered depending on the pain pathophysiology or need to control other concurrent symptoms in the individual patient.

Cancer Pain Management Using the World Health Organization Three-Step Analgesic Ladder

Nonopioid Analgesics for Cancer Pain Management

The nonopioid analgesics include acetaminophen and the NSAIDs, of which aspirin is the prototypic agent. These compounds are most commonly administered orally. Their analgesia is limited by a ceiling effect. Tolerance and physical dependence do not occur with repeated administration. Aspirin and the other NSAIDs have analgesic, antipyretic, anti-inflammatory, and antiplatelet actions. Others (e.g., ibuprofen) appear to produce fewer gastrointestinal side effects than aspirin. The COX-2 inhibitors potentially offer less gastrointestinal (GI) toxicity and without affecting platelet function. Acetaminophen, an analgesic and antipyretic agent equipotent to aspirin, is much less effective as an anti-inflammatory agent but does not interfere with platelet function. Survey data from the WHO demonstration projects suggest that 20% to 40% of patients obtain pain relief with the use of nonopioid analgesics alone.[13] If pain relief is not obtained, adding an opioid to a nonopioid provides additive analgesia

Opioid Drugs for Cancer Pain Management

The opioid analgesics, of which morphine is the prototype, vary in potency, efficacy, and adverse effects. These drugs produce their analgesic effects by binding to discrete opiate receptors in the peripheral and central nervous systems. It do not appear to have a ceiling effect. There are also series of drugs that are pure antagonists (i.e., they block the effect of morphine at the receptor). The antagonist drug most commonly used in clinical practice is naloxone, which is administered to reverse respiratory depression and other complications associated with opioid overdose.

1. *Start with a specific drug for a specific type of pain.*

   As defined by the WHO three-step analgesic ladder, the specific drug chosen depends in part on the degree of pain intensity and the type of pain. Opioid responsiveness is defined as the degree of analgesia achieved during dose escalation to either intolerable side effects or adequate analgesia. It has been suggested that neuropathic pain, which accounts for 15% to 20% of pain problems that are difficult to manage, is opioid-resistant and that opioid drugs should not be used in this patient population.[14]

   The clinician's armamentarium for managing cancer pain now encompasses a series of opioid alternatives to morphine, including congeners of morphine hydromorphone, oxycodone, oxymorphone - as well as methadone, levorphanol, fentanyl, and buprenorphine. The choice of agent depends on the clinician's knowledge about how to use the drug, patient factors such as age and renal function, route of delivery, opioid availability, and cost.

   Controlled-release oral morphine is currently available in a wide range of doses from 15 to 200 mg; differing products provide options for every 8-, 12-, and 24-hour administration. These preparations provide analgesia comparable to that of immediate-release forms and offer increased convenience. Oxycodone, which is commonly administered in a 5-mg dose at the second step of the WHO analgesic ladder, can also be used in the third step at higher doses. It is available in a slow - release preparation.[15] Its half - life is 3 to 4 hours. Oxymorphone is its active metabolite. Methadone represents a second-line drug for cancer pain patients who have had prior exposure to opioids. It is a relatively inexpensive oral

analgesic. The bioavailability of methadone is higher than that of morphine (85% vs. 35%, respectively). Its analgesic potency also differs, with a parenteral to oral ratio of 1:2 in contrast to 1:6 for morphine. Moreover, the plasma half-life of methadone is 17 to 24 hours.

With the development of a novel transdermal patch for administration and various transmucosal preparations, fentanyl is an opioid analgesic used effectively in cancer patients for management of both acute and chronic pain.[16] The half-life of fentanyl is 1 to 2 hours. 4 mg of intravenous morphine is equivalent to 100 mcg of intravenous fentanyl. Patches are currently available in 12.5 to 100 mcg/h doses and are changed every 72 hours. When a patient is started on the fentanyl patch, there is up to a 12- to 15-hour delay in the onset of analgesia, and alternate approaches must be used to maintain patients' pain control during this period.

Buprenorphine, a mixed agonist/antagonist opioid drug, is used to treat chronic noncancer pain and drug addiction and is also available in a transdermal preparation for cancer pain management. It is reported to be a useful agent in patients with moderate to severe pain, and it does not accumulate in patients with renal dysfunction.

2. *Know the equianalgesic dose of the drug and its route of administration*. Knowing the equianalgesic dose (i.e., the dose of one analgesic drug that is equivalent in the pain-relieving potential of another analgesic drug) can ensure more appropriate drug use.

3. *Administer analgesics regularly after initial titration.* Medication should be given regularly to maintain the plasma level of the drug above the minimum effective concentration for pain relief. In the initial titration, patients should be advised to take their medication as needed to determine their total 24-hour requirements.

4. *Gear the route of administration to the patient's needs.* Various methods of opioid drug delivery have been developed in order to maximize pharmacologic effects and minimize side effects. Most patients require at least two routes of drug administration, and 20% need up to four approaches during the course of their cancer pain treatment.

   The oral route is preferable and easy. Orally administered drugs have a slower onset of action, delayed peak time, and longer duration of effect. Drugs given parenterally have a rapid onset of action but a shorter duration of effect.

   For the rectal route, oxymorphone, hydromorphone, and morphine are available in suppository form. The transdermal route is a convenient way to deliver a potent short-acting opioid on a continuous basis. Various parenteral routes include intermittent and continuous subcutaneous, intravenous, epidural, intraventricular, and intrathecal infusions.

   Use of intermittent and continuous epidural and intrathecal opioid infusions is based on the demonstration of opioid receptors in the dorsal horn of the spinal cord and the availability of opioid drugs to suppress noxious stimuli at the spinal cord level. Localized selective analgesia is produced without motor or sensory blockade. However, distribution of the drug directly into the cerebrospinal fluid is 10 to 100 times greater. Existing studies demonstrate that this approach is used with approximately 10% of cancer patients to maximize analgesia and minimize side effects.

5. *Use a combination of drugs.* By using a combination of drugs, the physician can increase analgesic effects without escalating the opioid dose.

6. *Anticipate and treat side effects.* The side effects of the opioid analgesics often limit their effective use. The most common side effects are sedation, respiratory depression, nausea, vomiting, constipation, and multifocal myoclonus and seizures.

7. *Manage tolerance.* The earliest sign of developing tolerance is the patient's complaint that the duration of effective analgesia has decreased. Increased opioid requirements are most commonly associated with disease progression rather than with tolerance alone. Because the analgesic effect is a logarithmic function of the dose of opioid, a doubling of the dose may be needed to restore full analgesia. Tolerance to the respiratory effects of opioid doses occurs. This degree of tolerance makes it safe for patients to increase their opioid doses for analgesia. Tolerance to one opioid does not lead to complete tolerance to another opioid.

8. *Taper drugs slowly.* The long-term administration of opioid analgesics is associated with the development of physical dependence; thereafter, the sudden cessation of the opioid analgesic produces signs and symptoms of withdrawal: agitation, tremors, insomnia, fear, marked autonomic nervous system hyperexcitability, and exacerbation of pain. Slowly tapering the dose of the opioid analgesic prevents such symptoms.

9. *Anticipate complications.* Overdose with opioid analgesics occurs either intentionally, when a patient takes an excessive amount of drug in a suicide attempt, or unintentionally, when the recommended dose accidentally produces excessive sedation and respiratory depression. In both instances, the complication can be treated effectively with naloxone.

Adjuvant Drugs

Adjuvant drugs are used to enhance opioid analgesia, provide analgesia for certain types of pain (e.g., neuropathic pain, bone pain, and visceral pain), and treat opioid side effects or other symptoms associated with pain.[17] They are an integral part of the WHO analgesic ladder.

Adjuvants to Enhance Analgesia - Acetaminophen, NSAIDs, hydroxyzine, and dextroamphetamine have been demonstrated to provide additive analgesia to patients chronically receiving opioids.

Adjuvant Analgesics for Neuropathic Pain

Neuropathic pain has a variable responsiveness to opioid drug regimens and may be less responsive than other types of pain. Some of the commonly used adjuvant drugs for managing this population of patients are described in the following sections.

Antidepressants - The tricyclic antidepressants continue to be the most useful group of psychotropic drugs applied in pain management.[18.19] Their analgesic effects are mediated by enhancement of serotonin activity. Data from controlled trials indicate that both the tertiary amine tricyclic antidepressants (amitriptyline, doxepin, imipramine, and clomipramine) and the secondary amine compounds (desipramine and nortriptyline) have analgesic effects. These drugs have been reported to be effective in treating continuous dysesthesias as well as intermittent lancinating dysesthetic pain.

Anticonvulsants - The role of anticonvulsants in the management of patients with neuropathic pain is based, in part, on the fact that the mode of action is to stabilize membranes and alter sodium and calcium influx.[20] Many patients with neuropathic pain complain of paroxysmal, brief, lancinating pains are the one benefited the most. The drugs most commonly used include gabapentin, carbamazepine, and phenytoin and pregabalin.

Local Anesthetics - The use of both brief intravenous local anesthetic infusions (lidocaine) and maintenance oral anesthetic drugs has demonstrated some efficacy in the management of chronic neuropathic pain, particularly in those patients with both lancinating and continuous dysesthesias. Mexiletine is the oral local anesthetic for which there are pilot data to support analgesic efficacy.[21]

Cutaneous Local Anesthetics - The use of cutaneous anesthesia has been suggested to be most helpful in patients who have significant allodynia and marked hyperesthesia. The use of high-concentration lidocaine (5% and 10%) has also been reported to be effective in patients with significant allodynia associated with postherpetic neuralgia.[22]

Corticosteroids - A series of controlled and uncontrolled surveys have demonstrated that the use of chronic corticosteroid therapy to reduce pain in patients with breast and prostate cancer improves quality of life.[23,24] The major indications for corticosteroid use include refractory neuropathic pain, bone pain, pain associated with capsular expansion or duct obstruction, and headache due to increased intracranial pressure.

Adjuvant Drugs for Bone Pain - Numerous investigators have identified a management approach for bone pain, which includes the use of specific surgical palliative approaches, radiotherapeutic approaches, hormonal therapies, and bone resorption inhibitors.

Patients with multifocal metastatic bone disease that is refractory to routine treatments may benefit from the use of a series of agents, including the bisphosphonate compounds, gallium nitrate, calcitonin, and radiopharmaceuticals. Bisphosphonate drugs such as pamidronate, zoledronate, clodronate, and etidronate bind to bone hydroxyapatite, inhibiting osteoclast activity, and are highly effective in the management of bony metastatic disease and in multiple myeloma.

Strontium-89 and samarium-153 are bone-seeking radiopharmaceuticals that have been recognized as useful in the treatment of bone pain secondary to metastatic disease.[25,26,27] Use is indicated in patients with refractory multifocal pain due to osteoblastic lesions who have a life expectancy of longer than 3 months, who have sufficient bone marrow reserve

Psychological Approaches

Studies strongly support an association between cancer pain and psychological distress, predominantly manifested as mood disturbance, anxiety, and depression.[28]

Established behavioral therapies for cancer pain fall into three categories: (1) comprehensive cognitive behavioral therapy (CBT); (2) hypnosis and imagery-based CBT; and, (3) psychoeducational interventions.[29]

Anesthetic and Neurosurgical Approaches

Anesthetic and neurosurgical approaches are most effective in treating patients with well-defined localized pain. Ten percent to 20% of cancer pain patients require these approaches, together with pharmacologic approaches, to obtain adequate analgesia.

ANESTHETIC and NEUROSURGICAL PROCEDURES-

Type of Procedure	Most Common Indications
Inhalation therapy with nitrous oxide	Breakthrough pain, incidental pain in patients with diffuse poorly controlled pain
Intravenous barbiturates (sodium pentobarbital)	Diffuse body pain and suffering inadequately controlled by systemic opioids
Local anesthetic by intravenous, subcutaneous, or transdermal application	Neuropathic pain in any site with local application to the area of hyperesthesia or allodynia
Trigger point injections	Focal muscle pain
Peripheral nerve block	Pain in discrete dermatomes in chest and abdomen or in distal extremities
Epidural nerve block	Unilateral lumbar or sacral pain; midline perineal pain; bilateral lumbosacral pain
Intrathecal nerve block	Midline perineal pain; bilateral lumbosacral pain
Autonomic blocks	
Stellate ganglion	Reflex sympathetic dystrophy
Lumbar sympathetic vascular insufficiency of the lower extremity	Reflex sympathetic dystrophy of the lower extremities; lumbosacral plexopathy
Celiac plexus	Midabdominal pain from tumor infiltration
Intermittent or continuous epidural infusion with local anesthetics	Unilateral and bilateral lumbosacral pain; midline perineal pain; neuropathic pain from the midthoracic region down
Intermittent or continuous epidural or intrathecal with local opioid analgesics	Unilateral and bilateral pain below the midthoracic region; often combined with local anesthetics
Intermittent or continuous intraventricular infusions with opioid analgesics	Head and neck pain and upper chest pain
Chemical hypophysectomy	Diffuse bone pain

Site	Procedure	Indications
Nerve root	Rhizotomy	Useful in somatic and neuropathic pain from tumor infiltration of the cranial and, rarely, intercostal nerves.
Spinal cord	Dorsal root entry zone lesion	Useful in unilateral neuropathic pain from brachial, intercostal, and lumbosacral plexopathy and postherpetic neuralgia.
	Cordotomy	Useful in unilateral pain below the waist. Often combined with local neurolytic blocks in perineal and bilateral lumbosacral plexopathy; may be performed bilaterally.
	Myelotomy	Useful in midline pain below the waist but rarely used because it involves extensive surgery.
Brainstem	Mesencephalic tractomy	Useful in pain in the nasopharynx and trigeminal region.
Thalamus	Thalamotomy	Useful in unilateral neuropathic pain in the chest and lower extremity.
Cortex	Cingulotomy	Useful through a stereotactic approach for diffuse pain.
Pituitary	Transsphenoidal hypophysectomy	Useful in pain control of bone metastases in endocrine-dependent tumors, breast, and prostate.
Peripheral nerve	Transcutaneous and percutaneous electrical nerve stimulation	Useful in reducing painful dysesthesias from tumor infiltration of nerve or trauma (e.g., neuroma).
Spinal cord	Dorsal column stimulation	Of limited use in neuropathic pain in the chest, midline, and lower extremities.
Thalamus	Thalamic stimulation	Of rare use in neuropathic pain in the chest, midline, or lower extremity.

Future Directions

The study of pain in cancer patients offers a unique opportunity to use clinical observations to advance biologic knowledge. These studies can teach us the physiologic and psychological differences between acute and chronic pain problems, the importance of the evolution of psychological factors, the difference between pain and suffering, the clinical pharmacology of analgesic drugs, and the behavioral mechanisms humans use to suppress pain. The use of innovative approaches based on sound scientific principles and advances in research technology offers the opportunity to understand the complex phenomenon of pain.

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REVIEW ARTICLE

Scenario of Fungal Infection of Nasal Cavity and Paranasal Sinuses in Gujarat : A Retrospective Study

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KEY WORDS : Invasive and non- invasive fungal sinusitis, Aspergillus flavus.

ABSTRACT

Fungal infection of the nose and sinuses is an uncommon condition which is now being increasingly recognized. In this study we review 100 cases of fungal infection from various districts of Gujarat. Data was collected in a brief predetermined format. Samples like nasal lavages, sinus secretions, and tissue specimens were processed. Histopathological examination was done. The cases were divided into five categorise according to following histopathological features: allergic fungal sinusitis (n=35), sinus mycetoma (n=13), chronic indolent fungal sinusitis (n=10), acute fulminant fungal sinusitis (n=15), granulomatous invasive fungal sinusitis (n=27). All patients were treated surgically and were given antifungal therapy according to nature of diseases. Two patients had presented with loss of vision. Allergic fungal sinusitis and sinus mycetoma have 100% successful result, where as acute fulminant fungal sinusitis had poor prognosis. The aim of this study is to increase awareness among clinicians and provide more accurate treatment option to patients.

INTRODUCTION

Sinusitis or more accurately rhinosinusitis is a common disorder affecting 20% of the population [1] . Chronic rhinosinusitis accounts for more than 90% of all cases of rhinosinusitis, has a slow protracted course, and has different aetiologies, fungal infections being a major cause [2]. Histopathology is important to distinguish the invasive from the non-invasive type and classify the disease. Direct microscopy and culture helps in establishing the aetiology. [3] Early diagnosis and accurate classification of fungal rhinosinusitis may help in deciding the treatment protocol and preventing multiple surgical procedures and lead to effective treatment.

The first reported case was by plaignaud in 1971[4], but in detail was described by Schubert in 1885[5]. Fungal sinusitis was emerged as a more vital health in modern times because of increased travel into and out of endemic areas, immunodeficient state such as AIDS, immunosuppression from transplantation and chemotherapy and more prevalent use of long term broad spectrum antibiotic therapy. Poorly controlled diabetes also remains a problem.

This study was done to assess the effect of humidity and pollution on people from different districts of Gujarat, to distinguish clinico-pathological features of non-invasive fungal sinusitis from invasive fungal sinusitis and accordingly manage them and prevent recurrence.

MATERIAL AND METHOD

This is a retrospective study conducted from June. 2010 to May. 2013 at department of ENT, on 100 patients belonging to different districts of Gujarat.

One-hundred suspected patients were included in the study, agreed by verbal consent to participate in the study. Data was included in a pre-designed format. It included patient's identification number, name, age, sex, patient's history, clinical presentation. Apart from this nasal endoscopy was done in all patients. CT pns was carried out to look for extension and hyperattenution. Systemic diseases like diabetes, AIDS, renal failure,

Table I : CLASSIFICATION OF FUNGAL RHINOSINUSITIS[6]

Invasive fungal sinusitis	Noninvasive fungal sinusitis
Acute fulminant invasive fungal sinusitis	Saprophytic fungal infestation
Granulomatous invasive fungal sinusitis	Sinus fungal ball
Chronic invasive fungal sinusitis	Allergic fungal rhinosinusitis

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asthma were ruled out. Samples collected included nasal lavages, nasal secretions and tissue specimens. The tissue specimens were collected from the sinuses by endoscopic sinus surgery. A portion of surgically excised specimen was received in sterile container containing normal saline to mycology laboratory, and another part of the specimen was received in a sterile container containing 10% formalin in the histopathology laboratory for final histopathological diagnosis.

RESULTS

Regarding demographic findings, out of 100 cases of fungal rhinosinusitis, patients' distribution from various parts of Gujarat is likewise:

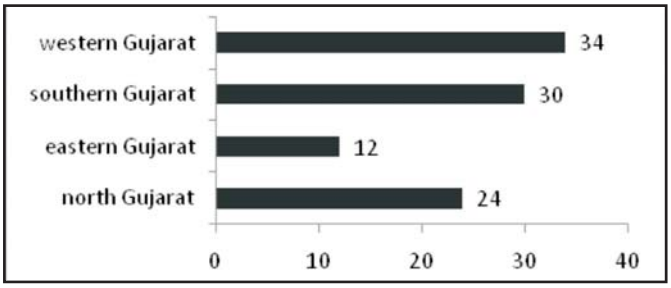

Fig I. Distribution of cases across Gujarat.

75 % of patients were living in areas of high humidity especially along coastal areas (Esq.: Tapi river, Sabarmati river and Arabian Sea), 35 patients which were diagnosed diabetic and immunosuppressed had no specific geographic location. Apart from these, areas with high pollution [esp. Ahmedabad] and dust may play an important role in aggravating the fungal infection.

The age group of patient with allergic fungal sinusitis was (18-35 yrs), with sinus mycetoma (25-60 yrs) and in invasive fungal sinusitis (45-75 yrs) with equal male to female ratio.

The clinical presentation of most the patient was nasal obstruction of the corresponding side, with or without headache and nasal discharge. 17 patients were asthmatic and sensitive to aspirin. 49 patients had nasal polyps with past history of polypectomy done in 24 patients. 21 patients had proptosis (unilateral). Two patients had loss of vision due to atrophy of optic nerve and compression of ophthalmic nerve. The duration of syndrome before diagnosis ranged from 1 month to 35 months.

Radiographically, most of the patients showed opacification and soft tissue mass involving multiple paranasal sinuses either in one or both sides. Anterior cranial fossa extension was seen in 12 patients without any middle or posterior cranial fossa extension. There was opacification with necrosis of multiple sinuses with extension into orbit in invasive forms.

The distribution of cases in the various histological subgroups was as follows: Allergic fungal sinusitis (n=35), sinus mycetoma (n=13), chronic indolent fungal sinusitis (n=10), acute fulminant sinusitis (n=15), granulomatous invasive fungal sinusitis (n = 27). Of all the cases of fungal rhinosinusitis, allergic fungal rhinosinusitis was the most common histopathological diagnosis.

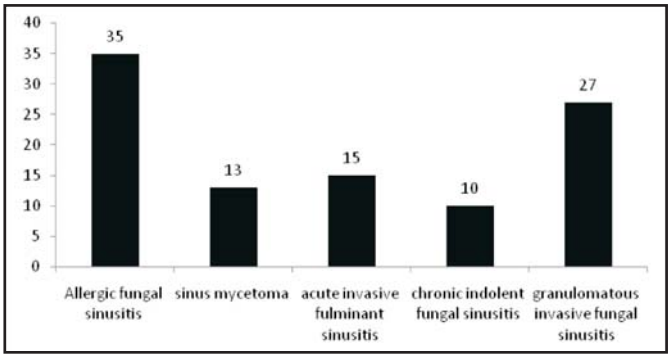

Fig. II. Distribution of cases in various histological subgroups.

Aspergillus flavus was the most common fungus, isolated in 17 cases of allergic fungal rhinosinusitis, also in sinus mycetoma; *Aspergillus flavus* was isolated in 10 cases and *Aspergillus fumigatus* from the 3 cases. *Mucor spp.* was the fungal species isolated in 13 cases of acute fulminant invasive fungal rhinosinusitis. In chronic indolent fungal rhinosinusitis, *Aspergillus fumigatus* was the most common aetiological agent identified, being isolated in 8 cases of the 10 cases of chronic indolent fungal rhinosinusitis. *Aspergillus flavus* was isolated in 23 cases of granulomatous invasive fungal rhinosinusitis. Aspergillus fumigates was commonly isolated in patients from Ahmedabad, A. flavus from saurashtra region.

All patients with allergic fungal rhinosinusitis were treated primarily with surgery to provide good drainage and aeration of the involved sinuses followed by antifungal therapy for 21 days and short course of steroids followed by intranasal steroid spray, where in invasive fungal sinusitis, aggressive treatment of primary disease along with surgical debridement. All patients were taught nasal douche for irrigation and remove of crust from nose.

DISCUSSION

Categorization of fungal rhinosinusitis as acute invasive, chronic invasive, fungus ball, allergic fungal or nonallergic eosinophillic fungal rhinosinusitis has important prognostic and management implications.

Table II comparison with various study.

Histological classification	Chakrabarti et al[7]	Panda et al[8]	Our study
Non-invasive fungal sinusitis (afs + fungus ball)	109	100	48
Invasive fungal sinusitis	67	78	52
Total	176	178	100

In our study, on the basis of clinical, radiological, histopathological and mycological findings, classified 100 patients of fungal rhinosinusitis and following observations were made: 48 cases (48%) were of non-invasive fungal rhinosinusitis including 35 cases of allergic fungal rhinosinusitis (72.91%) and 13 cases of fungal ball (27.09%), whereas invasive fungal rhinosinusitis constituted of 52 cases (52%) including 15 cases of acute fulminant invasive fungal rhinosinusitis (28.84%), 27 cases of granulomatous invasive fungal rhinosinusitis (51.92%) and 10 cases of chronic invasive fungal rhinosinusitis (19.23%). Allergic fungal rhinosinusitis constituted 35% of all the cases of fungal rhinosinusitis and was the most common histopathological diagnosis. Chakrabarti et al. classified the patients into allergic (12 patients), non-invasive without bony destruction (81 patients), non-invasive destructive (16), chronic invasive (55) and fulminant (12) [7] . Panda et al., in their study, categorized 178 patients diagnosed as having paranasal sinus mycoses into three disease groups- Allergic (8), non-invasive (92) and invasive (78) on the basis of histopathological and mycological investigations[8] . In a prospective study of 176 cases of fungal rhinosinusitis.

The diagnosis of allergic fungal rhinosinusitis (AFS) was developed for patients with recurrent nasal polyps and asthma in mind [9], but there is still not a clear definition and/or panel of criteria. Nasal endoscopy may be normal or show mucosal oedema, or polyps with or without allergic mucin (thick yellow–green mucus plugs) on one or both sides. Sinus CT scan may reveal heterogeneous and serpiginous sinus opacities, with or without pseudo-calcifications and bone lysis on one or both sides. Pathology consists of allergic mucin with detection of hyphae, eosinophils and Charcot-Leyden crystals. Mycology involves identification of various species on mucus fungal culture. Serum hyper-eosinophilia may be present. Type I hypersensitivity to fungal species is frequent. Large surgical removal of lesions, mainly via endoscopic sinus surgery is recommended. Postoperative systemic steroids are recommended by most authors for a duration varying from 2 weeks to several months, but the use of local steroids is not clearly codified. Antifungal agents (local or systemic) are recommended by some authors. In the initial studies, *Aspergillus fumigatus* was considered the primary etiologic agent of AFRS cases, but later, pigment-producing dematiaceous fungi-*Bipolaris spicifera, Exserohilum roibatum, Curvularia lunata and Alternaria spp.* were found as predominant etiologic agents in Western literature. [10] Data published from various studies from India differ from those reported in the western literature and state *Aspergillus flavus* as the predominant agent in cases of allergic fungal rhinosinusitis in the Indian sub-continent. A study by Saravanan *et al.*, in Chandigarh, reported that among the 32 patients in the allergic fungal rhinosinusitis group, the most common culture isolate was *Aspergillus flavus* (81%), followed by *Aspergillus fumigatus* (9%). *Bipolaris* species was isolated in only 2 patients (6%). [11] In our study of 29 cases out of 35 of allergic fungal rhinosinusitis, culture was positive,. The results were correlated with the histopathological findings, and it was found that *Aspergillus spp.* was the most common fungus isolated of allergic fungal rhinosinusitis with *Aspergillus flavus* being the most common species isolated 82.85% cases of allergic fungal rhinosinusitis. Inflammatory infiltrates and allergic mucin were found in all 35 cases, whereas non-invasive fungal hyphae and eosinophillic infiltrate was observed in 29 cases (82.85%).

When the fungal spores are not cleared because of immunodeficiency, they may germinate, produce filaments and then invade the surrounding tissues. Invasive fungal rhino sinusitis is therefore defined by the presence of fungal tissue invasion, detected on pathologic examination. This definition may correspond to different clinical forms: acute invasive fungal rhino sinusitis, chronic invasive fungal sinusitis and granulomatous invasive fungal sinusitis [12].

Acute invasive fulminate fungal sinusitis (AIFRS) was first described by McGill et al. in 1980. Fulminant aspergillosis in the paranasal sinuses represents an important cause of morbidity and mortality in patient whose host defence has been altered by primary disease like Patients affected by leukemia and lymphoma are especially at risk, in particular in cases of chemotherapy with aplasia and bone marrow transplantation.

Neutropenia is a key factor, especially when neutrophils are below500/ml. Other main factors are long-term glucocorticosteroid therapy and graft-versus-host disease. AIDS and type I diabetes patients are also at risk. Radiotherapy, long-term antibiotic therapy and malnutrition may also be risk factors for AIFRS. An unexplained fever in these patients must lead one to suspect AIFRS, especially if nasal congestion, rhinorrhea, epistaxis and/or headaches are reported. Clinical manifestation includes a rapidly progressive gangrenous necrosis of the mucoperiosteum causing early destruction of the bony walls of the nose and paranasal sinuses. Characteristically, the earliest lesion indicating involvement of the nose and paranasal sinuses is crusting of the anterior end of the inferior turbinate or adjacent part of the cartilaginous septum. This lesion may progress within days to involve the adjacent sinus wall or extend to the orbit and anterior cranial fossa, either by direct extension or along vascular channel, resulting in a fatal outcome. The rapid progressive course of fulminant aspergillosis contrasts sharply with the chronic indolent

fungal sinusitis. Mucormycosis (caused mainly by the genera *Rhizopusor Absidia*) represents a distinct entity, as it is generally encountered in type I diabetes patients. Of all the cases of fungal rhinosinusitis diagnosed in our study, 15 cases were diagnosed as acute fulminate invasive fungal rhinosinusitis on the basis of microbiological, histopathological and radiological findings. *Mucor spp.* was isolated in 13 cases, and histopathologically all cases showed inflammatory infiltrates with fungal hyphae invading into the mucosa and sub-mucosa. The therapeutic strategy must be defined according to a multidisciplinary approach (ENT, hematologist, mycologist, pathologist, ophthalmologist, neurosurgeon and anesthesiologist). Control of fulminate fungal sinusitis requires early recognition, aggressive surgery, systemic antifungal therapy and correction of the immunological deficits.

In contradistinction to the impressive clinical velocity of AIFRS, a second category of invasive fungal disease encompasses a more unhurried progression of illness, yet with similar histopathological findings. These particular varieties of invasive fungal sinus disease have been most stringently divided into two forms: chronic indolent fungal sinusitis (CIFS) and (granulomatous invasive fungal rhinosinusitis) GIFS.

CIFS, formerly known as chronic indolent fungal sinusitis, was first recognized by Milroy in 1989 and is now considered a form of slowly progressive invasive fungal disease [13, 14]. Chronic invasive fungal sinusitis (CIFS) occurs in patients with altered immune response such as diabetes mellitus, burns, trauma and steroid therapy. Patients present with nonspecific symptoms that mirror those of CRS, made remarkable by their long duration, slow progression, and refractoriness to standard antibiotic therapy [15,16,17]. Cases have been reported in immunocompetent and diabetic patients alike; therefore, diagnosis is often delayed until the development of vision changes, proptosis, facial deformity, seizures, or altered mental status mandate that the physician consider more ominous possibilities. This type of fungal sinusitis extends beyond the bony confines of the sinuses to the orbit or even to the anterior cranial fossa. Therefore, clinically it may mimic malignant neoplasm, Wagener's granulomatosis, osteomyelitis tuberculosis and rhinoscleroma. The most logical approach to the management of these patients seems to be a combination of radical surgery and antifungal chemotherapy. Michael *et al.*, [18] in a study done in South India, reported 21 cases (10%) of chronic invasive fungal rhinosinusitis among 211 cases of fungal rhinosinusitis diagnosed. *Aspergillus flavus* was the aetiological agent in 10 cases and *Aspergillus fumigatus* in 8 cases among all the 21 cases of chronic invasive fungal rhinosinusitis detected. In the current study, 10 cases of CIFS were reported on the basis of histopathological, microbiological, radiological and clinical findings. *Aspergillus fumigatus* was the aetiological agent in 8 cases and *Aspergillus flavus* was isolated in 1 case.

The distinction between CIFS and granulomatous invasive fungal rhinosinusitis (GIFS) is based on pathologic findings. Histopathologic study of GIFS identifies the familiar exuberant fungal proliferation with tissue invasion and a variable inflammatory infiltrate; however, the presence of multinucleated giant cell granulomas distinguishes GIFS from CIFS [19]. Das et al., [20] in their retrospective study on cases of fungal rhinosinusitis over a period of 5 years in Chandigarh, reported 48 cases of granulomatous invasive fungal rhinosinusitis (16.9%) among 284 cases of fungal rhinosinusitis. In our study, granulomatous invasive fungal rhinosinusitis was reported in 27 cases based on histopathological findings of presence of fungal hyphae invading into the adjacent tissue and granuloma formation. In 23 cases were caused by *Aspergillus flavus* as in accordance with previous studies. Most authors recommend aggressive surgery and systemic antifungal chemotherapy which is same in our study also.

Although each type of fungal sinusitis discussed above represents a fairly clinical entity, progression of allergic fungal sinusitis to the chronic indolent form might occur in long-standing, untreated cases. This view was supported by several authors. Hartwick and Batasakis revealed that 28% of patients with allergic fungal sinusitis have radiographic evidence of bone erosion and sinus expansion. Therefore early diagnosis and recognition of allergic fungal sinusitis is very important, not only because it is curable in the early stages, but also to prevent progression of the diseases into the more serious and destructive invasive forms.

CONCLUSION

Aspergillus species is the most common fungal infection of the paranasal sinuses in Gujarat. The causative organism is a spore forming filamentous fungus which occurs as a saprophytic in soil and decaying vegetable matter and spread by air borne transmission. Transmission between humans is unknown. The three species are commonly implicated in human pathogenicity. We found that factor affecting the pathogenesis of fungal sinusitis is environment and host related. Environmental factor explain the epidemiology of fungal sinusitis are agriculture, economy and warm moist climate. Genetic predisposition may also play a role in pathogenesis of this disease. Immuno-suppressive condition such as chemotherapy. AIDS, Renal failure also predispose to fungal sinusitis. 59 patients were from peripheral areas more into agriculture work.

Allergic fungal rhinosinusitis is diagnosed evidence for

histopathologically from the finding of eosinophillic mucin plugs containing fungal hyphae in patients with an elevation of immunoglobulin E antibodies specific to the cultured fungus. The treatment of allergic fungal rhinosinusitis is endoscopic surgical removal of allergic mucin and polyps and systemic steroid therapy. Systemic or topical antifungal may have a role, but evidence for their effectiveness is weak. Rapid diagnosis of invasive fungal rhinosinusitis in the immunocompromised patient, with the use of immediate fungal staining, culture, and biopsy, if possible, is critical to rapid implementation of therapy. The treatment of invasive fungal rhinosinusitis is reversal of the source of immunocompromise, appropriate antifungal therapy, and directed surgery. The treatment of sinus fungus balls is removal by endoscopic surgery.

Our recommendation to clinician working in areas of high prevalence of fungal sinusitis such as Gujarat esp. near highly humid and polluted area (esp. from southern and western Gujarat), is that any sinus contents as well as polyps from all patients with a history of repeated polypectomies should be sent for histopathologic examination, and that the pathologist should examine the polypectomies and sinus contents very carefully, and must be rule out for the presence of fungal hyphae.

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REVIEW ARTICLE

The Role of Micronutrients in ICU

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KEY WORDS : micronutrients, enteral nutrition, parenteral nutrition.

ABSTRACT

Nutrition support has become a standard of care in ICU treatment protocol.The knowledge of metabolic requirements is essential to define an artificial nutrition regimen. Optimum and early nutrition either by Enteral(EN) or Total Parenteral Nutrition(TPN) can improve the ICU outcome. The emergentdiscipline of clinical nutrition has tremendous potential to change the future of our knowledge and intervention strategies of artificial nutrition.

INTRODUCTION

Nutritional support is an integral, though often neglected, component of intensive care of the critically ill patient or acutely ill medical or surgical patients including trauma and burns. We have very well understood the cascades of metabolic derangement secondary to stress and starvation. The global prevalence of malnutrition varies from 10%-70% of all hospitalized patient.

Although great care is taken to provide adequate and optimal doses of micronutrient combinations; the essential role of micronutrients should not be overlooked. Micronutrients are helpful in intermediaries in metabolism and also for their potential roles in cellular immunity, antioxidant activity and wound healing. Micronutrients deficiency in critically ill patients may occur as preexisting condition in patient with poor nutritional status before hospitalization or as a result of severe illness or injury itself. SIRS is associated with redistribution of vitamins and trace elements from the circulatory compartment, organs and tissues which are involved in immune cell production and protein synthesis.

ROS (reactive oxygen species) released from several cell types has been emphasized as a final common pathway of tissue injury in ICU which leads to MODS and ARDS

The impact of vitamin D deficiency in ICU has not been studied properly till date but recent studies documented Vitamin D deficiency with acute life threatening hypocalcaemia, cardiac failure and increased mortality in critical ill patients. Vitamin D deficiency in ICU patient may be as high as 50% with undetectable levels of Vitamin D seen in 17%.[9]

CoenzymeQ 10 levels are abnormally low in patient with septic shock but the clinical significance of this abnormality is yet to be explored[10].

Metabolic derangement with artificial nutrition as an intervention:

Critically ill patients have lots of metabolic derangement in carbohydrate, lipid, aminoacid, protein and electrolyte metabolism which are proportionate to severity of an illness.[11]

The metabolic response to injury mobilizes aminoacids from lean tissue to support wound healing, immunologic response and accelerated protein synthesis for repairing process.

The goal of aggressive and early artificial nutrition is to maintain host defense by supporting this hypermetabolism and preserving lean body mass.

Today the artificial nutritional support of the critically ill patients represents a powerful metabolic therapy that stabilizes post injury metabolism, enhances the recovery phase and corresponds to a therapeutic intervention.

Micronutrient malnutrition in critically ill patients and artificial nutritional support:

Malnutrition is leading cause of morbidity and mortality in hospitalized patients and the scenario had worsened over last few decades as many patients stayed in critical care setup for many days to months.

Despite the needs of macronutrients are optimized through availability of various oral and parenteralsupplements there remains a cent percent micronutrient deficiency state due to ignorance on the part of health care provider and lack of availability of qualitative and quantitative good quality products.

Micronutrients requirements in ICU:

The total calories requirement of critically ill patient can be estimated with predictive equations or measured by

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indirect calorimeter but there are no means to predict and estimate need of micronutrients. A pragmatic approach is to attempt administer larger dose of micronutrients as usually these patients are hyper catabolic.[7,10]

Optimization of micronutrients in critical care:

Dietary supplementation with micronutrients that have physiologic effect on metabolic and immune functions have been shown to be beneficial in patients with critical illness special emphasis on selenium, zinc, Copper, Vitamin C & E. Vitamin B complex, etc. Micronutrient studies in critically ill remains few in relative term, with problems arising from a heterogeneity of patient population, large variability of patient within the same diagnostic category and absence of relevant clinical endpoints. Nevertheless, emerging evidence regarding the potential of micronutrient supplement in influencing clinical outcome in critically ill is encouraging. The sum total of available evidence still indicates that exact micronutrient requirement of the critically ill patient and related practice issues remain uncertain.[7]

DISCUSSION

This systematic review assessed the effect of micronutrient supplementation on adults recovering from critical illness and support previous finding that it may be associated with decrease in mortality especially 28day mortality.

Combined micronutrient supplementation in this review was not associated with a decrease in complication and Length of stay in hospital and ICU.

The present review did not find the evidence that parenteral nutrition is superior to enteral route of administration in terms of clinical outcome.

The current evidence and updated review confirm that timing, duration and dosing appear to be the key factors to ensure optimal clinical benefit. The timing of micronutrient supplementation is important and is probably a key factor because the repletion of micronutrients and specifically the antioxidants, would provide greater efficacy if administered before invasive oxidative injury (e.g.: severe sepsis or septic shock). During this acute phase the serum levels of micronutrients are observed with larger increase in ROS production.

Selenium was the most commonly used single nutrient, whereas Vitamin C and E(alpha tocopherol) were most commonly used micronutrients in studies of combined supplement including Zinc(Zn) and Copper(Cu).

This updated systemic review has highlighted the fact that there is still no clarity regarding optimal doses of micronutrients and which patients would benefit the most(or would be adversely affected), and that further large multicenter trials(including dose finding trials) are necessary.

Importantly, vast majority of trials reported no adverse or deleterious effect on micronutrient administration.

In terms of practical issues , micronutrients were administered mainly by intravenous route, with few studies using enteral route alone or in combination with IV route.

Although most studies reported decreasing CRP levels from baseline(for their experimental and control groups). It appears such that CRP levels decreases irrespective of supplements and as expected, pari pasu decreased resolution over time for some patients.

The importance of oxidative stress in critical care setting is well known but no single parameter can be declared gold standard to describe the redox status of the patient.Free radical are atoms or molecules containing unpaired electron .They strive to restore parity because of their instability. The so called Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNOS) are produced under normal aerobic metabolism; they are mainly produced by leucocytes and mitochondria and essential for cell signaling, proliferation, apoptosis and cell protection.

Another category of free radical is derived from nitric oxide metabolism (NOS) produced by endothelial metabolism. Excess free radical production without appropriated endogenous antioxidants (AOX) has been implicated to multiple pathologic conditions(oxidative stress as ischemia reperfusion syndrome, inflammation, MODS)

Antioxidants must inhibit or delay oxidation of a substrate. Antioxidant defenses are non-enzymatic(e.g. uric acid , glutathione, bilirubin, thiols, albumin and nutritional factors including vitamins selenium and phenols) and enzymatic(e.g. superoxide dismutase, catalase, glutathione peroxidases).

Critically ill patient are characterized by increased Reactive oxygen species(ROS) production. AOX released in critically ill has focused mainly on five micronutrient: Vitamin C & E , copper , selenium and zinc. The reinforcement of AOX by means of artificial nutrition, enhanced with AOX(vitamins and trace elements alone or in combination) seems safe and may have clinical and biological benefit.

When interpreting the findings of the review, the limitations of systematic reviews and met analysis as recognized and described in literature, must be bored in mind. Systemic reviews provide us with some of best available evidence and can aid, but never replace, sound clinical reasoning. Understanding a complex structure of decision making requires an appreciation of the ways in which knowledge, skill , values and research evidence are integrated in each patient- clinician encounter.

CONCLUSION

This review suggest a potential benefit of combined micronutrient supplementation in critically ill patients in term of some clinical outcomes like decrease in mortality, LICU and LOS but highlights that caution is warranted because nutrient interactions and nutrient toxicity are not clearly defined in critical illness. Timing, duration and appropriate dosing appear to be key factors to ensure optimal clinical benefit. But there is a need for more large, multicenter, standardized, prospective randomized control trials (RCT's) to assess the effect of different types and doses of combined and solitairemicronutrient supplementation in selected group of patients with different type of critical illness.

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ORIGINAL ARTICLE

Evalution of scrotal pathologies in clinically suspected cases by ultrasonography & colour doppler.

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KEY WORDS : Ultrasonography , Doppler , Scrotum

ABSTRACT

OBJECTIVE : The objective was to evaluate role of ultrasound and color doppler in scrotal pathologies in clinically equivocal cases and to determine whether it is testicular or extra testicular and determine the role of colour doppler in scrotal pathologies. **MATERIALS AND METHODS :** In the present study, 60 patients were scanned with the sector probe (3.5 MHz – 5 MHz) and linear probe (5 MHz- 7.5 MHz) on the ultrasound machine TOSHIBA XARIO ISTYLE.Detailed history was taken and through palpation of the scrotal contents was done before the sonographic examination during DECEMBER 2011 to SEP 2012. **RESULTS :** Out of 60 patients, 32 (53.33%) patients were between age group of 21 to 40years of age. Out of 60 patients, 30 patients (50%) had scrotal inflammatory disease, 6(10%) patients had malignant testicular tumor, 6(%) patients had varicocele. Out of 6 patients of malignant testicular tumor 3(50%) had seminoma & all of them were homogenously hypoechoic & 3(50%) patients had lymphnode metastasis. **CONCLUSION :** Ultrasonography and colour dopplerenables in clear demonstration of morphological alteration associated with acute inflammatory disease& differentiate it from testicular ischemia &torsion. Ultrasonography is highly sensitive in differentiating solid from cystic scrotal masses. Ultrasonography is highly sensitive in distinguishing scrotal mass as either testicular or extratesticular and clearly superior to clinical diagnosis. CT is mandatory only for evaluation of testicular tumor &it's spread.

INTRODUCTION

Until 1970's clinical examination of the scrotum including palpation and transillumination, was the main stay for the evaluation of the scrotal pathology. This method was however far from adequate because of tender swelling and gross scrotal contents resulting in low sensitivity and specificity often eluding the best of the clinicians. Sonography of the scrotum is simple to perform, safe, easily available noninvasive, without any radiation hazard, relatively inexpensive, widely available and portable. It causes no patient discomfort and can be done on outdoor basis.

The scrotum being superficial structure, ultrasound is routinely used for the investigation of patients presenting with scrotal symptoms. Scrotal ultra sound has reached a level of maturity that allows the technique to be the first and only imaging examination necessary to evaluate the scrotal contents. Gray scale sonography with use of high frequency transducers allows excellent visualization of morphologic changes associated with scrotal diseases. Colour flow imaging allows visualization of morphology and parenchymal blood flow characteristics and has led to increase in the clinical applications of scrotal sonography. It has largely replaced testicular scintigraphy, which had been the examination of choice in patients with suspected torsion.

MATERIALS AND METHODS

In the present study, 60 patients were scanned with the sector probe (3.5 MHz – 5 MHz) and linear probe (5 MHz-7.5 MHz) on the ultrasound machine TOSHIBA XARIO ISTYLE.

Detailed history was taken and through palpation of the scrotal contents was done before the sonographic examination during DECEMBER 2011 to SEP 2012.

The examination was performed with the patient in the supine position and additional scanning in the standing position and with Valsalva maneuver was done in cases of the varicocele.

The scrotum was elevated and supported.

A direct contact scanning technique with the use of the acoustic coupling gel was used. Through scanning was done in the sagittal, transverse and oblique sections.

DISCUSSION

Age incidence: In present study all patients between the age of 0 to 70 years of age and 32 out of 60(53.33%) patients were between the age of 21 to 40 years.

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Malignant testicular tumors

In present study it constitutes about 10% of total cases.

Clinical presentation –

In the present study, most patients of testicular malignancy presented as painless hard swelling.

It has been mentioned that the most common symptom of testicular cancer is a painless enlargement of the testis. Enlargement is usually gradual and a sensation of testicular heaviness is not unusual. (1)

In the present study, seminoma was the most common of all testicular tumor(50%), followed by mixed germ cell tumors(33.33%).

Echo pattern –

In the present study 3 out of 6tumors were heterogeneous while rests of 3 tumors were homogenously hypoechoic and all of them were seminomas.

In contrast to seminomas, other germ cell tumors were heterogeneous. So from the present study we can say USG findings alone could not be used to classify a neoplasm histologically.

Associated hydrocele –

Secondary hydrocele was present in 3 out of 6 cases (50%). It was seen in twocases of mixed germ cell tumor& onecase of seminoma.

It has mentioned that large hydroceles occur uncommonly with neoplasms but small hydroceles occur in 60% of patients with testicular tumors. (2)

Metastasis –

In the present study, lymph node metastases were present in 3 out of 6 cases (50%) patients.

In the present study lymph node metastasis in seminoma group of patients were in 1 out of 3 patientsand 2 cases of germ cell tumor show metastasis.

It has been mentioned that while retro peritoneum is the most commonly involved site in metastasis, visceral metastasis are seen in advanced disease.(1)

It has been mentioned that rather than relying solely on specific preset size criteria we should consider any lymph node at the primary metastatic site suspicious, even those that would be considered not enlarged (i.e. less than 10mm) by usual CT criteria, especially those located anterior to the mid portion of the aorta.(3)

Scrotal Inflammatory Disease

In present study it constitutes largest percentage of total cases and it constitutes50 % cases. Here were 4 patients of isolated epididymitis, 15 patients of epididymo-orchitis and 8 patients of isolated orchitis. Only one patient had pyocoele.

Out of 30 patients, 15 had acute and 2had chronic epididymo-orchitis. Patients of chronic epididymo-orchitis had tuberculosis and both patients had multiple hypoechoic ill-defined lesions in testes with heterogeneous epididymis and 1 0f them had foci of calcificationswithin.

Role of color Doppler in differentiating testicular tumors and orchitis:

Epididymo-orchitis as well as tumors >1.6 cm are hypervascular and thus both entities show increased blood flow on color Doppler study. On follow up scans if the patients do not improve with antibiotic therapy then diagnosis of the tumors should be considered.

Color Doppler scanning has limited role in the evaluation of testicular tumors. The combination of clinical history, physical examination, and grey scan USG findings facilitate the diagnosis in all the cases.

The hypervascularity of large neoplasm can't be differentiated from that inflammatory lesion.

Hydrocele

There were 6 patients of isolated hydrocele in the present study. Also hydrocele was associated with inflammation in 10patients and secondary hydrocele was present in 3 case of malignancy.

Hydrocele was easily diagnosed by sonography as an anechoic collection in the tunica vaginalis sac, but there were also cases with low level of echoes and fibrin strands.

There was one patient of pyocoele in the present study. On USGit showed fluid in the tunica vaginalis sac with multiple internal echoes and septations.

It was mentioned that pyocele or scrotal abscess is most often the complication of epididymo-orchitis which has the lining of mesothelial lining of tunica vaginalis.

Testicular Torsion

There were 4cases of testicular torsion in this patients presented with acute attack of testicular pain which was followed by decreased pain and sensation on the involved side.

On USG 3 patient had hypoechoic testis and another one was heterogeneous& hyperechoic and all were normal in size. Correlating clinical history and the palpation findings with USG findings, the diagnosis of testicular torsion was kept.

Grey scale findings are nonspecificand misleading in some cases of torsion. But here clinical examination and history can help us differentiate epididymo-orchitis as pain can be relieved by elevating the testis above pubic symphysis in latter while pain is not relieved in testicular torsion. This is known as prehn's sign.

Therefore, real time USG alone should not be used to evaluate testicular torsion. It is recommended that the diagnosis should continue to be made by clinical examination and history and colour doppler.

Criteria for the diagnosis of the testicular torsion.(4)

1. Absent arterial and venous flow
2. Increased RI on affected side (diminished or reversed diastolic flow)
3. Decreased flow velocity difficult to measure but may be subjectively inferred by relative difficulty in finding small, low amplitude scale on symptomatic side.

Pitfalls to be aware of when color Doppler USG includes torsion and incomplete torsion in which there will be presence of low velocity venous type of flow and pediatrics patient because there are smaller vessels, making it difficult to detect blood flow.

Undescended Testis

In the study there were 3patient of undescended testis.Size of testis was decreased in both the patient. In 2 patients it was on right side (66.66%) and in one patient it was on left side (33.33%).

It has been mentioned thatundescended testis is more common on the rtside (58%) than in the left side (30%) and bilateral in 20% because rt testis descends later than left testis normally. (5)

Size of testis was decreased in all the patient.

There is evidence that no imaging technique is useful for determining that testis is absent. This suggest that no imaging technique currently available can help the surgeon decide whether to operate or not, nor can the results of any currently available modalities can change the approach.

So in case of undescended testis diagnostic imaging technique can be useful in the following situation.

1. For the follow up the testis after orchidopexy.
2. For the follow up normally placed testis for malignancy.
3. For the follow up for malignancy in a patient of undescended testis who is older than 32 years and in whom a decision has been made not to operate.

Testicular Trauma

In present study there were 2 cases of testicular trauma. Most common features of blunt testicular trauma is altered abnormal echotexture. Haematocele and abnormal altered echotexture were present in both of the cases while abnormal contour is seen in only one patient.

A hematocele is the result of the venous bleeding from the testicle or the pampiniform plexus into tunica vaginalis, which appears on ultrasound as an extra testicular anechoic collection with low echoes within it.

Varicocele

There were 6 patients of varicocele. They showed dilated serpiginous tubular structures more than 3 mm in diameter and increase in size by valsalva maneuver and upright position.

The diagnosis of varicocele by sonography is considered if the veins in the pampiniform plexus are more than 3 mm and the diagnosis are confirmed if they change in size in upright position or during valsalva maneuver. Also reversal of color flow on valsalva adds to the diagnosis.

The grading of varicocele is as follow (4) Grade 1: *Not visible but palpable on valsalva maneuver* ***Grade2:*** *Less visible but palpable without valsalva* ***Grade3:*** *Always visually identified and palpable without valsalva maneuver*

There is no conclusive evidence to date that repair of subclinical varicocele improves semen quality and consequently fertility. Their presence my explain some of the previously unknown causes of idiopathic infertility.

Epididymal Cyst

There was 3 patient of epididymal cyst in the present study. They appeared as well defined anechoic cystic lesions in the epididymis. Both epididymal cyst and spermatocele appear as anechoic, well defined masses with increased through transmission and indistinguishable on USG.

Aspiration of the fluid can allow a definitive diagnosis to be made but it is seldom necessary since both lesions are benign.

Table I : Age Distribution

Age Group	No of Patients
0 To 10 Yrs	4
11 To 20yrs	4
21 To 30 Yrs	18
31 To 40 Yrs	14
41 To 50yrs	10
51 To 60 Yrs	8
61 To 70 Yrs	2
Total	**60**

Table II : Clinical Presentation

Clinical Signs/Symptoms	No of Patients
1 SCROTAL SWELLING	44
2 PAIN / TENDERNESS	34
3 FEVER	20
4 TRAUMAT TRAUMA	4
5 EMPTY SCROTAL SAC	4
6 BURNING MICTURITION	6

Table - III :- Incidence of Intratesticular / Extratesticular Lesions

Type of Lesion	No of Patients
Intratesticular	12
Extratesticular	26
Intra+Extratesticular	22
Total	**60**

Table – IV :- Comprehensive Analysis of Scrotal Lesions

	SCROTAL LESIONS		NO OF PATIENTS
1	MALIGNANCY		**6(20%)**
		SEMINOMA	3
		YOLK SAC TUMOUR	-
		EMBRYONAL CELL CARCINOMA	1
		MIXED GERM CELL TUMOR	2
2	INFLAMMATION		**30(50%)**
		ACUTE EPIDIDYMITIS	4
		ACUTE EPIDIDYMO-ORHCITIS	15
		CHRONIC EPIDIDYMO-ORCHITIS	2
		ACUTE ORCHITIS/TESTICULAR ABSCESS	8
		PYOCELE	1
		SCROTAL ABSCESS	-
3	EPIDIDYMAL CYST		**3(5%)**
4	ISOLATED HYDROCELE		**6(10%)**
5	UNDESCENDED TESTIS		**3(5%)**
6	TORSION		**4(6.66%)**
8	HEMATOCELE + TESTICULAR CONTUSION		**2(3.33%)**
9	VARICOCELE		**6(10%)**

Table V : Ultrasonographic Pattern of Testicular Tumor

HISTOLOGICAL TYPE	ULTRASONOGRAPHIC PATTERN		
	HOMOG. HYPOECH.	HETROGEN.	TOTAL
Seminoma	3	-	3
Mixed germ cell tumors	-	2	2
Embryonal carcinoma	-	1	1

Table VI : Ultrasound Apperance of Various Inflamattory Pathology:

SI NO	ECHOPATTERN & COLOUR DOPPLER	ACUTE EPIDIDYMITIS	ACUTE EPIDIDYMO-ORCHITIS	ACUTE ORCHITIS	CHRONIC EPIDIDYMO-ORCHITIS
1	HETEROGENOUS	-	4	1	2
2	HYPOECHOIC	3	10	6	-
3	ISOECHOIC	1	1	1	-
4	CYSTIC	-	-	-	-
5	TESTICULAR CALCIFICATION	-	-	-	1
6	FOCAL INCREASE IN VASCULARITY	-	4	3	-
7	DIFFUSE INCREASE IN VASCULARITY	4	11	5	-
8	FOCAL DECRESE IN VASCULARITY	-	-	-	1
9	DIFFUSE DECRESE IN VASCULARITY	-	-	-	1
10	NORMAL VASCULARITY	-	-	-	-

Table VII : Comparison For Varicocele Between Physical Examination and Colour Doppler

PATIENT NO	PHYSICAL EXAMINATION	COLOUR DOPPLER EXAMINATION
1	Left	Left
2	-	Left
3	-	Bilateral
4	Bilateral	Bilateral
5	Right	Right
6	Left	Bilateral

Image I : Right Testicular Seminoma Shows Homogeniously Hypoechoic Apperance

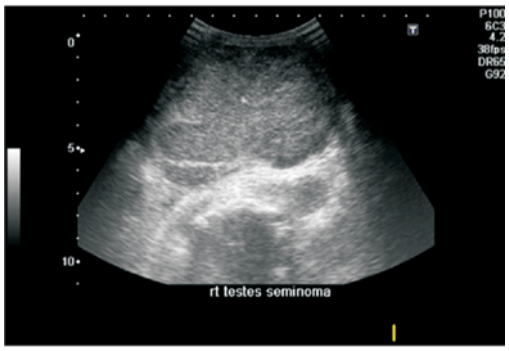


Image II : Varicocoele with Reversal of Flow

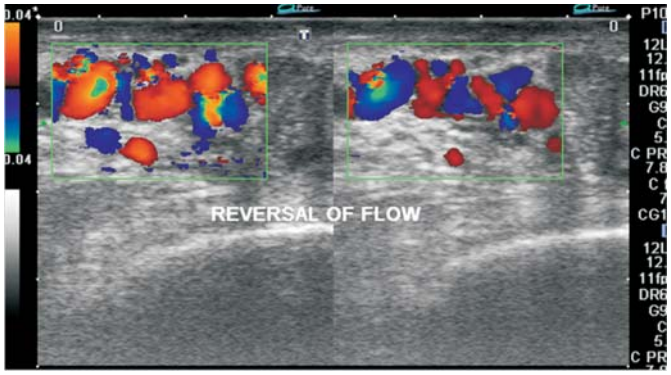


Image III : Torsion of Testis Showing No Colour Flow on Doppler

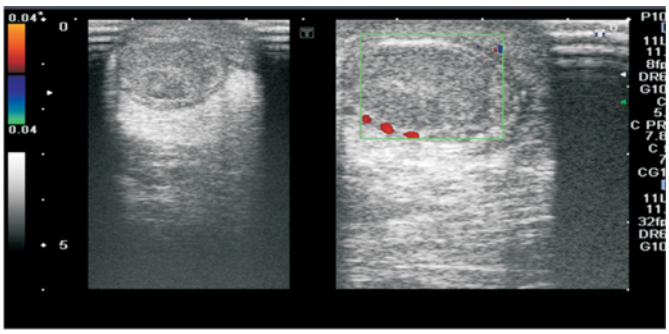


Image IV : Left Sided Acute Orchitis Show Hypoechoc Apperance With Increased Vascularrity

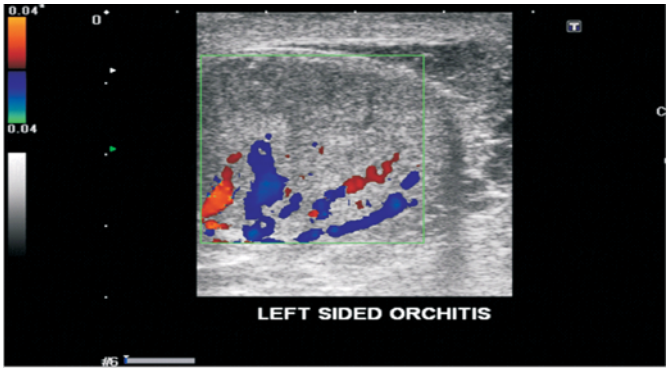
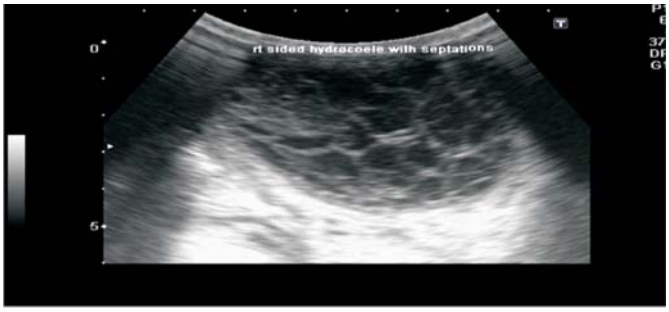


Image V: Hematocele Shwiong Fluid With Septations Within



Summary Andconclusions

1. The primary role of ultrasound in the evaluation of the scrotal pathologies is the detection of the lesions and to determine whether the lesion is intratesticular or extratesticular.
2. Ultrasound findings alone are not helpful to classify a tumor histologically and biopsy is necessary, however retrospectively we can say that most homogenously hypoechoic lesions are seminomas and most of the nonseminomatous lesions heterogeneous with areas of calcification and cystic areas.
3. Color Doppler findings of the tumor and the inflammatory lesions also overlap each other and thus to differentiate them repeat examination is necessary after a course of antibiotics to look for the resolution of the abnormal increase in vascularity in cases of the inflammatory lesions. Also correlation with the grey scale findings, history and clinical examination is helpful to differentiate between inflammatory and neoplastic lesions.
4. Ultrasound is very helpful in detecting the site and size of the lymph nodal metastasis and metastasis at the other sites like liver.
5. Ultrasound is very useful in evalution of painful scrotal condition like acute inflammatory disease and differentiates it from testicular torsion and salvaging the testes.
6. In the inflammatory condition, ultrasound is very helpful in detecting the changes in thesize ,echogenicity& vascularity of testis and epididymis, and associated findings i.e. hydrocele and skin thickening.
7. Ultrasound is very helpful in early detection of torsion of testis and thus help in early management and thus salvaging the testis.
8. Ultrasound is very helpful in detecting the complications of the inflammatory diseases like pyocele and abscess at earliest.
9. Ultrasound can easily identified hydrocele and most importantly it can rule out the underlying pathologies in cases of hydrocele as clinical evaluation is often limited.
10. In cases of undescended testis ultrasound helps in localizing the testis only when it is in the inguinal region and has limited value in intraabdominally located testes due to obscuration by the bowel gas, in those cases MRI can be helpful.
11. In the cases of scrotal trauma, ultrasound is helpful in detecting and staging the injury and thus helps in early management and thus salvaging the testis.

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ORIGINAL ARTICLE

A prospective comparative study of early and interval laparoscopic cholecystectomy in Acute Cholecystitis.

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KEY WORDS : Early laparoscopic cholecystectomy; Interval laparoscopic cholecystectomy; acute cholecystitis.

ABSTRACT

Background : Earlier interval cholecystectomy was usual practice in cholecystitis, but later cholecystectomy in acute cholecystitis preferably within 72 hours was proven to be as safe as interval cholecystectomy.

Method : A prospective comparative study of early laparoscopic cholecystectomy (ELC), n=25 and interval laparoscopic cholecystectomy (ILC), n=25 for acute cholecystitis was carried out in a series of 50 cases admitted in a single surgical unit of Govt. Medical College, Surat (Gujarat), India during the period of 1st July 2008 to 31st August 2010.

Results : Comparing two groups; patients undergoing ILC experienced a significantly shorter duration of surgery (1.5$\pm$1.41 vs. 2.27$\pm$0.63, $p < 0.045$) than in ELC and total hospital stay in ELC is more than in ILC (6.3$\pm$10.62 vs. 5.92$\pm$3.53, $p < 0.030$). There was no significant difference with wound infection rates (6/25, 24% vs. 5/25, 20%, $p > 0.05$) and other complications like URTI. On comparing conversion to open cholecystectomy (04 vs. 01, $p > 0.06$) in ELC more than ILC was statistically not significant (p value was > 0.05) ; only 1 case (4%) of biliary leak which was stopped in 48 hours in ELC group.

Conclusion : Both early and interval cholecystectomy are safe for treating acute cholecystitis, but operative difficulty and duration of surgery is more in early group.

INTRODUCTION

Cholecystectomy is the definitive treatment for patients with acute cholecystitis. Early cholecystectomy performed within 2 to 3 days of presentation is preferred over interval or delayed cholecystectomy that is performed 6 to 10 weeks after initial medical therapy. About 20% of patients fail initial medical therapy and require surgery during the initial admission or before the end of the planned cooling-off period [1].

Since last 20 years, increasing number of surgeons hasfavored a policy of early surgery. Several randomized studies in the early 1980 has shown that performing early cholecystectomy for acute cholecystitis was better than delayed cholecystectomy in terms of shorter hospital stay, operative feasibility and both had similar operative morbidity and mortality rates[1].

The present study is an endeavor to find out the intra-operative as well as post-operative morbidity and mortality in early laparoscopic cholecystectomy for acute cholecystitis and its benefit over traditional interval laparoscopic cholecystectomy and compare them with those already published.

Review of Literature

An English surgeon, Walton (1923) first advocated early operation for acute cholecystitis [2].Charles S. Jones et al (1960) suggested that early surgery as a general policy for management in acute cholecystitis might further reduce present mortality [3]. An added advantage of this policy would be correction of a misunderstanding, which has caused delay in definitive treatment.

Ross Boggs and Dunphy (1950) interviewing 151 surgeons found general agreement that the period between fourth and twelfth days from the acute attack were particularly dangerous but concluded that immediate operation was the treatment of choice no matter how long the duration of the disease [4].Pines and Robinowith (1954) concluded that after four days

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mortality and morbidity rises steeply [5].According to Reiss et al (1979) early surgery to be performed within 48 hours after full diagnostic investigation and adequate preparation [6].According to Jarvien et al (1979) early surgery for acute cholecystitis is that which is done within seven days of admission and delayed surgery is that which is done after a period of conservative treatment. They are then discharged from hospital and operated upon after a period of six months [7].Bhansali (1980) from his study advocated that for acute cholecystitis, initial conservative therapy followed by 3-6 weeks later operation should be done [8].

MATERIAL AND METHOD

A prospective study of 50 consecutive cases of acute cholecystitis admitted in a single surgical unit of Govt. Medical College and New Civil Hospital, Surat during the period of 1st July 2008 to 31st August 2010 was conducted after approval of local ethical committee and with consent of patients involved in the study. No discrimination was made in respect of age and sex on the selection of cases to be studied.

Every case was clinically examined to detect any relevant disease and routine laboratory investigations (urine, blood for total count, differential count, and hemoglobin percentage) were carried out. The functional capacity of Liver, ultrasonography of abdomen along with plain x- ray of the abdomen was done after admission. Out of 50 patients, early laparoscopic cholecystectomy was done in 25 patients; on the other hand conservative treatment followed by surgery after a gap of 6-8 weeks was performed in the rest 25 patients.

Conservative management was donewith nil by mouth, bed rest, nasogastric aspiration, intravenous fluids and antibiotics, analgesic and antispasmodics. Continuous observation of the patients, regarding pulse, temperature, rigidity, Lump and tenderness in the abdomen. The response of the patients to conservative treatment was noted till the date of discharge.Intraoperative findings were noted both in early and delayed surgery.Sub-hepatic abdominal drain was placed in all fifty patients. Other parameters observed were: need for blood transfusion, operative time, conversion of laparoscopic cholecystectomy to open cholecystectomy.

Any complication that occurred during conservative treatment and following surgery was noted. Thecomplications looked for wereabscess formation, itis empyema;increase in size of the lump; impending perforation;development, and or increase in jaundice;onset of septicemia;othercomplications due to prolonged bed rest,leg vein thrombosis and basal pneumonia;re-attack of acute cholecystitis following conservative treatment; post-operative complications like: wound infection, respiratory tract infection, prolonged ileus, hyperpyrexia, sub phrenic collection, and biliary fistula or leak. All data collected and statistical analysis was performed with Microsoft excel2010. Continuous data were compared with STDEV.P formula and categorical data were compared with Pearson's test. Values of $p < 0.05$ were considered statistically significant.

OBSERVATIONS & RESULTS

Comparing both groups ELC (Early laparoscopic Cholecystectomy) of 25 cases and ILC (Interval laparoscopic Cholecystectomy) of 25 cases, age and sex were comparable (Table I). On presentation, abdominal pain was present in all 50 patients; Fever (19 vs. 00), jaundice (01 vs. 01), nausea and vomiting (22 vs. 02) with p value 0 were observed (in ELC vs. ILC). On examination, icterus in single patient in both group; tenderness (25 vs. 00); rigidity (25 vs. 00); palpable lump (19 vs. 02) with p value 0 were present (in ELC vs. ILC). On investigation, bio-chemical investigations are not significant, ultrasonography showed gall bladder calculi in all 50 patients and in ELC group pericholecystic collection detected in 11 cases. Comparing two groups; patients undergoing ILC experienced a significantly shorter duration of surgery (1.5 ± 1.41 vs. 2.27 ± 0.63, $p < 0.045$) and total hospital stay in ELC is more than in ILC (6.3 ± 10.62 vs. 5.92 ± 3.53, $p < 0.030$). Intraopretively aspiration of distended gall bladder required ingroups (02vs. 01, $p< 0.02$), spillage of stones (02 vs. 01, $p< 0.02$), gangrenous gall bladder (02 vs. 00, $p< 0.04$), pus collection (01 vs. 00, $p< 0.02$) are expected and comparable. Partial cholecystectomy due to dense callot's triangle (02 vs. 00, $p< 0.04$) was pathognomic of acute cholecystitis.There was no significant difference with wound infection rates (6/25, 24% vs. 5/25, 20%, $p > 0.05$) and other complications like URTI. On comparing conversion to open cholecystectomy (04 vs. 01, $p > 0.06$) in ELC more than ILC was statistically not significant (p value was > 0.05) ; only 1 case (4%) of biliary leak which was stopped in 48 hours in ELC group; no other intra or post-operative complications; no 30 days readmission rate and no mortality in either group were noted.

Table I : Early versus Interval laparoscopic cholecystectomy in Acute cholecystitis [9].

Characteristic	ELC N=25	ILC N=25	P value
Age	19-65	23-66	0.089
Sex M/F	01/24	04/21	0.40
Symptoms			
Pain in abdomen	25	25	0
Fever	19	00	0.38
Jaundice	01	01	0
Nausea, Vomiting	22	02	0.4
On examination			
Icterus	01	01	0
Tenderness	25	00	0.5
Rigidity	25	00	0.5
Lump in RHC	19	02	0.34
USG-gall bladder calculi/pericholecystic collection	25/11	25/00	0.41
Duration of surgery - Average hours with SD (min.-max.)	2.27+0.63 (2.30-3.20)	1.5+1.41 (1.15-3.15)	0.045
Intra operatively-			
Aspiration required in distended gall bladder	02	01	0.02
Gangrenous Gall bladder	02	00	0.04
Spillage of stones	02	01	0.02
Partial cholecystectomy	02	00	0.04
Pus collection	01	00	0.02
Conversion to open cholecystectomy	04	01	0.06
Total hospital stay- Average days (min.-max.)	6.3+10.62 (2-17)	5.92+3.53 (5-10)	0.03
Complications			
Biliary leak	1 (4%)	0	0.02
Wound infection	6 (24%)	5 (20%)	0.02
URTI	1 (4%)	1 (4%)	0

Note that there was no mortality, no 30 days admissions in either group of patients.

DISCUSSION

Twenty five out of the fifty cases in the present series underwent early cholecystectomy. All twenty five cases were operated within 48 hours of acute attack.The aim of the study was to compare and evaluate the result of the present series with those already published.

Graham et al (1938) from their study mentioned certain factors that make early cholecystectomy for acute cholecystitis more difficult than one performed, in the developed period. The gallbladder is often tense and distended. The tissues are more friable and bleeding is profuse. There is more swelling in the cystic duct [10].Adam et al (1947) was of the opinion that surgical treatment should be carried out within 26-72 hours of onset of symptoms [11]. L.J. Lester (1947) [12] and Bhansali (1976) believed in conservative management for 6-8 weeks followed by surgery [8].But Zinninzer (1934) [13], Mentzer (1936) [14], Doubilet et al (1954) [15], Charles S. Jones et al (1960) [3], Wright et al (1960) [4], Ahmed (1992) [16]; all favored early cholecystectomy.

In ELC cases operation was not difficult due to the development of a cleavage plane between the gallbladder and surrounding structures which facilitates dissection of gallbladder. But four cases because of difficult Calot's triangle and excessive bleeding had to be converted to open from laparoscopic cholecystectomy and 3 patients required blood transfusion. The other twenty five patients were underwent delayed cholecystectomy after a gap of 6-8 weeks from the acute attack. In these cases operation was comparatively easier due to decrease in tissue edema, structures can be identified properly. Also there is less tissue friability. Conversion to open from laparoscopic cholecystectomy was needed in only 1 patient. Blood transfusion was not needed in any of the patient.

HOSPITAL STAY

R.A. Pyne (1969) in his study found that the average duration of hospital stay to be 16.6 days for delayed surgery [17]. In another study conducted by S.A. Khuwaith found that the average duration of hospital stay for delayed cholecystectomy to be 18.5 days [18]. William van Der Linden et al (1981) found average duration of hospital stay for the patients treated with early operation to be 10.1 days [19]. The mean stay for the patients of delayed operation group was 18.9 days.I. Ahmed (1992) in his study found that the average duration of hospital stay for early cholecystectomy group to be 10 days and delayed cholecystectomy group to be 15 days [16].In the present series the average duration of hospital stay for those patients who underwent early cholecystectomy was 6.3 days and 5.92 days for those who underwent delayed cholecystectomy.

DURATION OF SURGERY :

Average time taken for cholecystectomy in cases of early laparoscopic cholecystectomy is approx. 2 hr. 27 min. whereas in cases of interval laparoscopic cholecystectomy, it is 1hr 50 min. This is due to more adhesions and less experience of surgeons for doing cholecystectomy during attack of acute cholecystitis.

COMPLICATIONS

Linden et al (1970) described post-operative wound infection is the most common post-operative complication, which is more in those patients who undergo early cholecystectomy [20].According to Mc Arther et al [21], Jarvinen et al (1979) [8] and Ahmed (1992) [16]. Post-operative wound infection is more common in those patients which were undergone early cholecystectomy. Other postoperative complications that were recorded by Ahmed were - respiratory tract infection, prolonged ileus, hyperpyrexia, subphrenic collection, dyspepsia and recurrence of symptoms.

In the present series out of 50 cases, five patients (20%) of group of delayed surgery (ILC) suffered from postoperative wound infection. 1 (4%) patient suffered from upper respiratory tract infection.Out of the rest twenty five patients who had early cholecystectomy (ELC), 6 patients (24%) had postoperative wound infection, 1 patient (4%) had upper respiratory tract infection.

FOLLOW UP :

We have done follow up of the patients at our outpatient department from 2 to 4 years. 5 patients were lost in follow up due to unknown reasons. None of patients had developed any complications during follow up except for mild abdominal discomfort for which PPI (proton pump inhibitors) are given and patients' pain relieved. No patient had developed jaundice or biliary cirrhosis.

CONCLUSION

Though the factors like operative difficulty and duration of surgery are against the early group comparing delayed group; they depend on experience and skill of surgeon in laparoscopy, postoperative complications, morbidity and mortality are comparable in both groups. All over both early and interval laparoscopic cholecystectomy are safe for treating acute cholecystitis. Conversion of laparoscopic cholecystectomy to open should not be considered as complication as it is just a mode of treatment. Patients had to stay less in hospital if delayed surgery is done, rather than early surgery but previous admission in cases of delayed cholecystectomy had not been taken in to account.

admission in cases of delayed cholecystectomy had not been taken in to account.

Conflict of interest: The authors declare that they have no conflict of interest.

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ORIGINAL ARTICLE

Relationship of Serum Uric Acid Level to Maternal and Perinatal Outcome in Patients with Hypertensive Disorders of Pregnancy

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KEY WORDS : Severe preeclampsia, uric acid level, perinatal and maternal outcome

ABSTRACT :

Aim and objective : To Study Serum Uric Acid level elevation in Hypertensive Disorders of Pregnancy and its role on maternal and perinatal outcome.

Material and Methods : The Study was performed on two groups of women with hypertensive disorders of pregnancy; the first group (n=50) with a serum uric acid level of ≥6mg/dl was compared to the second group (n=50) with a serum uric acid level of <6mg/dl. Maternal and perinatal complications like eclampsia, HELLP(Hemolysis, Elevated Liver Enzymes, Low Platelets) syndrome, ARF(Acute Renal Failure), IUFD(Intra-Uterine Fetal Death), low apgar score, IUGR(Intra-Uterine Growth Retardation) were studied.

Results : A comparison between the two groups revealed that hyperuricemia in patients with hypertensive disorders of pegnancy is a strong risk factor for several maternal and perinatal complications with an increased risk of an apgar score <7 by 6.0 fold, IUFD by 20 fold, IUGR by 4.0 fold, eclampsia by 4.2 fold and cesarean section by 3.4 fold in patients with a uric acid level ≥6mg/dl as compared to those with a level of <6mg/dl.

Conclusion : Hyperuricemia in patients with hypertensive disorders of pegnancy is a strong risk factor for several maternal and perinatal complications.

INTRODUCTION

Hypertensive disorders are among the commonest medical disorders during pregnancy and continue to be a major cause of maternal and perinatal morbidity and mortality worldwide. In developing countries they rank second only to anaemia, with approximately 7-10% of all pregnancies being complicated by some form of hypertensive disease.[1]

Pregnancy may induce hypertension in women who are normotensive before pregnancy and may aggravate hypertension in those that are hypertensive before pregnancy.[2,3]Early screening for preeclampsia may allow vigilant antenatal surveillance and appropriate timing of fetal delivery in order to avoid serious sequelae.

In the non-pregnant population hyperuricemia is an independent predictor of cardiovascular and renal disease in both the general population and in subjects with chronic hypertension.

Elevated uric acid level in maternal blood, presumably due to decreased renal urate excretion is frequently found in women with preeclampsia. Various studies have been conducted to find out the relationship between elevated uric acid level and preeclampsia.[4]There are several potential origins for uric acid in preeclampsia; abnormal renal function, increased tissue breakdown, acidosis and increased activity of the enzyme xanthine oxidase/dehydrogenase.

Studies of serum uric acid level in normal and hypertensive pregnancy and its relation with the early diagnosis of preeclampsia, severity of preeclampsia and associated perinatal outcome have been done in various parts of the world by many workers [5,6.]

AIMS AND OBJECTIVES

To study level of serum uric acid elevation in Hypertensive Disorders of Pregnancy and its role in maternal and perinatal complications.

MATERIAL AND METHODS

The study was performed on 100 women with hypertensive disorders of pregnancy at Ob and Gy dept, B.J. Medical College and Civil Hospital, Ahmedabad from 2011 to 2012. Serum Uric acid levels were studied at the onset of parturition. The participants were categorized into two groups according to their serum uric acid level:

Group A, those with a serum uric acid level of ≥ 6mg/dl (n=50)

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Group B, patients with a serum acid level of <6mg/dl (n=50)

Maternal and fetal complications like Intra Uterine Fetal Death (IUFD), low apgar score, Intra Uterine Growth Retardation (IUGR), increased cesarean section rate and eclampsia were studied. Blood samples for serum uric acid were taken and determined by enzymatic colorimetric method.

Follow up levels were not measured. Only a single estimation of serum uric acid level at the onset of parturition was done.

RESULTS

Table-I : Association between Uric acid level and Type of Hypertension

Type of Hypertension	Uric acid ≥6 mg/dl	Uric acid <6 mg/dl
Chronic hypertension	5	3
Preeclampsia superimposed on chronic hypertension	6	2
Mild Preeclampsia	10	35
Severe preeclampsia	25	9
Eclampsia	4	1
Total	**50**	**50**

Table-II : Perinatal Outcome

Complication	Uric acid ≥6mg/dl	Uric acid <6mg/dl	Odd ratio(95%CL)	P value
Apgar <7	20	5	6.0(2.03-17.72)	0.001
Preterm deliveries	10	2	6.0(1.24-28.98)	0.02
IUGR	13	4	4.04(1.21-13.43)	0.02
IUFD	8	0	20.0(1.13-360.29)	0.04

IUGR (Intra Uterine Growth Retardation)
IUFD (Intra Uterine Fetal Death)

Table-III : Maternal Outcome

Complication	Uric acid ≥6mg/dl	Uric acid <6mg/dl	Odd ratio(95%CL)	P value
Cesarean Section	23	10	3.4(1.40-8.28)	0.006
Eclampsia	4	1	4.26(0.45-39.54)	0.20
Abruption	4	0	9.7(0.51-186.52)	0.12
HELLP	4	0	9.7(0.51-186.52)	0.12
ARF	1	0	3.06(0.12-76.95)	0.49
Maternal mortality	1	0	3.06(0.12-76.95)	0.49

HELLP (Hemolysis, Elevated Liver Enzymes, Low Platelets) **ARF (Acute Renal Failure)**

DISCUSSION

In present study, two groups, Group A (uric acid ≥6mg/dl) and Group B (uric acid <6mg/dl), both consist of 50 patients were studied. Mean age of the patients in Group A was 29±5.1 yrs and that in Group B was 28±4.8 yrs. Mean weight of the patients in Group A and B was 55.6±6.0 kg and 52.8±4.28 kg respectively. There was no significant difference in age and weight parameters of both groups. Out of 50 patients in Group A, there were 36 primigravida and 14 multigravida while in Group B, there were 20 primigravida and 30 multigravida patients.

Preeclampsia has been defined as a triad of hypertension, edema and proteinuria. A rising serum uric acid is now recognized as an early feature of preeclampsia and its measurement greatly increases the accuracy of diagnosis and helps to differentiate this disorder from essential and other chronic forms of pre-existing hypertension complicating pregnancy[7,8].

In a carefully controlled and extensive investigation, Lim and Frideman measured serum uric acid concentration in healthy pregnant females, patients with preeclampsia and patients with hypertensive vascular disease. They determined the mean serum uric acid level in the last trimester of pregnancy for the normal women to be 3.5±0.6 mg%. Patients with hypertension had similar concentration of serum uric acid, 3.7±1.1mg%, whereas the mean level for patients with histologically proven preeclampsia was 6.4±1.7mg%. Thus a significant increase in mean serum uric acid concentration was present in patients with preeclmpsia compared to those with hypertensive vascular disease and normal pregnant women[9].

Mustaphi and Gopalan found that an elevation of mean values for uric acid correlated with degree of severity of toxemia. Lim and frideman in 1998 found that the concentration of serum uric acid also correlated well with

severity of glomelur lesion. Anna and Leo concluded that the level of serum uric acid appears to be a sensitive index of severity of preeclampsia[10].

In group A, there were 10 pre-term babies , 8 IUFD, 13 IUGR and 20 babies had low apgar (<7) In group B, 2 pre-term babies, 4 IUGR, 5 babies with low apgar (< 7) and no IUFD. So these entire abnormal fetal outcomes were higher in Group A (uric acid ≥6mg/dl).

In group B, there were no complications like Abruptio placentae, HELLP syndrome, ARF and maternal mortality. Only one case of eclampsia in group B while in group A, there were 4 cases of eclampsia.

This study of 100 patients with hypertensive disorders of pregnancy shows that serum uric acid is an useful index of fetal status and this results are comparable to those of Lim and Frideman, Anna and Leokee-HakLim, Williams and Galernea.

This study indicated that in pregnant women with hypertension, measurement of serum uric acid is a better indicator of fetal consequences of preeclmpsia than measurement of blood pressure itself. In an established preeclmpsia case, the diagnosis is usually clinically evident and elevation of serum uric acid will simply confirm the diagnosis[11.] But since urate retention is an early feature of the disorder, serum uric acid measurement is of the greatest value where the diagnosis is in doubt.

According to Williamset.al., the time of onset of preeclampsia is of great importance in determining the final outcome of fetus because the only treatment for disorder is earliest delivery. Since preeclampsia is usually relentlessly progressive disorder, if it starts between 24 and 30 weeks of gestation, it may readily progress either to IUFD or to a dangerous illness demanding delivery at a time when neonatal survival is unlikely.

The time at which serum uric acid concentration begins to rise is an approximate indicator of the time of onset of the preeclampsia[12]. The value of measuring serum uric acid in hypertensive pregnancy is greatest between 24 to 32 weeks of gestation. Low values indicate a good prognosis for the fetus. Rising or high values at this time indicate high-risk cases which are better managed and treated in hospital. Early bed rest, monitoring of fetal well being in utero and anticipation of maternal problems related to preeclampsia then ensure the best chances for bringing the pregnancy to stage where planned delivery prevents serious maternal complications and gives the best possible chance of fetal survival.

CONCLUSION

The measurement of serum uric acid is thus of great diagnostic and prognostic value for fetus. This study shows that estimation of serum uric acid level in pregnancies complicated by both pre-existing hypertension and preeclampsia help to assess the severity of illness, and to identify those fetuses that are likely to have IUGR and high perinatal mortality and morbidity. Because, laboratory investigation of serum uric acid is simple, it can be easily performed in any laboratory.

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ORIGINAL ARTICLE

A comparative study of hemodynamic responses to intubation:fentanyl versus nalbuphine

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KEY WORDS : Fentanyl, Nalbuphine, hemodynamic changes and endotracheal intubation.

ABSTRACT

Introduction : The pressure response to laryngoscopy and endotracheal intubation has been recognized since long. These changes in the form of Tachyardia, hypertension and arrhythmia may be potentially dangerous. So, the aim of our study is to compare fentanyl and nalbuphine for control of hemodynamic changes during endotracheal intubation.

Material and Methods : Total of 60 patients were selected for the study. These patients were randomly divided into two groups **Group F** (Inj. Fentanyl dose 2µg/kg iv) and **Group N** (Inj. Nalbuphine dose 0.2mg/kg iv). All patients belong to ASAI &ASA II of both sexes aged 20-60 years, were included in this double blinded parallel grouped comparative randomized study. Pulse, blood pressure, ECG were monitored continuously and recorded before giving the study drug , after giving the study drug , at intubation then after at1,3,5,10,and 15 minutes after intubation.

Result : Both groups had increased heart rate during intubation but that was statistically insignificant (P>0.05). Fentanyl group had 12.5% rise in heart rate at time of intubation and Nalbuphine group had 13.6% rise during intubation which is almost equal.

Group N had significant rise in SBP and DBP during intubation compared to Group F.Maximum rise in SBP and DBP in Group N was 14.9% and 8.9% respectively. Where as in Group F it was 4.8% and 4.5% respectively. In Group N rise BP lasted longer after intubation compared to Group F.

Conclusion : Both the drugs show almost equal rise in heart rate at intubation.But increase in B.P was significantly more in Nalbuphine as compared to Fentanyl.

To conclude Fentanyl appears to be better than Nalbuphine when there is need to control hemodynamic response to laryngoscopy and intubation.

INTRODUCTION

Induction of general anaesthesia is known to induce clinically relevant changes in hemodynamic variables probably generated by direct laryngoscopy and endotracheal intubation. Tracheal intubation causes a reflex increase in sympathetic activity that may result in hypertension, tachycardia, and arrhythmia [1, 2]. A change in plasma catecholamine concentrations also has been demonstrated to be a part of the stress response to tracheal intubation [3].

The pressure response to laryngoscopy and endotracheal intubation has been recognized since long. In 1940, Reid and Brace first described hemodynamic response to laryngoscopy and intubation [4].

The rise in pulse and blood pressure are usually transitory, variable and unpredictable. These changes are of no consequence and are well tolerated by healthy individuals. But in patients with hypertension, heart disease and coronary artery disease, the pressure response can result in an increase in the cardiac workload[5].

The pressure response also assumes great significance in neurosurgical patients [6]. Most of these patients suffer from decreased intracranial compliance due to the presence of a tumour or a recent intracranial haemorrhage. Sudden increase in the blood pressure, as is seen during laryngoscopy and intubation, can result in a sudden steep rise in intracranial pressure and consequently, acute cerebral oedema and herniation of brain tissue.

Various drugs and induction agents like Thipentone, Propofol, Esmolol, Lignocaine, Magnesium, Vasodilators and Opioids etc. have been tried to prevent hemodynamic

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response of laryngoscopy but each drug has its own limitations [7-13].

Fentanyl was first synthesized in 1960 and found to be significantly more potent than commonly used opioids, such as morphine or meperidine. The large safety margin, relatively short duration of action, and minimal respiratory depression at analgesic doses observed for fentanyl soon made it the drug of choice for intravenous anaesthesia.[14] Its ability to provide cardiovascular stability and to block the stress response to surgical stimuli at high doses made it the mainstay of cardiac anaesthesia.

Nalbuphine is a semi-synthetic opioid agonist-antagonist analgesic of the phenanthrene series. It is chemically related to the widely used opioid antagonists, naloxone and naltrexone, and the potent opioid analgesic, oxymorphone. It is agonist at kappa receptor and act as antagonist at μ receptor [15]. Nalbuphine is a potent analgesic. Its analgesic potency is essentially equivalent to that of morphine on a milligram basis [16].

Nalbuphine, unlike other agonist-antagonist opioids eg.pentazocine or butorphanol, does not increase systemic blood pressure, pulmonary artery blood pressure, heart rate, or artial filling pressure. For this reason, nalbuphine may be useful to provide sedation and analgesia in patients with heart disease, as during cardiac catheterization.[17]

Fentanyl and Nalbuphine are most commonly used in our setup as a premedication. So our aim was to compare the effects of Fentanyl and Nalbuphine on hemodynamic responses to endotracheal intubation to help the selection of a better drug [18].

AIMS & OBJECTIVES

1. To study the effect of I.V Fentanyl (2μg/kg) and I.V Nalbuphine (0.2mg/kg) during laryngoscopy and intubation on
   - Heart rate (HR)
   - Systolic blood pressure (SBP)
   - Diastolic blood pressure (DBP)
2. To compare side effects and complications of both drugs.

MATERIAL AND METHODS

After obtaining approval from the ethics committee we studied 60 patients posted for surgery under general anaesthesia and requiring orotracheal intubation. We have conducted the study over a period of two years and analysed the data statistically.

These patients were randomly divided into two groups.

Group F : Inj. Fentanyl dose 2μg/kg iv

Group N : Inj. Nalbuphine dose 0.2mg/kg iv

All patients belonged to ASA I &ASA II of both sexes aged 20-60 years, weighing 40 to 70 kg were included in this double blinded parallel grouped comparative randomized study.

EXCLUSION CRITERIA

- Patient's refusal.
- Known allergy to the trial drugs.
- ASA III or more.
- Emergency Surgeries.
- Patients with difficult intubation.
- Patients with bronchospastic disease.
- Patients on beta blockers.

A detailed pre-anaesthetic evaluation of each case was done after noting the medical history, a thorough systemic examination was carried out to detect the presence of any systemic disorder. Routine and special investigations were done accordingly. All patients were kept nil orally 6-8 hrs prior to surgery.

All patients were premedicated with Inj Glycopyrrolate 0.2 mg iv, Inj ondansetron 4mg iv, Inj Ranitidine 50 mg iv and Inj Midazolam 1mg i.v10 min before giving study drug. Baseline Pulse, blood pressure, SPO2, ECG were recorded before premedication.

Group F received Inj Fentanyl 2 μg/kg i.v and Group N received Inj Nalbuphine 0.2mg/kg i.v. Both the drugs were diluted in 10 ml distilled water and injected i.v slowly over 1 minute.

After 3 min of oxygenation and administration of the study drugs, induction was done with Thiopentone sodium 2.5% i.v till the loss of eyelid reflexes and Inj suxamethonium 2mg/kg i.v. Laryngoscopy and intubation was performed 90 seconds after the administration of succinylcholine. All the patients were intubated with Macintosh curve blade laryngoscope within a period of 15seconds and we have excluded the patient who had taken more than15 seconds for intubation. Total time taken for intubation after injection of study drug was 5 minutes in all patients.

Anaesthesia was maintained with O2-N2O (50%-50%) & isoflurane 1%. Injection vecuronium was used for muscle relaxation.

Patients were not stimulated during the observation period and surgery was allowed to start after 15 min of intubation.

Pulse, blood pressure, oxygen saturation were monitored continuously and recorded before giving the study drug, after giving the study drug, at intubation then after at1,3,5,10,and 15 minutespost-intubation. The patient's ECG (lead II) was monitored by the attending anaesthetist for arrythmias and ST-T changes.

At the end of surgery anaesthesia was reversed with Inj

Neostigmine 0.05 mg/kg i.v and Inj. Glycopyrrolate 0.008mg/kg i.v. All the patients were monitored in recovery room for the pulse, blood pressure and Spo2.

Patients were observed intraoperatively and postoperatively for any complication like arrythmias, bradycardia, nausea, vomiting, respiratory depression, sedation , muscular rigidity and pruritus.

Unpaired 't' test was used for analysis of data between groups. Results were considersignificant for P values<0.05.The Statistical software namely SPSS 11.0 were used for the analysis of the data.

OBSERVATION AND RESULTS

Both The groups were comparable with respect to age, sex, weight and ASA physical status (Tab: 1). Baseline SBP and DBP were comparable between both groups (P>0.05). Increase in both SBP and DBP during intubation was more in group N compare to group F, which was clinically and statistically very highly significant (P<0.001). Even 15 min after intubation SBP in group N was significantly higher compare to group F (P<0.001) (Tab:2). Statistically significant difference in DBP between two groups also last up to 10 min after intubation (Tab:3).

Maximum rise in SBP in Group F was 4.8% whereas in Group N it was 14.9%. After intubation SBP started decreasing and 15 min after intubation it was 5.1% lower than basal value in group F whereas in groupN it remained higher than baseline (Tab:2)

Similarly Group N showed more rise in DBP(8.8%)during intubation compared to groupF (4.5%). 15 min after intubation DBP was 4.7% lower than basal value in GroupF whereas in Group N it was higher than baseline DBP(Tab:3).

Baseline heart rate between two groups was comparable (P>0.05). Both group showed rise in HR after intubation. But difference in HR between two groups at any time interval was statistically insignificant (P>0.05). In Group F maximum rise in HR was 12.5% during intubation and 15 min after intubation HR was 5.9% lower than baseline .In Group N maximum increased in HR was 13.1% during intubation and it was 7% lower than basal value 15 min after intubation(Tab:4).

TABLES AND GRAPHS ↑ ↓

TABLE-I : DEMOGRAPHIC DATA

	Group F	Group N	P-value
Age	36.26 ± 11.36	37.46 ± 10.73	0.67
Sex (M/F)	16 / 14	16/14	
Weight	50.50 ± 3.91	51.46 ± 5.84	0.75
ASA (I/II)	18/12	17/13	

Table -II: COMPARISON OF CHANGES IN MEAN SYSTOLIC BLOOD PRESSURE BETWEEN GROUP-F & GROUP-N

Time	Group F (mm Hg) Mean ± SD	Group F Percentage change from basal value (%)	Group N (mm Hg) Mean ± SD	Group N Percentage change from basal value (%)
Basal	125.4		122.4	
3 min after study Drug	118.07	↓5.4	118.47	↓2.4
During Intubation	131.53	↑4.8	139.6	↑14.9
1 min after intubation	129.73	↑3.4	135.73	↑11.8
3 min after intubation	125.93	↑0.4	133.2	↑9.7
5 min after intubation	123.67	↓1.3	131.2	↑8.07
10 min after intubation	122.27	↓2.4	127.6	↑5.1
15 min after intubation	118.53	↓5.1	124.67	↑2.6

FIG-I : COMPARISON OF CHANGES IN MEAN SYSTOLIC BLOOD PRESSURE BETWEEN GROUP-F & GROUP-N

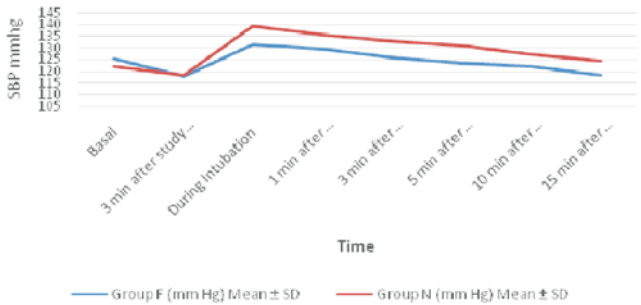

Table III: COMPARISON OF CHANGES IN MEAN DIASTOLIC BLOOD PRESSURE BETWEEN GROUP-F & GROUP-N (mm Hg)

Time	Group F (mm Hg)	Group F Percentage change from basal value (%)	Group N (mm Hg)	Group N Percentage change from basal value (%)
Basal	83.13		81.53	
3min after study drug	81.03	↓2.5	81.02	↓0.6
During Intubation	86.9	↑4.5	92.56	↑8.8
1 min after intubation	86.01	↑3.4	91.53	↑8.5
3 min after intubation	84.07	↑1.1	89.4	↑8.4
5 min after intubation	83.07	↓0.07	88.27	↑8.26
10 min after intubation	80.4	↓3.2	85.8	↑5.2
15 min after intubation	79.17	↓4.7	83.4	↑2.2

FIG-II : COMPARISON OF CHANGES IN MEAN DIASTOLIC BLOOD PRESSURE BETWEEN GROUP-F & GROUP-N

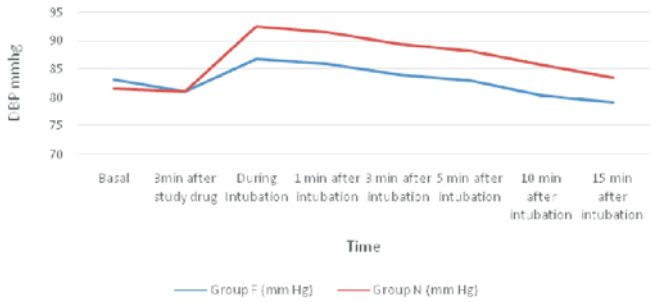

TABLE-IV : COMPARISON OF CHANGES IN MEAN HEART RATE BETWEEN GROUP-F & GROUP-N

Time	Group F (HR/min)	Group F Percentage	Group N (HR/min) change from basal value (%)	Group N Percentage change from basal value (%)
Basal	86.03		85.93	
3 min after Study Drug	84.93	↓3	82.83	↓3.6
During Intubation	96.83	↑12.5	97.33	↑13.6
1 min after intubation	94.37	↑9.6	92.23	↑7.3
3 min after intubation	89.83	↑4.4	89.63	↑4.6
5 min after intubation	86.93	↑1	85.83	0
10 min after intubation	82.93	↓3.6	80.03	↓6.8
15 min after intubation	80.93	↓5.9	79.83	↓7

DISCUSSION

Larygoscopy and intubation are two most consistent manoeuvres that lead to significant increase in blood pressure and heart rate. These changes are reported to be greatest immediately after intubation of trachea and last for 5-10 minutes [19].

If no specific measures are taken to prevent hemodynamic response of laryngoscopy, the heart rate can increase from 20% to 45% depending on the method of induction [42,45,46] and systolic blood pressure can increase from 36% to 45% [19,20].

To blunt these response, various methods have been tried like topical application of local anaesthetic, infiltration or nerve blocks, α adrenergic blockers, vasodilators,

calcium channel blockers, α 2 agonists[21-27]. But these drugs have no role for induction and maintenance of anaesthesia and also causes dangerous complication.

Narcotics have advantage of having perioperative role in anaesthesia. They can be used as sole or supplementary agent for induction of anaesthesia. Narcotics are very commonly used for intraoperative analgesia , therefore there is no additional cost involved.

Fentanyl is available in our country since 1998 and has various advantages like no histamine release , no bronchospasm, cardiostability, rapid onset and short duration of action. Nalbuphine is also cardiostable, potent analgesic, minimum side effect in the dose of 0.2-0.4 mg /kg and its action start within 2-3 minutes.

In our study patients were randomly distributed into two groups and there was no statistically significant difference in the distribution of age, sex, ASA Grading and weight of patients in both the groups (Table-1).

Fentanyl has been tried in various bolus doses for control of hemodynamic changes of laryngoscopy. Black et al [28] and Kay et al [28] found complete attenuation of hemodynamic response with 5µg/kg fentanyl. But large dose can lead to muscular rigidity, bradycardia, nausea and vomiting. Large doses may also cause post-operative respiratory depression especially in surgery with short duration (less than1 hour). McClain et al[29] reported apnoeic episodes in four out of seven patients who received 3.2 to 6 µg/kg fentanyl.

We selected the dosages in our study based on the assumption that nalbuphine is equipotent to morphine [30] .Fentanyl on an mg basis is about 80 times more potent than morphine [30] and a dose of 2µg/kg was therefore chosen to be almost equipotent to nalbuphine 0.2 mg/kg.

Nalbuphine was also used in the dose in which less side effects like nausea , vomiting, post-operative respiratory depression occur [31].

Fentanyl and nalbuphine were given 5 minutes before intubation which is a optimum time to administer these drugs to protect circulatory responses to laryngoscopy and tracheal intubation. Ko SH et al [32] had studied 2 µg/kg of fentanyl given at different time before intubation and they found that optimal injection time for fentanyl for control of cardiovascular changes is 5 minutes before intubation. So Similarly we have done intubation 5 minutes after injection of study drugs.

Khan et al has compared nalbuphine 0.2 mg /kg and Fentanyl 2µg/kg as total intravenous anaesthesia with propofol infusion in laproscopic surgery. These drugs were given 5 minutes before induction. They found significant increase in SBP and DBP in nalbuphine group which is similar to our result . DBP after intubation increased to a maximum of 13% in nalbuphine versus 3% in fentanyl.

Branko M et al studied fentanyl and nalbuphine for coronary Artery Bypass Surgery. In their study during and after intubation all patients given nalbuphine (and only one patient given fentanyl) required nitroglycerin to control MAP. They also found higher level of epinephrine, norepinephrine, vasopressin and cortisol in Group N in comparison to baseline value.Whereas in Group F it was within baseline values.

Results of Freye E & Levy JV also proved that nalbuphine is only partially effective in reducing the cardiovascular responses to laryngoscopy and tracheal intubation in comparison to fentanyl.

Changes in heart rate between fentanyl and nalbuphine group did not show statistically significant difference at any time interval ($p>0.05$). F.A.Khanet al found sigiificant increase in heart rate in nalbuphine group (25%) as compared to fentanyl group . The maximum positive or negative change in heart rate observed in this study in the fentanyl group was 6.4%..

Study of B.KY et al for comparison of fentanyl and nalbuphine for blocking the circulatory responses to tracheal intubation found significant rise in heart rate and bloodpressure in nalbuphine group .In contrast , neither an increase in blood pressure nor heart rate in group F.

Suprato et al found significant rise in heart rate and blood pressure after intubation in patients receiving fentanyl 1µg /kg given 15 minutes before intubation. SBP & DBP increased to 40% above baseline in fentanyl group 30 seconds after intubation. The inadequate effect of fentanyl to attenuate the hemodynamic response in this study may be related to the lower dose used and longer than optimal time lag from administration to laryngoscopy.

Any patient from both groups did not had any complication like arrhythmias, bradycardia, nausea, vomiting, respiratory depression or pruritus.

CONCLUSION

Both the drugs show almost equal rise in heart rate at intubation. But increase in both SBP and DBP was more in group N than group F.

To conclude Fentanyl appears to be better than Nalbuphine when there is need to control haemodynamic response to laryngoscopy and intubation.

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ORIGINAL ARTICLE

Bone Marrow involvement by Metastatic solid Tumors

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KEY WORDS : bone marrow, metastasis, solid tumors, trephine biopsy.

ABSTRACT

The bone marrow in addition to being the site of origin of numerous primary hematological malignancies is commonly involved by metastatic solid tumors. The presence of metastasis in the bone marrow usually means an incurable although not necessarily rapidly fatal disease. It is therefore imperative to rule out marrow involvement in any malignancy where curative treatment is being considered. We reviewed a three and a half years experience with bone marrow aspirates and biopsies positive for metastasis. In our study, marrow examination in 525 cases suspected for bone marrow metastasis was done. Seventy three out of 525 cases (13.9%) were positive for metastasis .Out of 73 cases,29 cases of paediatric age group and 44 cases of adult age group were positive. The common primary tumors metastasize to bone marrow in pediatric age group were neuroblastoma (41.3%), followed by retinoblastoma (24.13%), and Ewing's sarcoma(20.6%).While in adult age group Ewing's sarcoma (25%), followed by Carcinoma breast (9.09%), Carcinoma lung (9.09%), rhabdomyosarcoma (9.09%), and Carcinoma prostate (6.81%) were common. Seven cases of metastatic adenocarcinoma were detected. This study also demonstrates the usefulness of combining trephine biopsy with aspiration examination for increased detection of bone marrow metastasis.

INTRODUCTION

Bone marrow is one of the most common sites to be involved by tumors that metastasize via the bloodstream. Detection of metastatic tumors to the bone marrow is of great importance for the clinical staging of tumor spread because malignant infiltration of hematopoietic tissue can alter the clinical course of the disease. Metastatic tumor in the bone marrow may influence the response to treatment, overall survival, and resulting decreased hematopoiesis may force the clinician to scale down the dosage of drugs used. After introduction of chemotherapy assessment of bone marrow reserve has become a routine procedure in the evaluation of patient before and during therapy. This has revealed an unsuspected high frequency of metastatic spread to the bone marrow [1].

In adult, Ewing's sarcoma, carcinoma of the breast, lung, gastrointestinal tract and prostate accounting for majority of cases. In children, neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma and retinoblastoma constitute the majority of bone marrow metastasis [2].Bone marrow infiltration may be suspected on the basis of bone pain, pathological fracture, lytic or sclerotic lesions on X-ray, hypercalcemia, elevated serum alkaline phosphatase of unexplained hematological abnormalities. However, metastasis may be present in the bone marrow without any abnormalities being recognized in the bone scans, radiographic picture, serum chemistry and hematological parameters. This fact highlights the importance of using sensitive technique for the detection of bone marrow metastasis. [2,3]. Our experience during the past three and a half years with diagnosis of metastatic tumor involvement of the bone marrow was reviewed, and value of the aspirate versus biopsy was assessed.

MATERIALS AND METHODS

We carried out retrospective analysis of bone marrow involvement by metastatic solid tumors, diagnosed and treated at Gujarat Cancer & Research Institute, Ahmedabad, India from January 2003 to June 2006. Patient's name, age, sex, date of presentation and date of diagnosis were recorded. Total number of 525 suspected cases of bone marrow involvement, in which 244 paediatric cases and 281 adult cases were evaluated. A diagnosis of metastatic infiltration in bone marrow was made in 73 cases. Diagnosed cases of Lymphoma and Hodgkin's disease were not included in this study. The diagnosis was based upon finding tumor in either aspirate or biopsy, or both.

Bone marrow aspirates obtained from iliac crest were routinely stained by Wright stain and special stains like Periodic Acid Schiff and Alcian blue were used as and when required. The bone marrow biopsies obtained by

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Jamshidi needle (8G x 10cm) were fixed in 10% formalin solution and paraffin embedded 4 micrometer thick sections were stained with hematoxylin-eosin. Special stains were used as and when necessary.

OBSERVATION AND RESULTS

Total 525 cases suspected for bone marrow involvement were evaluated. In adults, 44 out of 281 cases (15.6%) were positive for metastasis. Only bone marrow aspirate was positive in 14 cases (31%), only trephine biopsy was positive in 11 cases (25%) and both aspirate and trephine biopsy were positive in 19 cases (43%). In pediatric age group 29 out of 244 cases (11.8%) were positive for metastasis. Out of 29 positive cases, in 20 patients trephine biopsy was not performed. Only bone marrow aspirate was positive in 21 cases, only trephine biopsy was positive in 2 cases and both marrow aspirate & trephine biopsy were positive in 6 cases.

PEDIATRIC CASES-Patient's age ranged from 6 month to 14 years in 29 cases. The male to female ratio was 1.3:1. Maximum number of cases were of neuroblastoma, (12/29) followed by retinoblastoma (7/29), Ewing's sarcoma (6/29), rhabdomyosarcoma, (2/29) and wilms' tumour (1/29). In one case, patient was diagnosed as malignant round cell tumour on bone marrow examination and then follow up was lost so final histopathological diagnosis could not be confirmed.

ADULT CASES-Patient's age ranged from 19 to 77 years. The male to female ratio was 2:1. In 35 out of 44 metastatic cases the primary site was known. Maximum numbers of cases were of Ewing's sarcoma (11/44), followed by Carcinoma lung (4/44), Carcinoma breast (4/44), rhabdomyosarcoma (4/44), Carcinoma prostate, (3/44) and medulloblastoma (3/44). Rest of the cases includes primary from rectum, stomach, ovary, nasopharynx, skin and neuroblastoma each. In seven cases, metastatic adenocarcinoma was identified but site of origin could not be ascertained. In two out of seven cases, primary could be from gastrointestinal tract and in one case, primary from lung was likely. In two cases malignant round cell tumour was identified and final histopathological diagnosis could not be done as patients were lost to follow up.

The most common presenting symptoms were back pain, abdominal pain and pyrexia of unknown origin. On peripheral blood examination, almost all patients were anemic. Thrombocytopenia was observed in 60% cases and leukoerythroblastic reaction was observed in 10% cases. Serum alkaline phosphatase was raised in all cases.

There was no significant difference in detection frequency between aspirate smears and trephine biopsy section in adult age groups. For some tumor categories, simultaneous use of both techniques resulted in superior rates of detection.

Table I. Frequency of Metastasis in Bone Marrow

	Total no of suspected cases	Total no of positive cases
Paediatric cases	244	29
Adult cases	281	44
Total cases	525	73

Table II. Primary tumor/site of Metastasis to Bone Marrow Paediatric age group:

PRIMARY TUMOR/ SITE	NO OF CASES
Neuroblastoma	12
Retinoblastoma	07
Ewing's Sarcoma	06
Rhabdomyosarcoma	02
Wilm's tumour	01
Unknown-Malignant Round Cell Tumour	01

Adult age group

PRIMARY TUMOR/SITE	NO.OF CASES
Ewing's Sarcoma	11
Carcinoma of Lung	04
Carcinoma Breast	04
Rhabdomyosarcoma	04
Carcinoma Prostate	03
Medulloblastoma	03
Carcinoma Rectum	01
Carcinoma Skin	01
Carcinoma Stomach	01
Carcinoma Ovary	01
Nasopharyngeal Carcinoma	01
Neuroblastoma	01
Unknown-Malignant Round Cell Tumour	02
Unknown-Metastatic Adenocarcinoma	07

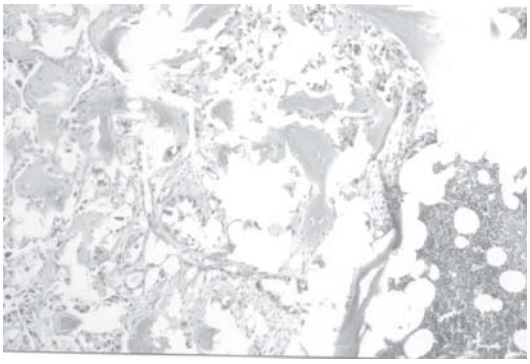

Figure : 1- BM trephine biopsy section, metastatic adenocarcinoma, showing group of Tumour cells with hyper chromatic nuclei and gland formation.

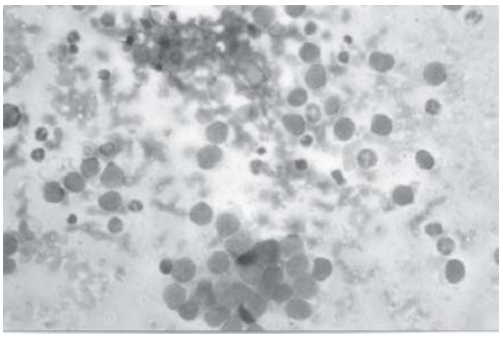

Figure: 2- BM aspirate, Malignant Round Cell Tumour, showing neoplastic cells Arranged in clusters and have high nucleocytoplasmic ratio and a diffuse chromatin pattern.

DISCUSSION

Bone marrow metastasis in non hematological solid tumors reported virtually in all types of malignancies both in Western and Indian literature [4]. Detection of metastatic tumor in the bone marrow is of great importance for the clinical staging of tumor spread, because it may influence the response to treatment and the overall survival [5,6]

This study includes 525 cases suspected for bone marrow metastasis. In the evaluation of an individual with suspected metastatic disease, tumor may be present in marrow & not be detected by other techniques [2, 7, 8].

In our study 44 out of 281 adult cases were positive for metastasis. The highest incidence of bone marrow involvement occurred in Ewing's sarcoma (25%), followed by Ca breast (9.09%), Ca lung (9.09%), rhabdomyosarcoma (9.09%), Ca prostate (6.81%) and medulloblastoma (6.81%) with a frequency almost similar to that reported by others [2,6, 9,10]. In pediatric age group 29 out of 244 cases were positive for metastasis. The highest incidence in pediatric age group was observed in neuroblastoma(41.3%), followed by retinoblastoma (21.3%), Ewing's sarcoma(20.6%) & rhabdomyosarcoma (6.8%) which was also almost similar to other studies [2,6,9,11].

The hematological abnormalities most suggestive of marrow infiltration were peripheral leukoerythroblastic picture(10%), anemia (100%), thrombocytopenia (60%) and elevated serum alkaline phosphates levels (100%) which is also observed by others. [5, 13, 14]

The frequency of bone marrow involvement by neuroblastoma in our study is 41.3%. Bone marrow examination is usually important in establishing the diagnosis, for accurate staging of the tumor, for monitoring the course and confirming the response to therapy particularly if autologous bone marrow transplantation is an option. In cases of neuroblastoma bilateral iliac crest bone marrow aspirates and trephine biopsies are indicated [4, 11].In general, patients with marrow involvement are considered to have poor prognosis .[15]

Bone marrow involvement is a frequent event in metastatic Ewing's sarcoma (52%) and is often multifocal and therefore requires extensive BM investigation. [10]

Carcinoma breast is one of the most commonly metastasizing in the bone marrow. In our study the incidence is 9.09%. There is strong correlation between the presence of tumor in the marrow and bone scans and x-ray evidence of skeletal metastasis [4].

Several studies have confirmed the frequent metastasis of prostatic carcinoma in to bone marrow [2]. In our study it is 6.8%.

As early as 1971, it was demonstrated that bone marrow metastasis was a frequent findings at the time of diagnosis in patients with small cell anaplastic carcinoma of lung [17.] The incidence ranges from 17% to 45% during life [4]. Marrow is seldom the sole site of metastasis. Although marrow metastases in non hematological malignancies are reported most commonly in breast, lung, prostatic carcinoma, Ewing's sarcoma & neuroblastoma, they occasionally are reported in almost all types of malignancies. In our study seven cases of metastatic adenocarcinoma were reported.

The demonstration of marrow involvement in early stage disease by application of newer technique is of interest. Immunohistochemistry, clonal growth, flow cytometry & PCR techniques will indicate a greater frequency of tumor infiltration than has been evident from standard histological methods [18.]

Bone marrow aspiration and trephine biopsy are relatively sensitive technique for detecting bone marrow infiltration by metastatic tumors. The advantage of the trephine biopsy with respect to smear preparation is that it preserves the histological architecture of the tumor cell clusters. Thus rosette formation and glandular structures were frequently found in the trephine biopsy section. In addition paraffin embedded particals permitted the utilization of special stain to further establish histological type. In contrast certain tumor types which subtly infiltrate the bone marrow such as rhabdomayosarcoma and neuroblastoma were difficult to detect on trephine biopsy section while the smear preparation permitted the recognition of typical features of malignant cells. Hence the two procedures should be regarded as complimentary [2, 4, 6, 19, 20]

In conclusion, bone marrow aspiration was slightly more sensitive than trephine biopsy (31% Vs 25%) and by using both the techniques, sensitivity was increased to 43%. Thus our results demonstrate the complimentary value of using the both preparatory techniques simultaneously.

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ORIGINAL ARTICLE

A Study on efficacy and safety of the drug misoprostol 600 mcg for prevention of postpartum hemorrhage by different routes of administration in routine management of 3rd stage of labor; a randomized placebo controlled double blind study.

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KEY WORDS : Misoprostol 600 mcg, postpartum hemorrhage, routes of administration

ABSTRACT :

Objectives - Based on our basic premise that routinely available oxytocics used in rural settings lose their potency over time due to lack of cold chain facilities and trained birth attendants in parenteral administration of oxytocics; a suitable drug with safe delivery is desirable. We designed a well controlled study to evaluate the newly approved drug- tablet misoprostol 600 mcg to evaluate its safety and efficacy in prevention of post partum hemorrhage using placebo and blinding technique in 340 subjects. **Methods -** Subjects were allocated randomly to rectal and sublingual route of administration after they fulfilled inclusion criteria with double blinding. We used combined methods of visual as well as quantitative assessment of blood loss to evaluate efficacy controlling the confounding factors by strict inclusion criteria. **Results -** Mean blood loss in cases allocated to sublingual route (170) was 82.76±48.96ml while in cases allocated to rectal route (170) was 111.85±63.51 ml. Side effects in sublingual route was 34.70% while that in rectal route it was 14.11%. The major side effect was shivering 22.64% (77 cases out of 340). Minor side effects were fever (1.17%), diarrhea (0.29%) and rigors (0.29%). No other side effects, morbidity or mortality occurred. **Conclusion -** Since shivering was less in rectal group 12.94% as compared to sublingual group 32.35% with acceptable blood loss we concluded that rectal route of misoprostol 600 mcg with controlled cord traction and uterine massage is safe and effective in prevention of postpartum hemorrhage applicable to rural settings. We state that we have ensured safety and autonomy of subjects throughout.

INTRODUCTION

PPH is an important cause of maternal mortality, accounting for nearly one quarter of all maternal deaths worldwide. Atonicity is most common cause. Active management of labor includes 3 aspects as per WHO guidelines 1.Uterine massage 2. Controlled cord traction 3.Use of uterotonic drugs.

Among these Uterotonic drugs, Oxytocin & Methergin must be handled & stored properly because they are unstable when exposed to light & high ambient temperature. Furthermore, these drugs must be injectibles. So, not only does this require qualified persons to administer these drugs, but it also requires a readily available supply of sterile syringes & needles that must be handled & disposed of properly. Even today large amount of deliveries occur with/without trained birth attendants in rural settings in India. Refrigeration facilities and cold chain are not available at all the times hence drugs lose their potency. Many of birth attendants are also not trained for giving parental injections.

So, there is a need of a drug which is safe, effective in prevention of PPH (postpartum hemorrhage), cheap, easily available, stable at room temperature not requiring storage facility or skilled person to administer.

Govt. of India has included Tab Misoprostol 600mcg for Prevention of PPH & in training of active management of 3rd stage of labor after delivery of baby for Auxiliary Nurse Midwives & staff nurses. WHO and Drug Controller General of India have also included Tab misoprostol for prevention & treatment of PPH in the list of essential drugs. Several studies are available worldwide on use of misoprostol as effective drug for prevention & treatment of PPH in different dosage form & routes (1-15). The drug Tab Misoprostol 600mcg is permitted & approved by Drug Controller General of India under rules 122-B of Drugs & Cosmetic Rule 1945 with effect from 14th Jan 2009 for the indication of prevention & treatment of PPH (vide permission letter no.MF-7059/06, file no.04-103/2001/DC dated 10/12/2006 and 14/1/2009).

MATERIALS & METHODS

Duration of study: 1st July 2010 to 31st Aug 2011.

Type of study: Randomized placebo controlled double blind comparative study.

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Agents used: Tab Misoprostol 600 mcg; Sublingual, Rectal Route (Active drug and Placebo)

Placebo: Constituents-Microcrystalline Cellulose, Sodium Starch Glycolate and Lubricant-Hydrogenated Castor oil. The tablets are exactly look alike the active drug with similar Embossing of word "PPH"

Indication: Prevention of PPH in routine management of 3rd stage of labor

Sample size: 170 in each route (340 Total)

Study design:

INCLUSION CRITERIA:

Normal/low risk pts assigned randomly (irrespective of gravidity) in age group of 19-35 years after informed consent.

EXCLUSION CRITERIA:

1. Pregnancy with Previous Caesarean Section
2. Mal-presentation
3. Severe Anemia
4. Operative Delivery
5. Ante-partum Hemorrhage
6. Traumatic PPH
7. Glaucoma, Asthma
8. Hypertension
9. Cardiac Diseases
10. Use of oxytocin infusion and prostaglandins in induction and/or augmentation of labor
11. Multiple Pregnancy
12. Hydramnios
13. Prolonged labor
14. Abnormal bleeding time
15. Pyrexia and vomiting
16. Parity > 4

METHOD OF CASE ALLOCATION

A total number of low risk cases satisfying inclusion/exclusion criteria are selected using lottery method exactly equal to the sample size and then again re-allocated to (a) Tab Misoprostol 600mcg sublingual (b) Tab Misoprostol 600 mcg rectal is done using same lottery method out of primary numbers drawn. Since we want to carry out placebo controlled double blind study we have used placebo tablets containing inert substance to remove bias. The blinding was done by third party other than the authors 1&2 to remove bias of selection.

We have ensured that each patient in the study received single active uterotonic drug (either rectal or sublingual) in the management of third stage by using combination of placebo tablets of same appearance by various route combinations in a double blind manner.

Each patient has received one sublingual tablet and one rectal tablet immediately after the delivery of anterior shoulder of the baby. (One placebo tablet & one active uterotonic tablet randomly and by blinding). Each patient has received uterine massage for 4 minutes and placental delivery is done by Controlled Cord Traction as prescribed by WHO. No other oxytocic has been administered except Tab Misoprostol 600 mcg unless patient develops PPH.

METHOD OF OBSERVATION (Figures 1, 2)

Figure 1 Brass V type Blood Collection Kit

Figure 2 Visual Assessment Pads 10 x 10 cms

After delivery of the baby all the fluid/liquor/blood is immediately removed from the delivery table and a fresh specially prepared plastic sheet (Brass-V type) with funnel attached to its lower part is replaced by the doctor who is blind to the drug used as uterotonic **(1, 2).**

He has also collected the specially prepared 10 x 10 cms delivery pads soiled after delivery of the baby for visual assessment of blood-loss **(3,4).** The total blood is collected in calibrated vessel from after the delivery of the baby, delivery of placenta and through the 4th stage of labor (1hour).

The frequency of observation of blood loss is grouped in following categories.

0-50ml, 51-100 ml, 101-150 ml, 151-200 ml, 201-250ml, 251-300ml, 301-350 ml, 351-400ml, 401-450 ml, 451-500 ml, 501-550 ml, 551-600 ml. etc (Blood collected in calibrated vessel plus soiled pads- quarter of pad soiled =5ml, half of pad soiled=10ml, ¾ of pad soiled=20 ml, fully soiled pad=30ml)

We have also observed the time lag between administration of the drug and contraction & retraction of the uterus and duration of the third stage of labor (delivery of baby to complete delivery of placenta). The observations for duration of third stage of labor are noted in minutes using stop clock.

We have also meticulously observed the side effects of the drugs mentioned in literature as well as other untoward effects and noted temperature, Pulse, BP, Respiration in case records. Cases are deleted from study if any case meets the exclusion criteria.

DECODING

After completion of all cases decoding is done and comparison and analysis of observed data is done using qualitative as well as quantitative data analysis methods. Literature comparison is done from available studies published.

NOTES ON RISK, SAFETY & RISK REDUCTION

Risk identified in study:

1. There is a time lag between onsets of action of Tab Misoprostol & Other routinely used injectible uterotonics as per drug literature (Rectal= 40.5 min ; Sublingual= 18min).
2. So, there may be chance of development of atony during use of Tab Misoprostol.
3. Also, S/E like diarrhea, shivering, fever, abdominal pain, nausea are associated with Tab Misoprostol which are mild in nature as reported in literature except pyrexia.

Notes on safety & risk reduction

1. Each patient has received uterine massage for 4 minutes.
2. Drug Misoprostol in dosage of 600 mcg is found to be safe if given S/L or Per Rectal as shown by review of literature and W H O recommendations for peripheral units owing to good shelf life as compared to other oxytocics.
3. If any patient develops hemorrhage in excess of 500 ml or develops any hemodynamic deterioration patient shall be managed as per routine therapeutic methods immediately using other oxytocics, surgical methods and intravenous fluids if required to ensure safety of the patient. As this study is designed to study only prophylactic use of Tab Misoprostol 600 mcg any case of PPH is managed by therapeutic methods as prescribed in literature.
4. The drug Tab Misoprostol 600 mcg is permitted & approved by Drug Controller General of India under rules 122-B of Drugs & Cosmetics Rule 1945 with effect from 14th Jan. 2009 for prevention & treatment of PPH.(Vide permission letter no. MF-7059/06, File No. 04-103/2001/DC dated 10/12/2006 & 14/1/2009).
5. We have also obtained permission from Institutional Ethics Committee for this study after due review.
6. We also state that we have alternate oxytocics drugs like inj. Oxytocin, inj. Methyl ergometrine, inj. Carboprost readily available in delivery room as well as surgically skilled persons available in case the subject develops PPH or other complication.
7. Having very specific inclusion & exclusion criteria to exclude high risk cases to ensure patient safety.
8. A Qualified senior person is always available during study.
9. Blood transfusion facility including components available to all patients and samples are tested for cross matching and bleeding time.
10. Full operative facilities are available and Drugs to deal with S/E always ready

NOTES ON STUDY BIAS:

Cases are selected by authors coming to labor room by prior simple randomization using lottery method and covering drugs in specific color coded foils as predesigned. Rectal tablets in RED and Sublingual tablets in SILVER FOILS and blinding is done by using placement of PLACEBO tablets by third party with a case to case meticulous record for decoding at the end of the study. Both the tablets- the active and placebo have same color, size, shape and embossing ("PPH").

CONSENT: Due consent to get enrolled in the study is obtained in vernacular and the patient has free choice to opt out at any moment. There is no element of monetary consideration, compulsion or denial of treatment if not opted for the study by the authors. The authors have followed the dictum of "primum non nocere" at all times during the study.

NOTES ON PROCUREMENT OF PLACEBO & ACTIVE DRUG:

We have procured the placebo tablets from Research & Development Department of Cipla, Sikkim, India. There is no financial consideration or favor and the drugs obtained are only for academic purpose. We have procured the active drug from our hospitals' tender mechanism prior to the start of study bearing batch numbers- A00606;March 2010, A000901;Apr 2010(Manu.Lic.M/455/2007). We

have not passed on the costs to the subjects coming for medical care in our department.

Placebo Tablets supplied by Medical Services Department Cipla Ltd., Mumbai Dated 10th Mar 2010 contained inert material.

OBSERVATIONS & DISCUSSION

The average blood loss in the third stage of labor is 250-350ml and 12% of women will lose > 500 ml. Use of uterotonics should reduce this proportion to 5% as per Cochrane Database Systemic Reviews. 2000, Issue 3.

The purpose of the study is to find out which route of administration of Tab Misoprostol 600mcg is better in view of amount of blood loss, duration of 3rd stage of labor and side effects and also to find out whether Tab Misoprostol 600mcg is suitable to be used as preventive measure for PPH in routine management of 3rd and 4th stage of labor especially in rural settings.

Table 1: General observations

	Group	S/L(n=170)	Rectal(n=170)	Total (n=340)
Age (yrs)	≤20	14	9	23
	21-25	76	100	176
	26-30 71	52	123	
	>30	9	9	18
Parity	1	3	1	4
	2	78	88	166
	3	72	68	40
	4 17 13	30		
Placental weight (gms)	≤300	0	1	1
	301-400	25	27	52
	401-500 108	102	210	
	501-600 31	29	60	
	601-700 4	11	15	
	701-800 2	0	2	
Baby Weight (kg)	<1.5	0	1	1
	1.5-2	14	13	27
	2.1-2.5	48	42	90
	2.6-3.0	84	80	164
	3.1-3.5	22	32	64
	>3.5	2	2	4
Total Blood Loss(ml)	≤50	33	23	56
	51-100	103	72	175
	101-150	22	37	59
	151-200 6	24	32	
	201-250 1	6	7	
	251-300 1	6	7	
	301-350 1	0	1	
	351-400 1	2	3	
	401-450 0	0	0	
	451-500 0	0	0	
Time Taken by uterus to contract (mins)	1	10	10	20
	2	99	96	195
	3	57	52	109
	4	3	10	13
	5	0	2	2
	6 6 0	1		
Duration of 3rd stage of labor (mins)	1	1	0	1
	2 3 6	9		
	3	44	36	80
	4	56	62	118
	5	35	37	72
	6 20 15	35		
	7	8	7	15
	8 3 7	10		

Table 2:Mean Blood Loss:

	Blood Loss(ml)		Duration of 3rd stage of labor(min)	
	Mean	95%CI	Mean	95%CI
S/L (n=170)	82.76±48.96	75.40-90.12	4.20±0.0008	0.00021
Rectal (n=170)	111.85±63.51	102.31-121.40	4.24±0.0009	0.00022
Both (n=340)	97.3±58.46	91.09-103.52	4.22±0.0009	0.00015

Z Value: 4.74 which is greater than 3 hence P is < 0.01 (More efficacy of sublingual Misoprostol)

Table 3: Side Effects:

	Side effect						
Route	Yes	No	Shivering	Fever	Diarrhoea	Rigor	Required Rx
Sublingual (n=170)	59	111	55	3	0	1	2
Rectal (n=170)	24	146	22	1	1	0	3
Both (n=340)	83	257	77	4	1	1	5

Chi-Square 19.52 Suggestive p value< 0.001(significance)

(Concluded that sublingual route having more association with side effects.)

We found that Mean blood loss in sublingual group was 82.76±48.96ml while in rectal group it was 111.85±63.51ml and it was 97.3±58.46ml in both groups combined. So the mean blood loss is significantly lower (p<0.01) in sublingual group as compared to rectal group. Z Value: 4.74 which is greater than 3 hence P is < 0.01

Analysis of the results shows more efficacy of sublingual Misoprostol (600mcg) as compared to rectal Misoprostol (600 mcg) in view of blood loss but no significant difference in duration of 3rd stage of labor.

Side effects:

On analysis it was found that shivering is the major side effect in both groups. Side effects in sublingual route was 34.70% while that in rectal route it was 14.11%. The major side effect was shivering 22.64% (77 cases out of 340). Minor side effects were fever (1.17%), diarrhea (0.29%) and rigors (0.29%). No other side effects, morbidity or mortality occurred. Shivering was less in rectal group 12.94% as compared to sublingual group 32.35%.

Chi-Square 19.52 Suggestive p value< 0.001 (significance) concluded that sublingual route having more association with side effects.

Statistical Analysis :

Data were analyzed on intent to treat basis by parametric and nonparametric tests, using Microsoft Office Excel 2007. For Estimation of significance of drug in relation to blood loss one-tailed Z –test (p<0.01) was used while for estimation of significance in view of side effects Chi-square test (p<0.001) was used.

Comparison with other studies :

We found mean blood loss in our study was 82.76±48.96ml in sublingual route, which is almost similar to 96.05±21.1ml in 600mcg by sublingual route and lower

than 126.24±49.3 ml in 400mcg by sublingual route by Singh et al**(5)**

Mean blood loss by rectal route in our study is 111.85±63.51ml in our study. Harriott j et al found that mean blood loss with misoprostol 400mcg by rectal route is 180.1 ±120 ml. Steven M et al **(6)** estimated 163.5ml mean blood loss with 800mcg rectal misoprostol.

The most recent study conducted in rural India was the first large, randomized, placebo-controlled trial testing the efficacy and safety of a regimen of oral misoprostol (600 mcg) in a community setting where a skilled provider is not in attendance. This study showed that misoprostol reduced PPH $\geqslant$ 500mL by nearly 50% compared with placebo (6% misoprostol vs. 12% placebo) **(7).**

Hoj et al. (2005) found that sublingual misoprostol (600 mcg) was significantly better than placebo for reduction of severe PPH $\geqslant$ 1000mL (11% misoprostol vs. 17% placebo) **(8).**

Although various routes and regimens have been tested, available evidence points to the use of a 600 mcg oral regimen for the prevention of PPH. The WHO Recommendations for the Prevention of Postpartum Hemorrhage recommends that regimen for use in settings where AMTSL is not practiced (Strong recommendation, moderate quality evidence, WHO 2007).

Our results show that in sublingual group 34.70% patient developed side effects while in rectal group it was 14.11%. Shivering is the major side effect in both groups accounting 93.2% in sublingual group and 91.66 % in rectal group.

Shivering (47%) and fever (44%) with misoprostol 800 mcg found in study by Winikoff B et al **(9).**

Results of a community-based randomized controlled trial in rural India shows that oral misoprostol(600mcg) had a significantly greater incidence of shivering (52% vs. 17%, $p < 0.001$) and fever (4.2%vs. 1.1%, $p < 0.001$) at 2 h postpartum compared with women who received placebo**(10).**

Randomized controlled trial by Mansouri HA et al in Saudi Arabia concluded shivering and pyrexia occurred in 161 (52.1%) and 86 (27.8%) women receiving oral misoprostol (600mcg), and in 81 (26.2%) and 47 (15.2%) of those who received rectal misoprostol(600 mcg), respectively (P=0.000 & 0.001) (11). A multicentre, double-blind randomized trial by Widmer M et al found misoprostol(600) versus placebo, had shivering [65%] vs. [32%]; 2.01, 1.79-2.27)**(9)**

A randomized controlled trial was performed at two district hospitals in Ghana by Steven MP et al resulted shivering was more common in the misoprostol (rectal 800mcg group (7.5% vs. oxytocin 0.9%; relative risk 8.0; 95% CI 1.86—34.36; P = 0.001). **(6)**

Thus, in our study the amount of blood loss using 600mcg Misoprostol by both the routes was found to be more efficacious as compared to the similar studies. We state that our study was well designed to reduce the effects of confounding variables by strict inclusion criteria, precision in measuring blood loss by standard time tested technique of Brass-V drape, visual assessment combined and by doing a randomized double blind placebo controlled study to remove the selection bias, and hence the results.

Strengths of this study :

Most studies available in literature on misoprostol as a uterotonic agent in prevention or treatment of postpartum hemorrhage have been insufficiently blinded. In our study we have done randomization and placebo controlled as well as double blinding to remove the selection and observational bias.

The placebo tablets are exactly look alike the active drug with similar Embossing of word “PPH”.

We have used strict inclusion as well as exclusion criteria to minimize confounding factors with different variables affecting the blood loss as well as side effects; a well controlled study. We were thus successful in recruiting normal or low risk patients in both the study groups improving quality of the study.

We have also taken steps for patient's safety and risk reduction. Every patient in our study has received active oxytocic (Misoprostol) drug for prevention of PPH by either route as compared to other studies reported in literature where only placebo were used to compare the effect of active drug which increases risk of PPH in group using placebo alone.

Coagulation profile was performed prior to recruitment in the study and specialist manpower as well as blood transfusion facilities were kept ready to improve safety.

None of the patient in our study has received any other oxytocics during labor.

None of the patient required blood transfusion or any surgical procedure during the study.

No maternal death was reported.

No SAE (serious adverse event) or serious ADR (adverse drug reaction) developed in our study.

Estimation of blood loss is known to be difficult and inaccurate as done in previous many studies. So for precise estimation of blood loss we have included both visual assessment and collection of blood in specially prepared BRASS-V type calibrated vessel.

Cost of the drug was totally borne by the hospital.

A well informed consent was taken from each patient for recruitment in study for autonomy and permission from institutional ethics committee was taken prior to start of the study.

CONCLUSION

Our premise that the rural birth attendants who do not have skill to administer injectibles at delivery and a suitable heat stable drug in absence of cold chain facilities was the start point of the study.

Since Misoprostol, prostaglandin E1 analogue, does not lose efficacy in absence of cold chain various administration routes were available to us. Here in this study we have successfully compared sublingual and rectal route for ease of administration considering rural settings.

Our randomized placebo controlled double blind study has concluded that Misoprostol 600mcg would play essential role and can be used as a safe agent in prevention of PPH with AMTSL.

Amount of blood loss is lower in sublingual group as compared to rectal group, but since side effects are more with sublingual route, rectal route should be preferred for routine use in AMTSL for prevention of PPH though both routes are effective for prevention of PPH.

We recommend that following method may be employed for prevention of Post Partum Hemorrhage as tested in our study and also prescribed by WHO for active management of 3rd and 4th stage of labor,

1. Controlled cord traction
2. Optimum uterine massage
3. Tab Misoprostol (600mcg) to be placed rectal at the delivery of anterior shoulder after ruling out contraindication of prostaglandin like asthma, liver disease.

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ORIGINAL ARTICLE

Oral care and culture sensitivity of organisms isolated from respiratory tract secretion of critically ill patients with ventilatory support admitted in I.C.U., I.C.C.U., of Dr Jivraj Mehta Smarak Healh Foundation, Ahmadabad.

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KEY WORDS : Respiratory secretion, ventilator support, culture and sensitivity, Oro care Brush.

ABSTRACT

The purpose of this study was to detect antibiotic resistant pattern of organisms isolated from the respiratory tract secretion. So that indiscriminate use of antibiotics can be prevented and arousal of resistant to antibiotics can be minimize.

Introduction : Critically ill patients who are on ventilator support, suffering from different diseases and post operative complication are at greater risk of cross infection during their stay in the hospital. Ventilator associated pneumonia is one of the major causes of Hospital acquired pneumonia.

Oral bacteremia are usually normal flora with up to 350 different species[1] The dorsal posterior aspect of the tongue contains layers of debris and harbors millions of organisms, and this oral flora can rapidly cause pneumonia, if not dealt effectively. Xerostomia and Mucositis are common cause In critically ill patients[2]. If critically ill and incubated patients does not receive effective oral care then bacterial plaque develops on the teeth within 72hrs[2] which can contribute to the bacterial infection down the tract.

Our aim of this study is to know the common types of organisms isolated from the respiratory secretion and their sensitivity pattern. This will help in proper selection of antibiotics, so that indiscriminate use of antibiotics can be prevented and arousal of antibiotic resistant in bugs can be minimized. Specialized flexible Oro Care brush either with chlorhexidine or with betadine was used for effective mouth care.

MATERIAL AND METHOD

Respiratory tract secretion form hundred critically ill patients requiring ventilator support admitted in I.C.U., I.C.C.U., of Dr Jivraj Mehta Smarak Health Foundation, Ahmedabad were collected and cultured on Nutrient, Mac Konkey's and Blood agar as per standard protocol. The isolates were identified by different biochemical reactions. The antimicrobial susceptibility testing was performed by Kirby–Bauer disc diffusion method.[3] Gram negative bacilli were tested against Ampicillin(10µg), Ampi+Sulbactum(10/10µg),Cephoperazone(30µg), Ceftriaxone(30µg), Cephoperazone+Sulbactum (30/10µg), Cefipime(30µg), Cefipime+Tazobactum (30/10µg), Imipenem (10µg), Meropenem (10µg), Levofloxacin (5µg), Gatifloxacin (10µg), Ciprofloxacin (5µg), Doxycyclin (30µg), Amikacin (30µg), Gentamicin(30µg), Aztreonam (30µg), Piperacillin + Tazobactum (100/10µg), PolymyxinB (300U), Colistin. Gram positive cocci were tested against Penicillin, Cephalothin (30µg), amikacin (30µg), Gentamicin (30µg), Clindamycin (30µg), Levofloxacin (5µg), Gatifloxacin (30µg), Ciprofloxacin (5µg), Vancomycin (30µg), Erythromycin (15µg), Linezolid (30µg), Clindamycin (2µg), and Cefoxitin (30µg). Sensitivity of bugs to Cefoxitin (30µg) was used as a marker for MRSA or MSSA. **The results were interpreted according to standard CLSI guideline**[3]. Disc of Ceftazidime (30µg) + Ceftazidime/Tazobectum (30/10) were used as a marker for ESBLpositive producers. ≥ 8 mm Increasing the diameter of zone of inhibition near the disc containing combined betalactam and betalactamase inhibitors as compare to zone of inhibition near betalactam alone used as marker for ESBL producing strain.[3] Resistance to combination of BL+BLI and cefoxitin was used as a screening test for the detection of AmpC beta lactamase production.[4]

RESULTS

Hundred samples were collected from the respiratory tract of patients admitted in I.C.U., I.C.C.U., of Dr Jivraj Mehta Smarak Health Foundation, Ahmadabad.

Out of hundred patients 63 patients were male and 37 patients were female.

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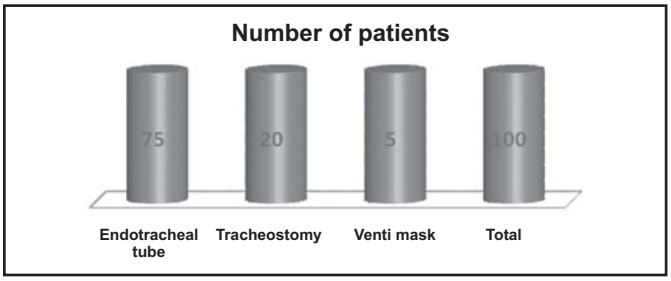
Table : 1 Age group & Gender

Years	Male	%	Female	%
15-20	02	2.08	04	10.00
21-30	05	10.41	01	3.33
31-40	04	8.33	04	13.33
41-50	11	20.83	02	06.66
51-60	10	16.66	12	33.33
61-70	12	8.33	10	20.00
>70	19	33.33	04	13.33
Total	**63**	**9.97**	**37**	**99.98**

Table : 2 Days since on ventilator.

Days	Male	%	Female	%
1-3	29	52.08	16	40.00
4-6	17	22.91	13	33.33
7-10	05	2.08	02	6.66
>10	02	2.08	01	3.33
Intermittent	03	6.25	01	3.33
No ventilator	07	14.58	04	13.33
Total	**63**	**99.98**	**37**	**99.98**

Table: 3 Mode of ventilator



Out of total 100 patients culture was not recovered in 4 patients, in remaining 96 patients there was no growth in 8 patients, in 62 patients single organism was isolated and remaining 26 culture mixed organisms were isolated. In four cases where culture was nit recovered were on intermittent venti mask respiratory support.

Table : 5 Culture status

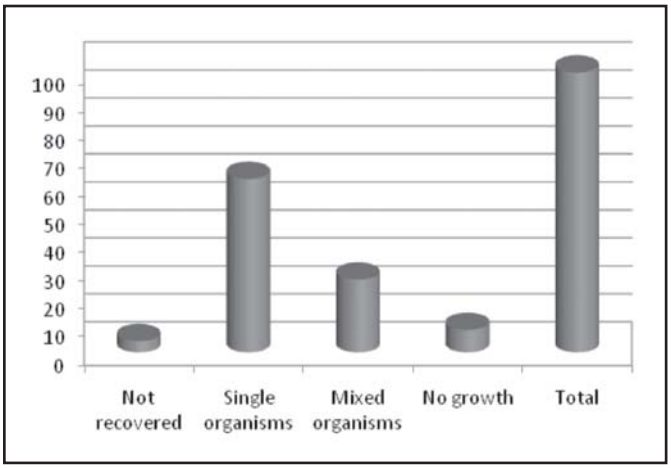


Table : 6 Organisms isolated

Organisms isolated	Number	%
Pseudomonas aeruginosa	15	24.19
Klebsiella pneumoniae	21	33.87
Escherichia coli	04	6.45
Candidia species	15	24.19
Acinetobacter baumanii	04	6.45
Staphylococcus aureus (MRSA)	03	4.84
Total	**62**	**99.99**

Klebsiella pneumoniae(33.87%) is the most common organism isolated followed by *Pseudomonas aeruginosa*(24.19%), *candida species*(24.19%), *Escherichia coli*(6.45%), *Acinetobacter baumanii*(6.45%), *Staphyloccocus aurueus*(4.84%).

Table : 7 Mixed organisms

Mixed organisms	Number	%
Pseudomonas+Klebsiella	14	53.84
Pseudomonas+candida	02	7.69
Pseudomonas+Acinetobacter	04	15.38
Klebsiella+candida	02	7.69
Klebsiella+Acinetobacter	02	7.69
Klebsiella+E.coli	02	7.69
Total	**26**	**99.99**

Pseudomonas+Klebsiella(53.84%) most commonly isolated mixed organisms followed by Pseudomonas + Acinetobacter (15.38%), Pseudomonas + candida (7.69%), Klebsiella + Candida(7.69%), Klebsiella + Acinetobacter (7.69%), Klebsiella + E.coli (7.69%).

DISCUSSION

The main aim of this study is to make aware about commonest oarganisms isolated from different specimens and their sensitivity pattern so that indiscriminate use of antibiotics and arousal of antibiotics resistant in bugs can be prevented. Study also help to know about prevalence of ESBL and AmpC beta lactamase producing bugs in the hospital.

Table : 8 Organismsproducing ESBL, AmpC beta-lactamase and Carabapenemase.

Organisms	Number of Isolates	ESBL producing	AmpC roducing	Carbape-nemase
E.coli	06	03(50.00%)	01(16.66%)	0
Klebsiella pneumoniae	41	28(68.29%)	08(19.51%)	04(9.75%)
Pseudomonas aeruginosa	35	22(62%)	06(17.14%)	03(8.57%)
Acinetobacter baumanii	10	08(80%)	01(10%)	00
Total	**92**	**65(70.65%)**	**16(17.39%)**	**07(7.60%)**

Amongst the total 92 culture positive samples we have detected 65(70.65%) ESBLs, 16(17.39%) isolates as possible AmpC producers and 7(7.60%) isolates as Carbapenemase producers. Our findings co relates with the study at Chennai [4]and at Saudi Arabia[3]. Further investigation of this phenotypic screening method for identifying possible AmpC producers seems warranted. ESBL, AmpC beta lactamase and Carbapenemase production most commonly found in *Enterobacteriacae* family followed by non fermenters like *Pseudomonas aeruginosa* and *Acinetobacter baumanii*[5] Prevalence of ESBL, AmpC beta lactamase and Carbapenemase producers amongst total Gram negative organisms were (70.65%) ,(17.39%) , and (7.60%)respectively[6].

CONCLUSION

The bacterial disease burden in India is among the highest in the world, consequently antibiotics will play a critical role in limiting morbidity and mortality. Oral care is also equally important in preventing infection going down the tract causing pneumonia, special flexible Orocare Brush designed to give better cleaning of the oral cavity with use of oral antiseptics is also a useful contibutory factor over and above other factors like use of proper antibiotics. Management of common and lethal bacterial infections has been critically compromised by the appearance and rapid spread of antibiotics resistant bacteria. The resistant is affecting patients and therapeutic outcomes with concomitant economical consequencies.

The present study emphasizes the high prevalence of multidrug resistant organisms producing β-lactamase+ AmpC betalactamase enzymes belongs to Enterobacteriacae family. To combat these problems, epidemiological studies should be undertaken in hospital settings to monitor the source of infection early detection of these β -lactamases in a routine laboratory could help to avoid treatment failure. Further more strict antibiotic policies and measures to limit the indiscriminative use of Cephalosporins and Carbapenems in the hospitals should be under taken to minimize the emergence of this β-lactamase producing organisms.[8] Use of Specialized Felxible Oro care Brush either with betadine or chlorhexidine can be use for proper cleaning of oral cavity to prevent the spreading down of infection.

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ORIGINAL ARTICLE

Combined Use of Intrathecal Fentanyl and Neostigmine as an Adjunct to Bupivacaine for Post Operative Analgesia after Abdominal Hysterectomy.

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KEY WORDS : Fentanyl, Neostigmine, Abdominal hysterectomy, Intrathecal, Bupivacaine.

ABSTRACT

Aim : To evaluate the analgesic efficacy of combined use of intrathecal fentanyl and neostigmine as an adjunct to Bupivacaine for postoperative pain relief.

Material & Method : 60 patients posted for abdominal hysterectomy under ASA I/II were randomly allocated in 2 groups. All the patients received 15 mg hyperbaric bupivacaine 0.5% plus 1 ml of test drug. **Group C** (Control group) will receive normal saline as 1 ml solution. **Group FN** (Fentanyl- Neostigmine group) will receive combination of fentanyl 20µg and Neostigmine 20 µg as 1 ml solution. Pain and nausea were evaluated using a 10-cm visual analog scale (VAS) where "0" is no pain and "10" is the worst pain.

Observation : We observed significant delayed post operative analgesia in group FN as compare to group C (FN- 476.7 ± 19.4 min vs C- 130.9 ± 3.61, P<0.001). The analgesic requirement in first 24 hours was significantly low in group FN as well. Patients were observed for side effects such as nausea, vomiting, hypotension, bradycardia, pruritus etc.

Conclusion : Combined use of intrathecal fentanyl and neostigmine as an adjunct to Bupivacaine at very low dose is quite effective in terms of prolong duration of rescue analgesia with lower rates of side effects.

INTRODUCTION

Pain is one of the main postoperative adverse outcomes especially after abdominal hysterectomy. Single analgesics, either opioid or nonsteroidal anti-inflammatory drugs (NSAIDs), are not able to provide effective pain relief without side effects such as nausea, vomiting, sedation, or bleeding.[1]

Intrathecal (IT) neostigmine and fentanyl have been used as an adjunct to spinal anaesthesia (SA) for prevention of acute perioperative pain. Previously it has been shown that spinal neostigmine and spinal fentanyl were both efficacious in terms of prolong duration of rescue analgesia and better pain relief. But studies have shown that they both synergize their action if used together.[1] Issue related to the side effects caused by neuraxial use of neostigmine was still important, considering this fact we have used lower dose of spinal fentanyl and neostigmine combination as an adjunct to Bupivacaine to minimize side effects along with better post operative analgesia.

We planned to evaluate efficacy and tolerability of combined use of intrathecal neostigmine and fentanyl as an adjunct to bupivacaine for post operative analgesia in patients posted for abdominal hysterectomy under Spinal anaesthesia.

MATERIAL AND METHODS

After obtaining the institutional ethics committee clearance and written informed consent, 60 adult patients of American Society of Anaesthesiologists (ASA) 1 or 2, undergoing abdominal hysterectomy under regional anaesthesia, were included in the study. Patients were randomly allocated into three groups of 30 patients each. The concept of visual analog scale (VAS), which consisted of a 10-cm line with 0 equaling "no pain at all" and 10 equaling "the worst possible pain," was introduced before surgery.

Intravenous (IV) preloading was done with Ringer's lactate as a bolus of 6–8 ml/kg given over 15 min before SA. Patients were premedicated with 0.004 mg/kg Inj. Glycopyrrolate and Inj. Ondensetron 0.1 mg/kg before induction. A 23-G spinal needle was introduced through the L3–L4 interspace with patient in the sitting position. A total volume of 4 ml was injected IT, at a rate of 0.25 ml/sec. The IT drug injected was 15 mg hyperbaric bupivacaine (3 ml) plus the test drug (1 ml).

Group C (Control group) will receive normal saline as 1 ml solution.

Group FN (Fentanyl-Neostigmine group) will receive

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combination of fentanyl 20µg and Neostigmine 20 µg as 1 ml solution. (Fentanyl 1ml contain 50 mcg from which 20 mcg was taken and diluted upto 0.5 ml NS and Neostigmine 1 ml contain 500 mcg which was taken in insulin syringe from which 0.4 kappa was taken which was diluted upto 0.5 ml and together this was combined as 1 ml of study drug solution).

Patients were placed in the supine position immediately after spinal injection. One anesthesiologist prepared the drug and administered the IT drug, while another anesthesiologist, who was blinded to the drug randomization, monitored the intraoperative and postoperative period.

Intraoperative sensory and Motor blockade of lower extremities was for the first 20 min after injection of the IT drug. Blood pressure, heart rate and SpO2 were monitored continuously throughout the surgery. A decrease in mean arterial pressure of greater than 25% below the baseline preanesthetic value or less than 60 mmHg was treated by incremental doses of 6 mg Inj. mephenteramine IV. A decrease in heart rate of more than 15% below the baseline or 50 beats per min was treated by Inj. atropine 0.6 mg IV.

Duration of rescue analgesia was the time until VAS pain scores were ≥ 4 cm or when the patient's first requested for supplemental analgesia, whichever appeared first. Subsequently, Inj. Diclofenac sodium AQ was administered 1.5 mg/kg as the rescue analgesic. The total number of rescue analgesics administered in 24 h was noted. Postoperative assessment included pain scores and postoperative nausea and vomiting (PONV) scores (5-point scale) recorded for 24 hour postoperatively. One or more emetic episodes were treated using ondansetron 4 mg IV. For patients experiencing more than one episode of nausea, the scores were averaged.

The data were analyzed statistically using unpaired t-test by using Graphpad Prism ver. 9.0 in which P <0.05 was considered significant. Data was presented in terms of mean ± SD.

RESULTS

A total of 60 patients were recruited for the study. Both groups showed no significant differences regarding age, weight, height, gender, and duration of surgery (P > 0.05) (Table 1).

Table 1 : Demographic Profile

	Group FN	Group C	P value	
Age (years)	42.87 ± 1.31	41.48 ± 1.87	0.46	NS
Weight (kg)	51.36 ± 6.34	50.85 ± 8.96	0.58	NS
Height (cm)	159.2 ± 8.42	163.3 ± 9.23	0.32	NS
Gender (M/F)	0/30	0/30		
Duration of Surgery	132.6 ± 28	130.1 ± 27	0.68	NS

NS- Non Significant S – Significant

Table 2 : Characteristics of Spinal Block

	Group FN	Group C	P value	
Max. limit of Sensory block	T6 (T10-T6)	T7 (T10-T6)	0.06	NS
Time of peak sensory block (min)	11.9 ± 3.2	11.8 ± 3.9	0.57	NS
Time of complete motor block (min)	10.1 ± 3.2	10.4 ± 3.1	0.42	NS

NS- Non Significant S - Significant

The intraoperative hemodynamic characteristics were comparable and intraoperative mephentermine consumption was similar among the groups.

Table 3 : Analgesia Profile

	Group FN	Group C	P value	
Duration of 1st Rescue Analgesia	476.7 ± 19.4	130.9 ± 3.61	0.01	S
Total no. of rescue analgesia	3.9 ± 1.3	6.7 ± 1.1	0.01	S
VAS at 1st Rescue analgesia	4.2 ± 0.9	4.7 ± 0.8	0.23	NS

NS- Non Significant S - Significant

Figure 1 : Ponv 5-Point Scale

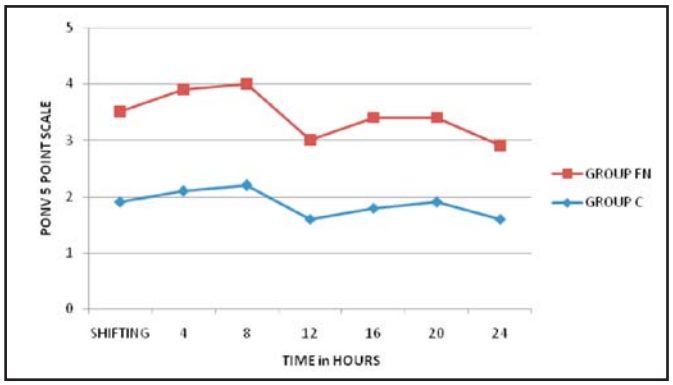

Table 4 : Side Effects Profile

SIDE EFFECTS/ COMPLICATIONS	GROUP FN	GROUP C
Nausea	7 (23.3%)	2 (6.67%)
Vomiting	4 (13.3 %)	0
Hypotension	1 (3.3%)	0
Bradycardia	1 (3.3%)	0
Pruritus	1 (3.3%)	0
Headache	0	0

Table 4 indicates side effects profile. Seven patients in the Group FN complained of Nausea and three of them had 1-2 episode of vomiting. All seven required antiemetic (Ondansetron) once and only one patient twice. However, no patient in the control group required any antiemetic postoperative while one patient from Group FN had mild pruritus over face. That doesn't require any medication. While no patients from control group had pruritus. No patient in any group had sedation score >2 at any time postoperatively.

DISCUSSION

Pain in the postoperative period is a critical factor that impedes recovery from surgery and anaesthesia.[1] Total abdominal hysterectomy (TAH) is usually performed through a Joel Cohen incision and patients experience considerable abdominal pain which require adequate post-operative analgesia.[2]

Our study results demonstrated that IT combination of Fentanyl and Neostigmine provided effective analgesia with prolong duration of rescue analgesia.

There is a potential synergism between fentanyl and neostigmine along with bupivacaine as reported in an animal study by Wang et al.[3] Intrathecal opioids bind to a family of G-protein-linked pre- and postsynaptic opioid receptors in Laminae I and II of the dorsal horn. Receptor activation leads to G-protein-mediated potassium channel opening (mu and delta) and calcium channel closure (kappa), with an overall reduction in intracellular calcium. This reduces the release of excitatory transmitters (glutamate and substance P) from presynaptic C fibres, but not A fibre terminals with consequent reduction in nociceptive transmission.[4] There are significantly greater number of opioid receptors located presynaptically compared with postsynaptically. Binding of opioids to postsynaptic receptor sites in the dorsal horn result in potassium channel opening and indirect activation of descending pathways from the brainstem.[5]

Lipid soluble opioids also resemble local anaesthetics in terms of their pKa, molecular weight, and partition coefficients that may explain some of the analgesic effects of CSF opioids. Using a pig model,[6] They have demonstrated that fentanyl rapidly partitions into receptor and non-receptor binding sites (epidural fat, myelin, and the white matter). This has been ascribed to its high octanol:water partition coefficient (860), resulting in a high volume of distribution in spinal cord. After fentanyl administration, CSF concentration decreases rapidly; epidural space concentration increases; plasma concentrations increase rapidly with resultant systemic effects; and there is limited cephalad spread with segmental analgesia. lipophilic opioids with higher octanol:water coefficient and lower pKa values are retained for longer periods in the spinal cord resulting in longer duration of action.

The inhibition of spinal cholinesterase by neostigmine results in an increase of endogenous acetylcholine, which is most likely released from intrinsic cholinergic neurons within the dorsal horn of the spinal cord. These cholinergic neurons terminate in the vicinity of primary afferent express muscarinic receptors. The endogenous acetylcholine produces analgesic effect through muscarinic presynaptic inhibition of glutamatergic afferents, similar to how it has been described in the neostriatum. Muscarinic receptor antagonists have been shown to reverse the analgesic effects of IT neostigmine. A tonic cholinergic activity is an important prerequisite for the effectiveness of neostigmine. The enhanced analgesic efficacy of IT neostigmine results from greater release of spinal acetylcholine from the more intense and prolonged discomfort of postoperative pain, and consequent action at muscarinic M1 and M3 and presynaptic nicotinic receptors present in the cholinergic interneurons at the lamina III and V of the dorsal horn.An action at nicotinic receptors at the dorsal horn ganglion and at the spinal meninges has also been suggested[7].

Lauretti et al.[8] had also combined both these drugs at dose of 25µg each and 10µg each. They have mentioned that 25µg provided prolonged analgesia with higher rate of side effects while 10µg provided not much effective

analgesia. Because of this, we have used 20µg in our study which has provided prolonged duration of analgesia with minimal number of side effects.

Pain score immediately after and in 1st 24 hours and duration of rescue analgesic in group FN were significantly better in comparison with control group that is mainly because of combine use of both the drugs synergise their effects which led to prolong duration of rescue analgesia[1].

Lauretti et al.[8] has also used IT fentanyl and neostigmine as an individual drug.They have demonstrated that duration of rescue analgesia for individual drug was lower as compare to combination of both these drugs. It indicates synergism of combined use of both drugs.

Lauretti et al.[1,8,9],showed a dose-independent reduction of postoperative analgesia requirement, but a dose-dependent increase in the incidence of PONV following addition of various doses of IT neostigmine and fentanyl (ranging from 10 to 25 mcg) to 15 mg of hyperbaric bupivacaine 0.5%. So for that reason, we have used low dose (20mcg) IT neostigmine with fentanyl (20mcg). In our study, PONV 5 point scale was on higher in group FN as compare to group C which was found similar in previous studies as well. We have obsereved 7 cases of nausea in group FN out of which 3 require additional dosage of Ondensatron post-operative as well as compare to just 2 cases in control group[3].

Almeida et al[10], demonstrated a trend toward more nausea with higher doses in patients undergoing major gynecological surgeries. These observations are further supported by the present study[12].

In our study, the time to reach maximum level of sensory block and the peak level attained was not influenced by the use of IT neostigmine. Similar effect was demonstrated by Lauretti et al[8],in patients undergoing vaginal hysterectomy. This is possibly due to a difference in the onset of action of IT neostigmine, IT fentanyl and IT bupivacaine.The time to development of complete motor block was also not altered.

Pruritus was a common complication in the patients receiving intrathecal fentanyl, although in most cases, it was so mild as not required treatment[13]. Respiratory depression is a known complication of intrathecal opioids[14], but we had not found any clinical manifestations of respiratory depression. This is not surprising, because it has been shown that even a much larger dose of 25 µg intrathecal fentanyl in elderly patients did not lead to respiratory depression[15].

CONCLUSION

We conclude that combined use of intrathecal fentanyl and neostigmine as an adjunct to Bupivacaine at very low dose is quite effective in terms of prolong duration of rescue analgesia with lower rates of side effects.

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ORIGINAL ARTICLE

Role of HRCT in Predicting Disease Activity of Pulmonary Tuberculosis

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KEY WORDS : TUBERCULOSIS , HRCT

ABSTRACT

Patients with pulmonary tuberculosis may or may not have their sputum positive for the acid fast bacilli. However underlying pathology may involve the lung parenchyma. High resolution computerised tomography scan helps in assessing the pattern of involvement of lung parenchyma and predicting disease activity, irrespective of the microbiology results. According to my study tree in bud appearance, scattered nodules and consolidation are features of active disease and traction brochiectasis, collapse etc are features of inactive disease.

INTRODUCTION

In developing countries, pulmonary tuberculosis is still a common disease particularly among the socioeconomically disadvantaged, elderly and chronically debilitated individuals.

The chest radiograph has been a major tool in the diagnosis of tuberculosis and is used in conjunction with tuberculin skin test as a means of detecting the disease.

Although chest radiographs usually provide adequate information for the diagnosis of active pulmonary tuberculosis, early disease can be missed.

High resolution computed tomography is found to be sensitive in detection of subtle or occult parenchymal disease and also to determine the extent of the disease.

Analysis of CT images on the basis of pathologic correlation is helpful in understanding the morphology of pulmonary tuberculosis.[1]

Typical CT findings of active postprimary pulmonary tuberculosis include centrilobular nodules and branching linear structures (tree-in-bud appearance), lobular consolidation, cavitation, and bronchial wall thickening. The CT findings of inactive pulmonary tuberculosis include calcified nodules or consolidation, irregular linear opacity, parenchymal bands, and pericicatricial emphysema.[2]

AIMS AND OBJECTIVE

To determine the pattern of HRCT findings in active & inactive Pulmonary Tuberculosis.

To determine the value of HRCT in predicting disease activity in Pulmonary Tuberculosis.

MATERIALS AND METHODS

A retrospective correlational study was conducted over a period of six months on 100 patients from June 2013-November 2013, referred to our department with suspected pulmonary tuberculosis.

The patients were subjected to HRCT on Siemens Sensation (64 slice), plain scans obtained and the patterns of disease activity and inactivity were analysed.

These features were then correlated with sputum AFB examinations / bronchoalveolar lavage.

Statistical analysis was done by graphpad software. P values were calculated wherever required using fisher's and chi square test. P value less than 0.05 was considered significant.

Scanner Used	Siemens Somatom sensation 64slice
KV / mAs	120Kv/200mAs
Detector Collimation	1 mm
Slice Thickness	1 mm

Inclusion & Exclusion criteria

Inclusion Criteria :

- Patients suspected with pulmonary tuberculosis and newly diagnosed cases on treatment, with or without positive chest radiograph findings, and 3 sputum AFB examinations/ bronchoalveolar lavage and positive for tuberculosis.
- Patients of any gender and age.

Exclusion Criteria:

- Patients with known malignancy

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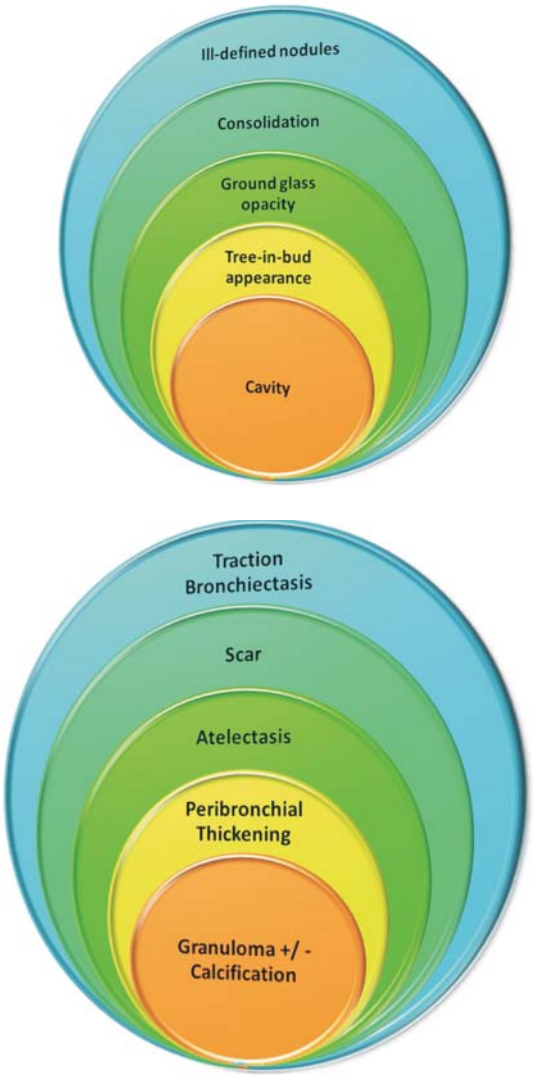
- Patients who are immuno compromised
- Pleural pathology

HRCT analysis : Descriptive terms



RESULTS

- 38 females and 62 males aged 1 to 87 years, with an average age of 44.15±22.6 were in the study.
- The clinical signs and symptoms of active pulmonary tuberculosis comprised of 84% cough, 53% fever, 33% hemoptysis, 63% sputum, 36% night sweats, and 55% weight loss.
- According to microbiology results, 44 patients (44%) had their sputum positive for TB, while 56 patients(56%) had their sputum negative.
- In patients with active disease, 71% had ill defined nodules, 67% had consolidation, 75% had tree in bud appearance and 41.6% had cavitations and 50% had peribronchial thickening.
- In patients with inactive disease 63.3% had traction bronchiectasis, 53.3% had atelectasis, 20% had calcified granulomas and 30% had peribronchial thickening.
- In right lung 99% lesions involved upper lobe, 89% involved middle lobe and 85% involved lower lobe. In upper lobe 25 to 50% of the lung parenchyma was commonly involved.
- In left lung 98% lesions involved the upper lobe and 86% involved the lower lobe. In the upper lobe 25 to 50% of the lung parenchyma was commonly involved.
- Though certain lesions are present predominantly in the active and inactive disease, their presence cannot always be correlated with sputum positivity / negativity. This may be due to co existence of lesions in both active and inactive disease or inadequate sputum collection.
- Mediastinal lymphadenopathy does not have a significant correlation with disease activity. However most of the tuberculous lymphadenopathy is associated with central caseation necrosis.

TABLE-1
Distribution of the various lesions in the total 100 patients

Findings	Sputum positive(n=44)	Sputum negative (n=56)
Ill-defined nodules	31 (71%)	4 (7%)
Consolidation	29 (67%)	6 (10%)
Tree-in-bud	33 (75%)	2 (3.3%)
Cavity	18 (41.6%)	4 (6.6%)
Ground glass opacity	7 (16.6%)	2 (3.3%)
Traction bronchiectasis	7 (16.6%)	35 (63.3%)
Atelectasis	4 (8.3%)	29 (53.3%)
Calcified granuloma	0 (0%)	11 (20%)
Peribronchial thickening	22 (50%)	17 (30%)

Ill defined nodules, consolidation and tree in bud appearance is seen more in sputum positive patients and seen relatively less in sputum negative patients. Traction bronchiectasis, atelectasis and calcified granulomas are seen more often in the sputum negative patients than the sputum positive patients.

TABLE--2
Lobar distribution of the lesions in right lung

Right lung (n=100)	0%	<25%	25-50%	>50%
Upper lobe	1(1%)	17(17%)	60(60%)	22(32%)
Middle lobe	11(11%)	33(33%)	42(42%)	14(14%)
Lower lobe	15(15%)	41(41%)	20(20%)	24(24%)

99%of the lesions involve the upper lobe, 89% involve middle lobe and 85% involve the lower lobe. in the upper lobe, 25-50% of the lung parenchyma is involved more commonly.

TABLE-3
Lobar distribution of the lesions in left lung

Left lung	0%	<25%	25-50%	>50%
Upper lobe	2(2%)	15(15%)	67(67%)	16(16%)
Lower lobe	24(24%)	20(20%)	41(41%)	15(15%)

98% of the lesions involve the upper lobe and 86% of the lesions involve the lower lobe. in the upper lobe 25-50% of lung parenchyma is involved in most of the cases.

TABLE-4
Correlation between the sputum findings and radiological findings.

	HRCT +ve for TB	HRCT –ve for TB
Sputum positive for TB(n=44)	43	1
Sputum negative for TB(n=56)	54	2

By fisher's test, p value is 1. Hence the correlation is insignificant. It is not necessary that sputum positive patients only show positive HRCT findings.

TABLE-5
Correlation between sputum findings and lymph nodal size

Lymph node size (small diameter)	Less than or equal to 10mm	More than 10mm
Sputum positive for TB (n-44)	16	28
Sputum negative for TB (n=56)	26	30

By fisher's test, p value is 0.4 i.e., the correlation is insignificant. The lymph node size criteria cannot be used for determining the disease activity.

TABLE-6
Correlation between lymph nodal size and central caseation necrosis.

Lymph node(> 10mm)	Caseation present	Caseation absent
Sputum positive for TB (n-28)	20	8
Sputum negative for TB (n=30)	26	4

By fisher's test, p value is 0.2 i.e., the correlation is insignificant. The central caseation cannot be correlated with the sputum negativity or positivity.

FIGURE-1

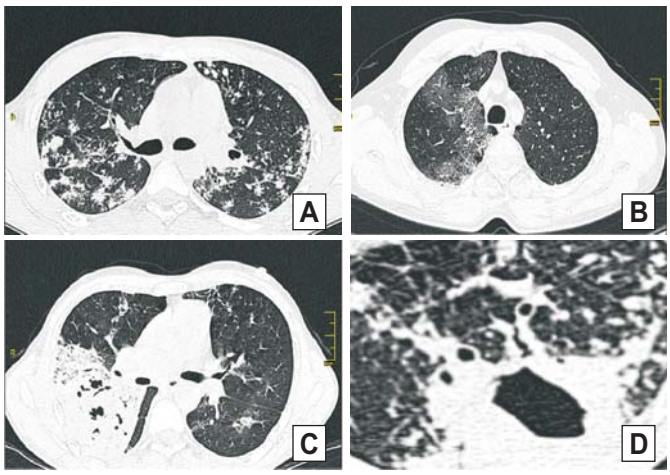


FIGURE-1

Figure 1a shows multiple linear branching opacities with surrounding nodlar infiltration, suggestina a tree-in-bud appearance. Tree-in-bud appearance signifies endobronchial spread, an active form of the disease.figure 1b shows ground glass haze involving apical and anterior segements of right upper lobe. Figure 1c shows patch of lobar consolidation with an air bronchogram and 1d shows central cavity with surrounding consolidation.

FIGURE-2

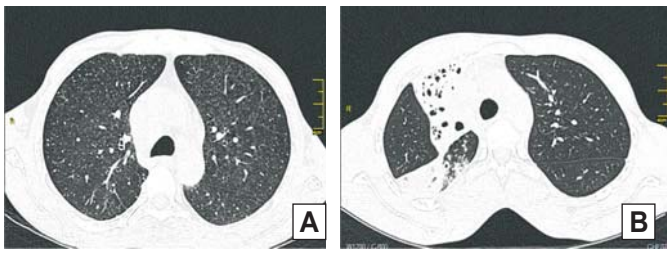


FIGURE-2

Figure 2a shows multiple tiny nodules depicting military pattern, scattered through out bilateral lung parenchyma. Military pattern indicates haematogenous spread of tuberculosis. Figure 2b shows atelectasis of the apical segment of the right upper lobe.

DISCUSSION

38 females and 62 males aged 1 to 87 years, with an average age of 44.15±22.6 were found in the study.

The clinical signs and symptoms of active pulmonary tuberculosis comprised of 84% cough, 53% fever, 33% hemoptysis, 63% sputum, 36% night sweats, and 55% weight loss.

According to microbiology results, 44 patients (44%) had their sputum positive for TB, while 56 patients(56%) had their sputum negative.

Primary TB occurs most commonly in children but is being seen with increasing frequency in adults .[3]

In this study post-primary tuberculosis is seen in adults.

In a Japanese study, Nakanishi et al reported that even in cases of sputum negative smears, high-resolution computed tomography (HRCT) scan can predict the risk of pulmonary TB and it can identify the patients with high probability of pulmonary TB. 116 patients with negative sputum smears for acid-fast bacilli, but with a suspicion of pulmonary tuberculosis were studied. I was found that nodules, tree-in-bud appearance and consolidation were significantly associated with an increased risk of pulmonary TB.[4]

In this study the commonest findings in active disease are ill defined nodules, tree in bud pattern, consolidation, cavitation and ground glass opacities.

In a study by Yeon et al cavity was a consistant finding of reactivation TB.[5-8] Tree-in-bud signs also correlate with the activity of the disease .[9]

Im et al correlated HRCT findings in active tuberculosis with pathologic findings and found that 97 percent of patients of active tuberculosis had tree in bud appearance on HRCT to suggest bronchogenic spread of disease.[9-13]

In active disease, the airway lumen are irregularly narrowed with thick walls, whereas in chronic disease, the airway lumen are narrowed smoothly with thin walls. [14-16]

Thus our study again proves that, centrilobular nodules and a tree-in-bud appearance in HRCT is more sensitive indicator of early endobronchial spread in active disease. Thus CT scan may also prompt diagnosis, even when microbiology reports are pending.

Also, our results showed that although infiltration was the dominant HRCT manifestation, "centrilobular nodule" and "tree- in-bud" appearances were the main findings in the majority of active pulmonary tuberculosis cases.

In the study we found that 97% of the patients with active disease had positive findings of tuberculosis on HRCT and also 96% of the patients with sputum negativity had positive findings of tuberculosis on HRCT. In this study commonest findings in inactive disease are traction bronchiectasis, atelectasis, calcified granulomas and peribronchial thickening.

This finding suggests that HRCT is a useful tool to estimate the underlying disease in sputum negative patients and to determine the prognosis.

Airspace consolidation, related to parenchymal granulomatous inflammation does not show any predilection for a particular lung zone.[17] . In this study the parenchymal disease predominantly involves the upper lobe in both right and left lungs with involvement of 25-50% of the lung parenchyma in most of the cases.

The lymphadenopathy is usually unilateral and seen commonly at hilum or paratracheal region. CT shows enlarged nodes with central low density areas representing caseous necrosis [18,19].

In this study mediastinal lymphadenopathy was found to be an insignificant factor in predicting disease activity. However caseation is found in majority of lymph nodes greater than 10mm.

CT also is useful in the evaluation of long-standing destructive pulmonary lesions and tracheobronchial tuberculosis[20].

This study concludes that HRCT is a powerful and reliable investigation in the diagnosis of tuberculosis , when other means of diagnosis (e.g., culture, BAL) fail to settle the matter, are not available or time consuming.

CONCLUSION

- Ill-defined nodules, consolidation, tree-in-bud appearance and cavitation are best indicators of active disease.
- Traction bronchiectasis, atelectasis, calcified granulomas and peribronchial thickening are indicators of inactive disease.
- HRCT is a useful tool in the diagnosis and management as it can differentiate active from inactive disease with greater sensitivity.

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ORIGINAL ARTICLE

Role of Antibiotics in Clean Surgeries : Prophylaxis V/S. Conventional

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KEY WORDS : Surgical, Infection, Peri Op. antibiotics, Prophylaxis

INTRODUCTION

Antimicrobial agents were once hailed as magic bullets that promised to eradicate infection. Unfortunately this promise has not been fulfilled. The use of antimicrobial agents to prevent surgical infection has become a subject of controversy and disappointment in clinical practice. Despite advances in surgical science, infection still remains responsible for most of the post-operative morbidity and mortality. The basic surgical skills of post-operative precaution, pre-operative preparation, excellent surgical technique, fastidious wound care and post-operative management are corner-stones of infection prophylaxis. Antibiotics for prolonged period may be harmful to both individual and hospital colony whether they are given as prophylaxis or for therapy. Routine use of antibiotics for a prolonged period after clean surgery is not justifiable. With the fear of developing wound infection after surgery we use to administer antibiotics for a period of 7-10days even in clean and clean-contaminated cases. This is not only expensive but also lead to hospital acquired infection and resistance to not only that particular antibiotic but also other antibiotics of the same group. By clean surgery we mean that an uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital or infected urinary tract is not entered. Wounds are closed primarily and, if necessary, drained with closed drainage. Antibiotics which provide coverage throughout the peri-operative period will reduce the infection rate of wound and also other infectious complications of body.

MATERIAL & METHODS

The study is a randomized prospective and comparative evaluation of prophylactic administration of three doses of broad spectrum cephalosporin group of antibiotic Ceftriaxone with 5 days conventional course of post-operative antibiotics in clean surgeries.

Two groups were established on the basis of numerical status. Patients with odd numbers were taken for three dose trials whereas those with even numbers were taken for five days course of antibiotics. The study was not blind.

The study admitted 50 patients 25 in each group, men and women 18 years and more undergoing clean operation from July 2012 to August 2013.

Initial dose of antibiotic, 1gm Ceftriaxone was administered one hour before surgery by intravenous route. Two more doses of Ceftriaxone were given second at immediately after shifting the patient to ward and third 12 hours after the second dose. In patients with 5days course the first dose was given immediately after operation and continued for five days two days intravenously and three days oral (Cefixime).

EXCLUSION CRITERIA

Concurrent or previous treatment with antibiotic was not allowed. Following group of patients were not eligible for enrolment in the study- Patients with hypersensitivity or history of adverse drug reaction to cephalosporin group, patients less than 18 years, patients with significant degree of renal impairment, severe hepatic disease, on steroid therapy, obese, suffering from diabetes mellitus, or tuberculosis.

RESULT

Total 50 patients were included in this study and 25 were given 3 doses of antibiotics preoperatively (Group A) and 25 were given 5 days conventional antibiotics (Group B).

TABLE 1 : AGE & SEX DISTRIBUTION

SEX		**GROUP A**	**GROUP B**
SEX	MALE	15	15
	FEMALE	10	10
TOTAL		25	25
MEAN AGE	RANGE		
	18-30	8	5
	30-50	9	12
	MORE THAN 50	8	8
TOTAL		25	25

Table 1 shows the age and sex distribution in the study which was not significant.

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TABLE 2 : INFECTION GRADING

GRADE	GROUP A		GROUP B	
OF INF.	7TH DAY	10TH DAY	7TH DAY	10TH DAY
GRADE 1	1	0	1	0
GRADE 2	0	0	0	0
GRADE 3	0	1	1	1
GRADE 4	0	0	0	0

1. One patient in Group A developed grade I infection on 7th post-operative day.
2. One patient in Group B developed grade I infection on 7th post-operative day.
3. One patient in Group B developed grade III infection on 7th post-operative day and another one on 10th post-operative day.
4. One patient in Group A developed grade III infection on 10th post-operative day.
5. No patient in either group developed grade II or grade IV infection.
6. No patient developed non wound infections.
7. The infection rate in Group A is 8% and in Group B is 12%.

TABLE 3 : STATASTICAL ANALYSIS OF THE DATA

INFECTION (Y/N)	GROUP A	GROUP B	TOTAL
YES	2(4%)	3(6%)	5(10%)
NO	23(46%)	22(44%)	45(90%)
TOTAL	25(50%)	25(50%)	50(100%)

The two sided P value is 1.000 which is statistically insignificant.

As the number of subjects in each group are not enough to make the results to match the studies but however the results are somewhat comparable.

TABLE 4 : TYPE OF SURGERIES IN EACH GROUP

SR. NO.	CASES	GROUP A	GROUP B	TOTAL
1	INGUINAL HERNIA	7	8	15
2	UMBILICAL HERNIA	2	5	7
3	PERI-UMBILICAL HERNIA	1	1	2
4	EPIGASTRIC HERNIA	1	1	2
5	FIBROMA	0	1	1
6	FIBROADENOMA	3	2	5
7	HEMANGIOMA	1	1	2
8	LIPOMA	3	1	4
9	VARICOCELE	1	0	1
10	VARICOSE VEINS	1	0	1
11	HYDROCELE	2	3	5
12	ORCHIDECTOMY	1	0	1
13	SPINDLE CELL TUMOR	0	1	1
14	HEMITHYROIDECTOMY	1	0	1
15	GYNECOMASTIA1	1	0	1
16	INCISIONAL HERNIA	0	1	1
TOTAL		25	25	50

As no fixed criteria were established regarding discharge of the patient, this study does not compare the economical advantages of hospital stay with other studies.

DISCUSSION

An effective prophylactic regimen should be directed against the most likely organisms. Infections can be prevented when effective concentrations of the drug are present in the blood and the tissue during and shortly after the procedure. Therefore, antibiotic prophylaxis should begin just before the operation. Beginning earlier was found to be unnecessary and potentially dangerous, while beginning later was found to be less effective[1]. A single dose prophylaxis before surgery was found to be sufficient. If surgery is delayed or prolonged, often a second dose is advisable if antimicrobial agent with short life is used. Post-operative administration is unnecessary and harmful.

Pre-operative use of antibiotics to prevent wound infection was demonstrated by Bernard and Cole (1964)[2].

A study conducted by Classenet al[1]. has shown that patients who received pre-operative antibiotics early developed 3.8% wound infections. Patients who received antibiotics perioperatively developed 1.45% infections compared to those who received antibiotic postoperatively and developed 3.3% wound infections[1]. To find out the economical savings achieved with the right prophylaxis to prevent surgical wound infections, a study was done by Fernandes[3].Our study also showed an economical advantage in using only 3 doses of peri-operative antibiotic prophylaxis.The American guidelines[4]for surgical prophylaxis, worked out recently by the CDC, have not modified their general structure and have strongly influenced the protocols and the prescriptive behavior of other countries.Incidence of wound infection following clean surgery is 1.8% as claimed by Curse and Foord[5]. As most of the wound infections are detected within three days after surgery, this indicates that these infections are acquired during operative procedure. The contaminating bacteria could have been present either in the skin or were inoculated during surgery[6,7]. In our study standard skin preparation was done for all patients, which decreased the exogenous bacterial load; however, the organisms situated deep within the skin pores cannot eliminated completely.

Various authors have studied the efficacy of single dose antibiotics in preventing wound sepsis/infections.

SR. NO.	WORKERS	YEAR	% OF INFECTION
1	SANCHEZ26	1958	5.6%
2	JOHNSTONE27	1962	8.7%
3	SNIDER28	1968	2.3%

All of the above studies support the results of the present study that a 1-day peri-operative antibiotic prophylaxis is almost as effective as multiple-dose antibiotics. Hence, a single-day prophylaxis is recommended to reduce the financial burdens, the emergence of resistant strains and to avoid the side effects of the drugs.

CONCLUSION

Three dose antibiotics are sufficient in preventing wound infection. Prolonged administration of antibiotics is unnecessary and costlier. Wound infection is equal in both sex and not associated with sex predominance. Prolonged use of antibiotics is associated with emergence of resistant strains and super-infections, which can be prevented by cost-effective short term antibiotic prophylaxis.

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ORIGINAL ARTICLE

Coronal plane "Hoffa" fractures of the distal femoral condyle treated using an anterior approach

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KEY WORDS : Hoffa fracture – anterior approach - fixation

ABSTRACT

Introduction : Coronal plane "Hoffa" fractures of the distal femoral condyles are a rare entity. Lateral fractures are three times more common than medial fracture. They are commonly associated with supracondylar fractures of the distal femur however as an isolated injury they are rare.

Material and methods : At our institute during a two year period 07 cases of Hoffa fracture were treated using an anterior midline approach. The parapatellar arthrotomy was carried out according to the side of the fracture

Results : All fractures united within 4 months. There were no instances of infection or nonunion.

The mean range of motion was -3 Extension to 135 flexion. The average Tegner Lysholm knee score was 88. All patients achieved satisfactory joint function and regained their walking ability with good clinical results.

Conclusions : Direct reduction and stable fixation of Hoffa fractures leads to good clinical and radiological outcomes of these rare injuries. The direct midline anterior approach allows excellent visualization and enough space for fixation of these fractures. The midline scar can be easily utilized for future total knee replacement if required, without worrying about soft tissue problems.

INTRODUCTION

Coronal plane Hoffa fractures of the femoral condyle are rare injuries first reported by Hoffa [1] in 1904. Patient Series in published literature with more than 10 patients are very few. The lateral side is more commonly injured than the medial side.[2,3] The mechanism of injury has been reported to be a direct antero-posterior force to the flexed and abducted knee for lateral condylar fractures and direct impact to the medial side of the knee in flexion for a medial condylar fracture. The objective in treatment of these fractures is to achieve anatomical reduction of the articular surface and stable fixation.[2,3,4] Generally according to the location of the injury the incisions have been described. For lateral injuries a direct lateral approach and for medial injuries a medial approach. Starr et al described a extensive swashbuckler approach for addressing these fractures.[5] There is paucity of data recommending which surgical approach and what implants and in which configuration are the most appropriate. We have utilized a midline anterior approach for all Hoffa fractures with multidirectional screw fixation. The parapatellar arthrotomy depends on the side of injury. The purpose of this study was to evaluate the clinical outcome of our surgical technique in the treatment of Hoffa fractures.

MATERIAL AND METHODS

Seven adult patients with Hoffa fractures were treated using an anterior midline approach during a two year period from 2010 to 2012. Five patients had lateral condyle fractures and two had medial condyle fractures. All patients were evaluated with standard radiographic AP and lateral views for the knee and if more comminution was present then additional computed tomography scans.

Surgical Technique

The patient is positioned in supine position. Tourniquet is used during the surgery. Appropriate broad spectrum antibiotics are administered before the surgery and continued fro a period of 48 hrs postoperatively. A midline incision is made, and a medial or lateral parapatellar arthrotomy is performed according to the location of the fractured condyle. The fracture surfaces are cleaned and the displaced fragments anatomically reduced and fixed with bone clamps. We have found that the reduction is easier with the knee in 90 degree flexion and once the reduction is done we completely flex the knee which helps to maintain the reduction. Fixation is carried out first with cannulated 6.5 mm or 4 mm screws placed perpendicular to the fracture surfaces. Screws are inserted from the

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nonarticular anterior surface of the distal femur. If screws are inserted from the articular surface then countersinking of the screw head is carried out. Additional screws are placed in different directions to augment the fixation once compression is achieved. Routine closure in layers over negative drains kept for 48 hours was done.

Postoperatively a commercially available AKBK knee brace was applied for immobilization. Initially only range of movement exercises were carried out. Weight bearing on the injured limb was not allowed for a period of 6-8 weeks thereafter full weight bearing with support with gradual progression to unassisted walking was done.

Evaluation

All patients were evaluated at 1, 2, 4,6,12 months postoperatively. Radiographs of the knee in different standard views were taken to evaluate the union as well as postoperative displacement of the fragments. Clinically they were evaluated using the Tegner Lysholm knee score. The grading of the results are as follows >90 excellent, 84-90 good, 65-83 fair, < 65 poor.

RESULTS

Six patients were injured due to motor vehicle accidents while one was injured due to fall from height. One patient presented at one month following injury. Two patients had associated injuries in the other limb. At four months all fractures were healed clinically and radiographically. Average healing time was 13 weeks (range 10- 17 weeks). There were no cases of superficial or deep infections. The mean range of motion was -3 degrees (range -10 to 0) to 135 degrees (range 120 to 150). There were no implant removals. The Tegner Lyscholm knee score mean 88 (range 80 to 96) showed all patients had satisfactory results. All patients regained their walking ability with good range of movements.

The radiographs were analyzed for status of union, step off and gap at the fracture site. All patients had less than 2 mm step off which did not progress on the further check x-rays. No patient had loss of reduction requiring a revision surgery.

Table 1 Patients Demographics

Patients	Age/Sex	Femoral Condyle	Side	Surgical Approach	Tegner Lyscholm Knee score	ROM of knee
1	19/F	Lateral	Left	Direct midline LPPA	96	-10 Ext to 150 Flx
2	35/M	Lateral	Left	Direct midline LPPA	90	-5 Ext to 146 Flx
3	54/M	Lateral	Right	Direct midline LPPA	80	0 Ext to 120 Flx
4	32/F	Lateral	Left	Direct midline LPPA	88	-3 Ext to 134 Flx
5	42/M	Lateral	Right	Direct midline LPPA	87	0 Ext to 133 Flx
6	21/M	Medial	Right	Direct midline MPPA	83	0 Ext to 127 Flx
7	27/M	Medial	Right	Direct midline MPPA	91	-3 Ext to 135 Flx

ROM – Range of Movement, Ext- Extension, Flx- Flexion
MPPA Medial parapatellar arthrotomy, LPPA Lateral parapatellar arthrotomy

DISCUSSION

Intra-articular coronal plane “Hoffa” fractures of the distal femur are rare injuries and difficult to treat. Conservative management often leads to unsatisfactory results and non union. The long term consequences of malunion, nonunion and degenerative changes of a major joint require serious consideration. Open reduction and internal fixation is mandatory for good outcomes.

In published literature there has been no standardized surgical approach in treating these fractures except that by Holmes et al where they described an anterior midline approach with parapatellar arthrotomies according to the fracture location.[3,5, 6] The Hoffa fractures are frequently associated with comminution at the articular surface. With the direct lateral or medial approaches it is very difficult to address the comminution which is located in the central part of the distal femoral condyle. Moreover along

with proximal migration of the distal fragment there is an element of rotation of the femoral condyle which is difficult to correct using the direct approaches. The anterior midline approach provides excellent visualization of the fractures condyle which makes it easier to address the problems of articular comminution, rotation and also is useful in future as if a total knee replacement is required then there is a single midline scar which can be utilized to perform the arthroplasty with no skin problems due to multiple scars..

The standard method of fixing these fractures is using cannulated screws in compression mode.[7, 8] However as these are shear fractures the parallel screw configuration sometimes leads to fixation failure. The parallel screw configuration perpendicular to the fracture line provides compression however it is not able to resist shear in comminuted fractures. We had augmented our fixation using extra screws in multiple directions along with the compression screws to prevent displacement. This allows us to mobilize the knee in the early postoperative period without fear of loss of reduction.

Minimally invasive methods to treat these fractures have been described along with the help of arthroscopy[9] for visualization of the reduction however although the soft tissue injury was less, rigid compression and fixation of the fractures was not possible thus not able to prove their superiority over open techniques.

The drawbacks of our study were the limited number of patients. Also there was no direct comparison with other modalities of treatment. As these fractures are a rarity a multicenter trial comparing the outcomes using different approaches and different fixation techniques can increase the knowledge regarding this fracture.

Our series of operatively treated Hoffa fractures is different from other series in published literature. Here a standardized approach was employed with stable internal fixation using strategically placed screws. The anterior midline skin incision with parapatellar arthrotomy provides excellent visualization of the fracture and distal femoral articular surfaces for achieving a perfect anatomical reduction and rigid fixation. The excellent fracture stability provided by the multidirectional screws prevents loss of reduction. In our hands this method had led to reproducible good results without significant complications.

Table 2 Comparison with other series

Authors	Cases	Surgical approach	Complications	Outcome
Lewis et al [12]	7 lateral	MPPA or direct lateral	None	2 Good, 3 fair, nonoperative 1 fair 1 poor
Holmes et al [3]	3 medial 2 lateral	MPPA or LPPA	None	Mean Knee society score 173 Range (160-180)
Kumar et al [11]	3 lateral	Direct lateral	None	2 Excellent
Ocguder et al [10]	1 medial with PCL and tibial spine #	MPPA	Quadricepsplasty At 5 months	130 flexion
Present series	5 lateral 2 medial	Direct anterior With MPPA or LPPA	None	Mean Tegner Lyscholm Knee score 88 2 fair, 3 good 2 excellent

MPPA Medial Parapatellar arthrotomy **LPPA** Lateral Parapatellar arthrotomy **PCL** Posterior cruciate ligament

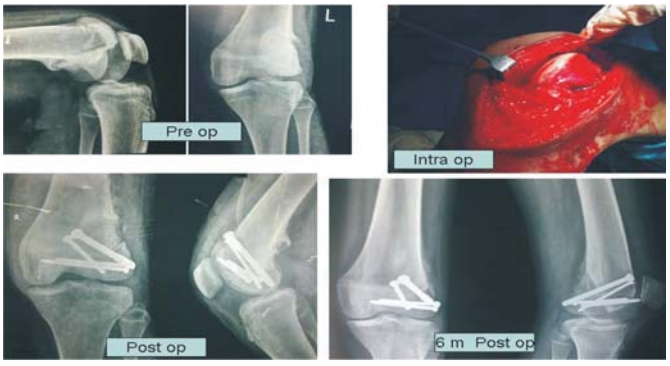

Figure 1

Case 1 : 19 yr old female with 1 month old lateral Hoffa fracture treated using anterior midline approach and lateral parapatellar arthrotomy

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ORIGINAL ARTICLE

A Comparative Study of Accuracy of Non-contact Infrared Thermometry and Axillary Digital thermometry in neonates

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KEY WORDS : Infrared thermometer, temperature, neonate.

ABSTRACT

Introduction : Thermoregulation and accurate temperature measurement remains a key element of new-born care. Axillary Digital Thermometry is the accepted method in neonates. **Objective :** To compare the accuracy of forehead infrared thermometry with axillary digital thermometry in neonates. **Design :** Randomised controlled trial, a prospective study **Setting :** NICU of a tertiary care teaching centre. **Method :** Body temperature of neonates admitted in NICU and under radiant warmer, was measured using both the methods. **Results :** Statistical analysis by Bland-Altman plot suggests that the two methods do not agree well. **Conclusion :** Infrared Thermometry is inaccurate and needs further improvement for regular use in NICU.

INTRODUCTION

Neonates are more thermo-labile, so accurate temperature recording remains an essential component of the neonatal care. Measurement of temperature in neonates can be obtained by rectal, axillary, and tympanicthermometry.[1]The gold standard is the mercury-in -glass thermometer.[2] But such a device must be held in place for a relatively long time in order to achieve accurate temperature measurement. Axillary digital thermometer for measurement of neonatal temperature being safe fairly accurate and convenient and can be taken by semiskilled personal.[3] has replaced the previously used mercury thermometer. The best method to measure temperature should reflect the accurate body temperature and should not be affected by external factors.

'Minimal contact' being the order of the day in NICU care, forehead non-contact infrared thermometry being a simple, fast, convenient method seems to be promising[3]. The forehead is a very good area to measure temperature as it is supplied by temporal artery which receives high blood flow from the carotid artery[3][7].

We compared the temperature of neonates kept under radiant warmer in NICU measured by infrared forehead thermometer and axillary digital thermometer.

OBJECTIVE

To compare the results of two methods of temperature measurements by non-contact infrared thermometer and digital thermometer in neonates and determine the agreement between two methods.

METHODS

A prospective comparative study was carried out in tertiary care teaching hospital NICU.Unlike previous studies all neonates admitted in NICU and kept under warmer, irrespective of their gestational age and causes of hospitalization were taken into the study. Axillary temperature was taken after wiping underarm with dry towel and digital thermometer probe tip was placed under the arm so the tip remained in contact with skin and temperature recording was recorded after the beep sound from the digital thermometer. Forehead temperature was taken with infrared thermometer at approximately 0.5-1 cm distance from the forehead at glabella.

Digital thermometer used in study was TB 100 ROSSMAX and infrared thermometer was THERMOFINDER FS 300. All temperatures were taken by trained nurses' staff and doctors.

Temperature recording were taken on neonates kept under open care servo-controlled radiant warmer with the skin probe set at a temperature of 36.5°C. A room temperature of 25°C-30°C was maintained. A single reading from each method was recorded every 6 hourly in 35 neonates for 7 days in 35 neonates in ages of 1-28 days. The temperature recording was done in °C. To study the statistically agreement between two methods, newer method of comparison Bland and Altman plot method was applied. A mean difference of 0.5°C was considered clinically acceptable.

RESULTS

All the collected data were statistically analysed. Temperature measurement by axillary digital

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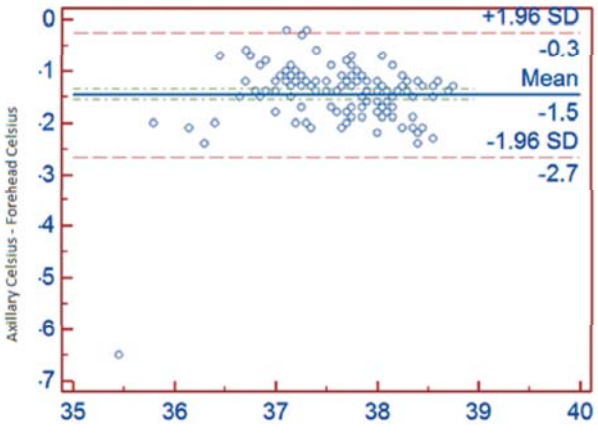
thermometer and noncontact infrared thermometer do not agree well (mean difference = -1.5, 95% limits of agreement: [-2.7,-0.3])by Bland and Altman[4] method. Infrared thermometer readings are not correlated with digital thermometer. So infrared thermometer used to replace digital thermometer for neonates temperature measurement gave unsatisfactory result.

DISCUSSION

After introduction of infrared thermometer various studies were done to compare the infrared thermometer result with other method for temperature measurement. Infrared thermometer was reported to be simple, non-invasive, and rapid. Chiappini , et al. reported a good agreement (mean difference= 0.07°C , 95% limits of agreement:[-0.06,0.76]) between infrared forehead thermometry and axillary thermometry using glass thermometer in paediatric population.[5] In contrast Fortuna, et al. compared IRFT to rectal thermometry in 200 children aged 1 month to 4 year with a mean age of 1.4 y and reported a broader 95% prediction band (on the order of 4°F) which is clinically not useful.[6] A similar study conducted by Sethi et al, did not show agreement between the axillary and forehead method (mean difference -0.5°C, 95% limit of agreement[-2.3,1.2],[7] while Seher et al, reported similar result with slightly narrower band for 95% confidence limits (mean difference=0.2°C, 95% limits of agreement [-1.2,1.6] in adult population.[8]However, unlike those previous studies, this study included only those neonates which was under servo-controlled radiant warmer with a set skin temperature of 36.5°C. In current study we found higher mean difference and slightly lower narrower bandwell (mean difference = -1.5, 95% limits of agreement: [-2.7,-0.3] . Infrared thermometer results are not satisfactory compared to digital thermometer when correlated with set skin temperature of neonates under servo controlled radiant warmer. Many factors may be responsible for these differences in results in different studies.

	DIGITAL THERMOMETER		INFRARED THERMOMETER		WARMER SET TEMPERATURE
	AVERAGE	RANGE	AVERAGE	RANGE	
FT	37.04	36.1-37.9	38.52	37.2-39.6	36.5
PT	36.86	34.8-38.1	38.30	36.8-39.5	36.5

Mean and Range of all temperature readings



Bland-Altman plot showing comparission of body temperature by axillary and no touch technique (°C) of all neonates.

CONCLUSION

Non- contact infrared thermometry is a newer technique of temperature measurement is simple, rapid, and easy ascompare to other traditional methods. Temperature readings howeverareaffected by the various factors like warmers, phototherapy, nearby wall of room temperature, etc. So the results achieved were not satisfactory. It needs some improvement in technology to become accurate for temperature measurement for a routine use in NICU.

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ORIGINAL ARTICLE

Clinical and Epidemiological Profile of Diphtheria in Tertiary Care Hospital

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KEY WORDS : Diphtheria, Immunization, resurgence

ABSTRACT

Background and aim : There has been a recent resurgence in the cases of diphtheria, mainly in the developing countries. The aim of our study is to study the clinical profile and epidemiology of diphtheria cases admitted to our hospital over a period of one year.

Materials and methods : This study was conducted at Civil Hospital Ahmedabad , patients of 0 to 12 years of age presenting with fever and sore throat with typical greyish white membrane , and diagnosed as diphtheria during the period of January 2013 to December 2013 were included in the study.

Results : It was observed that highest incidence of diphtheria was seen in the 0 to 5 years of age group (58%) the male to female ratio was 1.833:1. The majority of patients came from rural (47%) tribal areas (39.5). immunization status was the most determining feature in susceptibility as 32 patients out of 38 were unimmunized at the time of presentation.

Conclusion : The recent rise in the incidence of Diphtheria shows the pressing need for increasing immunization coverage in areas having less healthcare facilities & creating awareness regarding necessity of diphtheria vaccine.

INTRODUCTION

Diphtheria is an acute infectious disease of the upper respiratory system caused by toxigenic strains of *Corynebacterium diphtheriae/Corynebacterium* other than *diphtheriae.* The organisms are locally invasive and secrete soluble exotoxins, which can lead to serious consequences mainly involving the heart muscle, nervous system and kidneys. Death can occur due to myocarditis leading to circulatory failure within the first 10 days of infection. If diagnosed early, the infection responds to appropriate antibiotics and prompt antitoxin therapy. Factors contributing to morbidity and mortality include patient's immunization status, age at infection, clinical type, and time of intervention. Clinical correlation with laboratory findings (microscopy and culture) helps in the confirmation of the diagnosis, and onward transmission of data helps the health authorities to spread awareness, boost immunization programs, and prevent community spread.

Most of the vaccine preventable diseases showed a decline after introduction of Expanded Program of Immunization in 1978 and Universal Immunization Program in 1985. The reported incidence of diphtheria in the country during 1987 was about 12,952 whereas during the year 1999, there were only 2,725 cases showing a decline of about 79%1. It is still endemic in our country. The last decade has seen resurgence of diphtheria in both developed and developing countries where it was previously well controlled. Considering the recent resurgence of Diphtheria, it was decided to study the clinical profile and epidemiology of diphtheria cases in the year 2013.

The aim of this study is to assess the incidence of clinical diphtheria and its mode of presentation, trends of the disease, such as the frequency in children and adults, seasonal variation, gender predisposition, relationship between clinical disease and immunization status, and the role and limitations of laboratory investigations.

MATERIALS AND METHODS

This study was done at Civil Hospital Ahmedabad, B. J. Medical College from January 2013 to December 2013. Patients of 0-12 year's age presenting with fever and a sore throat having difficulty in swallowing with a greyish white membrane and diagnosed as diphtheria, were included in the study.[6]

The immunization status was documented as per the information given by the parents. Those who had received three primary doses at 4–6-week intervals starting at 1 month of age, followed by booster doses at 18 months and 5 years were recorded as “Immunized”. Those who had not received any dose were considered

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"Unimmunized". Patients who had missed one or more of the three primary doses or booster doses were included as "Partially immunized".

The following data were recorded: age, sex, clinical symptoms and signs, laboratory findings including Throat Swab smear for C.Diphtheria and culture, Complete Blood Count with Peripheral smear for Malarial Parasite (CBC,PSMP) Renal function Tests (RFT) with Serum Electrolytes in all Patients, Chest X-ray, and ECG, CPK-MB, CPK-Total, Electromyography-Nerve Conduction study (EMG-NCV) were done as and when indicated

Throat swabs for direct microscopy for *Corynebacterium diphtheriae* and culture for *Corynebacterium diphtheriae* were collected soon after admission. Staining of the smears was done by Gram Stain and Albert–stain method, and culturedon Nutrient Agar, Mc Conkey Agar, Tellurite Chocolate Agar, and Löffler's Serum (last two being selective media) and were identified based on differences in biochemical reactions, as per standard methods.

All patients were given ADS and appropriate antibiotics.

Those patients who developed complications were given treatment in the form of Tracheostomy and ventilator support.

The patients included in the study came from different socioeconomic strata, religions and ethnicity, and region of residence, giving a diversity in the subjects and practices.

OBSERVATION

There were a total of 38 patients admitted with diphtheria in the period between January 2013 to December 2013 comprising 0.67% of the total admissions.

The highest incidence was seen between the age of 1-5 years (58%), with 22 patients belonging to this group. Out of the 38 patients, 24 (63%) were males and 14 (37%) were females with male: female ratio of 1.833:1. Majority of patients were from rural areas (47%) whereas 39.5% of patients were from tribal areas. The highest number of patients belonged to lower socioeconomic scale (76.3) as per Kuppuswamy Classification, this could be because our hospital mainly caters to patients coming the lower socioeconomical class and these patients have poor access to immunizations and health care system. Immunization status was the most sticking factor affecting the susceptible to the disease. Out of 38 patients, 32 patients were unimmunized, out of which 8 patients were succumbed to disease. 1 patient was partially immunized and 5 patients were fully immunized, out of which 1 patient was succumbed to disease. Cases of diphtheria was seen through out of year and great number of increase was seen during month of August to month of December. The commonest clinical features were fever and sore throat which was seen in almost all patients. 9 patients had bull neck on presentation, 10 patients had features of circulatory collapse, 6 patients had feature of oliguria on presentation. 2 patients had complaint of difficulty to swallow. 2 patients had complaint of weakness. Out of 38 cases, 35 patients (92%) had tonsillo pharyngeal diphtheria, 2 patients (5.26%) had laryngeotracheal & 1 patient had (2.63%) had nasal diphtheria.

This could be due to poor immunization coverage, less health care facilities in outreach areas.

- 24 patients were undernourished and 21 patients had anemia.
- Throat swab for Corynebacterium Diphtheria by Albert stain & gram stain were positive in 6 patients, whereas culture was positive in 3 cases.
- All the patients were given ADS (Anti Diphtheria Serum) except one patient who had positive reaction to the test dose.
- Tracheostomy was required in 11 patients, out of which 5 patients expired, 4 were discharged after tracheostomy closure, while 2 patients were discharged with tracheostomy tube in situ.
- Complications were seen in 19 patients, with the commonest being myocarditis seen in 20 patients (26.38%) followed by acute renal failure in 7 cases (18.4%), palatal palsy in 2 cases (5.26%), poluneuropathy in 2 patients (5.26%), and tracheostomy failure in 9 (23.67%) cases.
- Out of 38 cases, 27 patients were discharged, 2 patients took discharge against medical advice, 9 (23.67%) patients died.
- The major contributing factors were myocarditis and acute renal failure.

DISCUSSION

Diphtheria is a fatal bacterial infectious disease known since ancient times. It's name is derived from the Greek word meaning "Leather" pointing towards pseudomembrane, the hallmark of the disease. In Ayurveda it's called *"Ghatsarpa"* suggesting a snake winding tightly around neck of a pot. Talking in the terms of epidemiology, the trends are changing with shifting of affected population age group towards preschool and adolescents because of immunization. The current state of control of disease in developed countries is very much under control but vaccine dependent and hence fragile, as suggested by intermittent outbreaks[2]. While the state of achieving control in developing countries and india is still a long way to go.[1]

The disease is caused by C. diphtheria mostly out of the other members of Corynibacterium species. The four subtypes are Mitis, intermedius, Belfanti, and gravis. These aerobic, non capsulated, non spore forming, gram positive bacilli acquire the toxigenic property by bacteriophages. The toxin, composed oif two subunits A & B, is responsible for various local and systemic effects of infection while pseudomembrabe produced due to necrotic effect at local site is responsible for respiratory tract effect. The toxin acts by inhibiting proteib synthesis by coimnbining with NAD+. The primary site of infection of this obligate human pathogen can be mucosa of respiratory tract (nasal, pharyngeal, laryngeal) cutaneous, ocular, ear or vulvo-vagina.

The clinical manifestations can vary from mild to severe to life threatening depending on immune status of host and severity of infection. The life threatening complication in initial course of disease is respiratory tract obstruction caused by adherent pseudomemrane, edema and bullneck. The systemic side effects are myocarditis (typically occurring after 2-5 weeks of initial infection), tubular necrosis and thrombocytopenia. Case fatality rises due to neurological complications involving diaphragm and respiratory muscles. This fatal infection has to be differentiated from similar streptococcal and EBV infections. The CDC criteria for laboratory diagnosis[3] involves isolation of bacteria from specimen via gram stain, Albert's stain or culture. Case classification classifies it as Probable (clinically compatible but not laboratory confirmed or epidemiologicaly linked to confirmed case) and Confirmed(clinically confirmed that is laboratory confirmed or epidemiologically linked)

The early and prompt treatment prevents mortality. Specific antitoxin is mainstay of management, where horse sera is used without waiting for laborarory confirmation to neutralize the unbound toxin in blood. Corynebacterium is susceptible to antimicrobials like penicillins, erythromycins, clindamicin and metronidazole. Therapy is to be given for 14 days. It is important to maintain isolation, treat carriers and prevent spread.

The vaccine containing diphtheria toxoid is the major contributor in bringing down its prevalence. The combined DPT vaccine was developed in early1920's. the schedule for DPwP or DTaP is at 6,10 and 14 weeks of age with first booster at 1 ½ years of age and second booster at 5 years of age. DPT is known for its adverse effects due to its pertusis component. The efficacy after doses is 75-85%

It is necessary to achieve universal coverage of DPT all over the world to prevent mortality due to diphtheria. At least 80% coverage of DPT is required to control the disease. A review of global data shows that there were a total of 4489 reported cases of diphtheria in 2012 out of which 2500 were estimated deaths. The global 3 dose coverage of DPT is 83%. Indian figures depict that 87% of total districts have achieved more than 80% coverage.

CONCLUSION

Our study shows that there are significant numbers of cases of diphtheria presenting to a tertiary care hospital in time frame of one year, indicating a recent resurgence of diphtheria.

In view of the poor immunization status of patients and high incidence of complications, it is imperative to take proactive steps towards improving immunization coverage, particularly in rural and outreach areas.

TABLE I : AGE DISTRIBUTION

<1 year	1-5 year	6-10 year	10-12 year
Nil	19	15	4

TABLE II : SEX DISTRIBUTION

Sex	No. of pts	Percentage
Male	23	61%
Female	15	39

TABLE III : RESIDENCE

Residence	No. of pts
Rural	19
Urban	5
Tribal	15
Total	38

TABLE IV : TYPE OF DIPHTHERIA

Type of Diphtheria	No. of pt's
Nasal Diphtheria	1
Laryngo Tracheal Diphtheria	2
Cutaneous Diphtheria	0
Tonsillopharyngeal Diphtheria	35
Total	38

TABLE V : COMPLICATIONS

Complications	no. of pts	percentage
Myocarditis	10	26.83%
Acute Renal Failure	7	18.40%
Palatal Palsy	2	5.26%
polyneuropathy	2	5.26%
Tracheostomy fistula	1	2.63%

TABLE VI : CAUSE OF MORTALITY

Cause of Death	No. of pts	Percentage
Myocarditis	7	18.40%
Acute renal failure	2	5.25%

FIGURE I : SEASONAL VARIATION

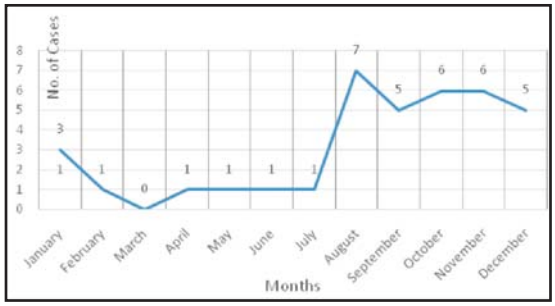


FIGURE II : IMMUNIZATION STATUS

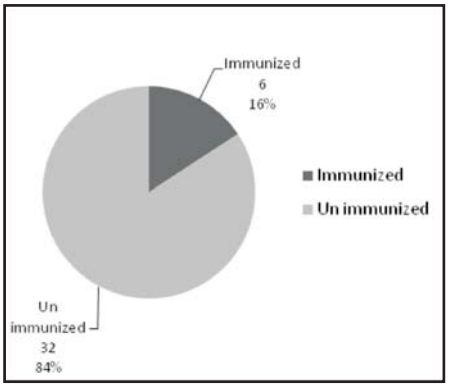
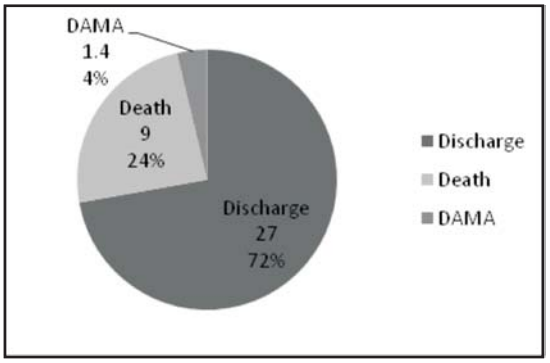


FIGURE III : OUTCOME



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CASE REPORT

Successful maternal and fetal outcome in a patient with coronary artery disease and type II Diabetes Mellitus

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KEY WORDS : Coronary artery disease in pregnancy, Diabetes Mellitus in pregnancy

INTRODUCTION

The prevalence of coronary artery disease is increasing as a result of changing lifestyle patterns, including cigarette smoking, diabetes and stress. Age appears to be one of the major determinants of pregnancy-related myocardial infarction. At the age of 40 years and older, the incidence of myocardial infarction is three per 10,000 deliveries.[1]

Increased cardiac workload and greater myocardial oxygen demand during pregnancy puts the heart in a situation where myocardial ischemia may have a more severe course. Before the current practise of percutaneous coronary intervention (PCI), the estimated mortality among pregnant women with ACS was 20%.[1,13] Currently, with the application of PCI, maternal mortality rate has dropped to 5%.[1] Coronary artery disease and diabetes mellitus type II in pregnancy has traditionally been considered to be a rare event. However with team efforts of obstetrician, cardiologist, endocrinologist, anesthesiologist and neonatologist, we can have best possible maternal and fetal outcome with least adverse results.

CASE REPORT

A 23-year-old female, G1P0A0, came to an antenatal OPD with history of 2 months amenorrhoea, with past history of coronary angioplasty before four months. Patient was relatively asymptomatic before four months, then she developed chest pain constricting in nature, radiating to left shoulder and arm for one week. There was no previous medical or drug abuse history. The risk factors were strong family history for coronary heart disease and obesity. Her mother, father and paternal uncle had history of coronary heart disease. Her BMI was 29. She was admitted in intensive cardiac care unit. Her ECG showed anterior wall myocardial infarction. Her 2-D ECHO findings were: LVEF 20%, anterior wall apex and inferior wall hypokinesia suggestive of acute anterior wall myocardial infarction. Angiography showed 99% bifurcation lesion in mid left anterior division involving ostium. She underwent percutaneous transluminal coronary angioplasty, stenting to LAD on 8th March 2011. 2-D ECHO after PTCA on 11th March 2011 showed: Normal size Left Ventricle with adequate systole, LVEF 54%, IVS hypokinetic, no LV hypertrophy.

After coronary angioplasty she was on: Tab Clopidogrel 75 mg bid, Tab Aspirin 150mg bid, Tab Rosuvastatin 20mg HS, Tab Metoprolol XL 25 mg oid, Tab Ivabradine 5mg bid, Tab Digoxin 0.25mg oid 5 days in a week. She was diagnosed to have diabetes mellitus type II at the time of angioplasty and advised subcutaneous Inj Human Insulin R BBF (16 U),BL (10 U), BD (8 U) . She conceived after 2 months. Her LMP was 20th May 2011.

She took regular ante-natal visits to our institute throughout pregnancy and continued insulin and Clopidogrel, Rosuvastatin, Aspirin in same dosages during pregnancy. Diabetic profile was carried out every 2 weeks interval. Throughout pregnancy, optimal glycemic goals were pre-meal, bed time and overnight glucose 60-99 mg/dl, peak post prandial glucose 100-129 mg/dl, mean daily glucose <110 mg/dl and A_1C <6.0. Her ultrasound at 20 weeks gestation showed normal growth and no congenital anomalies. Her ECHO at 32 weeks of gestation showed normal size Left Ventricle with adequate systole, LVEF 54%, IVS hypokinetic, no LV hypertrophy. At 30 weeks of gestation, her diabetic profile(with Insulin)was very high, She was admitted and advised to take Inj. Human Mixtard(30/70) BBF (12U), BL (20U), BD (18U) & Inj. HNPH (12 U) at 10 pm.

She was admitted to department of Obstetrics and Gynecology at 38 weeks of gestation. On examination, her vital datas were normal. Per abdomen examination showed fundal height corresponds to 36 weeks, cephalic presentation, high floating head, fetal heart rate 144/bpm. On per vaginal examination, narrow midpelvis and outlet. USG at 38 weeks gestation showed single live fetus with cephalic presentation, 38 weeks maturity, estimated fetal

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weight- 3.5 kg, placenta fundo posterior and polyamnios-AFI 25. Umbilical and middle cerebral artery doppler velocimetry was normal. Non stress test was reactive. Cardiologist advised Tab Digoxin(0.25 mg) and Tab Metoprolol XL (25mg).

Her thyroid profile, diabetic profile, lipid profile and homocystine levels were normal. Opinion of cardiologist, endocrinologist and anaesthesiologist were taken and followed. Decision for caesarean section was taken due to contracted pelvis. Rosuvastatin, Aspirin and Clopidogrel were stopped 5 days before surgery. Morning dose of insulin was omitted on the day of surgery. Morning dose of Tab Digoxin(0.25mg) and Tab Metoprolol XL(25mg) were given. Under general anesthesia caesarean section was performed. CVP monitoring was done during cesarean section and for 48 hours postoperatively. A single live female baby, 3.5 kg was delivered with Apgar score 8 and 10 at the end of 1 and 5 minute. Prophylactically, romovac negative suction drain was kept beneath rectus sheath which was removed after 72 hours. She was shifted to intensive cardiac care unit for 48 hours post operatively. Rosuvastatin, Aspirin and Clopidogrel were restarted after 48 hours of surgery. During postoperative period insulin was given according to sliding scale for 48 hours. Post operative period was uneventful.

DISCUSSION

The incidence of myocardial infarction in pregnancy has been estimated to be 6.2 per 100 000 deliveries with mortality rate 5.1%-11%[1,4] in recent reviews. Prior estimates of mortality have reported it as substantially higher at 37% and estimates of incidence substantially lower at 2.8 per 100 000 deliveries.[1] This incidence is approximately 3-4 times higher than the estimated age associated risk for non-pregnant women.[4] Anterior coronary circulation was more commonly involved.[4] Ladner et al found that in pregnancy women with anterior wall myocardial infarction, 38% occurred in ante partum, 21% in intra partum and 41% in 6 week post partum.[14]

The increased stroke volume and heart rate during pregnancy causes an increased myocardial o_2 demand, while the decreased diastolic blood pressure and related physiological anemia results in decreased myocardial perfusion that may contribute to the ischemia when coronary blood flow is compromised. Within pregnancy Badui & colleagues identified that woman in the 3rd trimester had the highest risk of anterior wall myocardial infarction.[5] With labour, myocardial ischemia may be precipitated by further increase in myocardial o_2 demand driven by pain, uterine contraction and anxiety. After delivery, caval compression is relieved and blood flow is shifted from the systemic circulation resulting in further stress on the myocardium and likely contributing to the increased incidence of myocardial infarction in the puerperium.

A classification scheme has been established to identify the associated risks with certain medications in pregnancy that are safely used in treatment of AMI in non pregnant state.[5] Beta blockers (Metoprolol class B, Atenolol class C) have been used successfully, however fetal bradycardia, hypoglycemia, hyperbilirubinemia and apnea can occur. A meta-analysis looking at anti platelet agents found that low dose aspirin is safe in pregnancy.[6] Clopidogrel (class B) has very limited data for its use in pregnancy. It is recommended that it is stopped 1 week prior to any regional anesthesia procedures.[4,13] Statins (class X) are not recommended in pregnancy. But a recent systemic review found that most data of human teratogenicity were only case reports and that overall risk is likely minimal.[4,11-12] In our case, there was no congenital anomaly of fetus inspite of Clopidogrel, Aspirin, Rosuvastatin, Metoprolol given during pregnancy.

PCI and stent replacement reported favorable fetal and maternal outcomes.[15] It is important to weigh the risks and benefits of each potential therapy and monitor the management according to the clinical presentation. Currently, with the application of PCI during pregnancy, maternal mortality rate has dropped to 5%.[1] In our case, PTCA before pregnancy gave favorable maternal outcome.

Pregnancy profoundly affects the management of diabetes. Excellent glycemic control in the 1st trimester continued throughout pregnancy is associated with the lowest frequency of maternal, fetal & neonatal complications Maternal hyperglycemia during the 1st few weeks of pregnancy is strongly associated with spontaneous abortions and major congenital malformations. Glycemic thresholds for the increased risk include A_1C >6.3%[3,8]. After 12 weeks gestation, hyperglycemia induces fetal hyperinsulinemia, accelerated growth and excess adiposity. Macrosomia is associated with increased rates of operative delivery & birth trauma, fetal death and neonatal hypoglycemia, hypertrophic cardiomyopathy, polycythemia & hyperbilirubinemia.[3] Control that is too tight (mean plasma glucose <80-90 mg/dl) was associated with fetal growth restriction, which carries its own set of neonatal and child development problems[3]. Fetal hyperglycemia causes

fetal hypoxia & acidosis, which may explain the excess stillbirth rates still observed in poorly controlled diabetic woman.[3] In our case, there was good glycemic control in 1st and 2nd trimester, but hyperglycemia at 30 weeks which was managed by starting Human Mixtard and HNPH insulin.

The least hemodynamically burden route of delivery is to be considered. In most cases, caesarean delivery is only performed for obstetrical indications because a vaginal delivery minimizes stress. In more recent reviews, no convincing support for one method of delivery over the other has been found.[2] In our case patient had cephalo-pelvic disproportion, so caesarean section was considered. Ergot alkaloid immediately after delivery was avoided because of the risk of coronary artery spasm.

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CASE REPORT

Anaesthetic Management of Cerebellar Hemangioblastoma Having Von-Hipple Lindau Syndrome

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KEY WORDS : Von-Hippel Lindau syndrome, Cerebellar hemangioblastoma, General anaesthesia

ABSTRACT

Von-hipple lindau syndrome is an autosomal dominant neoplastic syndrome characterized by development of various benign or malignant tumors and cysts in many organ systems. The anesthetic management of such patient can be challenging. We present a case report of VHL syndrome that underwent suboccipital craniotomy under general anaesthesia.

INTRODUCTION

Von hippel lindau disease is an autosomal dominant neoplastic syndrome of variable expression. It is characterised by the development of various benign or malignant tumors and cystic lesions in many organ systems[1]. The characteristic lesion is the capillary hemangioblastoma in the retina (60-70 % of the patients). Majority of the CNS lesion are located in the cerebellum. Renal and pancreatic cyst, hypernephroma, erythrocytosis and pheochromocytoma (often bilateral) are also associated with this disease[2].

In this patient many pathology of the VHLS were present, like pancreatic and renal cysts, retinal problems with the loss of vision of right eye, renal cell carcinoma for which he underwent nephrectomy + adrenalectomy, cerebellar hemangioblastoma and polycythemia (Hct – 49.8%).

CASE REPORT

A 39 year old male patient of 60 kg weight posted for craniotomy for cerebellar hemangioblastoma having VHL Syndrome was referred for preoperative evaluation. Patient presented with complaints of headache, vomiting & gait disturbances since 2 months. VHL syndrome was diagnosed before 1 year, as a part of preoperative evaluation for nephrectomy. At that time, patients had no CNS complaints, but at present his complaints warranted admission.

Patient had normal cardio-respiratory examination except mild high blood pressure 160/100 mm of Hg for which he was on tablet Amlodepine 5mg since one week. Pt was fully conscious with Glassgow coma scale of 15 with normal tone, power and reflex in all four limbs.

Before 1 year, he was evaluated and diagnosed as renal cell carcinoma with adrenal mass. He was operated for right nephrectomy & adrenalectomy under general anaesthesia. During USG of abdomen presence of pancreatic cysts and small cysts on the lower pole of left kidney were also detected.

He had, vitreous hemorrhages before 20 years for that he was treated by laser photocoagulation. Inspite of that vision loss occurred in right eye.

Patient was a known case of diabetes mellitus since 2 yrs and was on oral hypoglycemic drugs for 1 year. At present he was on regular human insulin subcutaneously as per dose (10-10-10 IU before breakfast, lunch and dinner respectively) with a good glycemic control. Patient was also on anticonvulsants, antiemetic and dexamethasone for his CNS complains.

His Hb was 16.8 gm%, HC-49.8% and RBS-136 mg/dl. LFT, RFT, electrolytes, chest X-ray & E.C.G were normal. MRI brain suggested right cerebellar haemangioblastoma (5*5*3.5cm) which was increased in size compare to previous year (2*2.5*0.5cm). Fourth ventricle was compressed & shows mild obstructive hydrocephalus.

On day of surgery, morning dose of insulin was omitted and all other drugs were given preoperatively.

After adequate pre-oxygenation, patient was induced with injection glycopyrrolate bromide 0.004mg/kg, injection fentanyl citrate 2mcg/kg, injection thiopentone sodium 5mg/kg and injection vecuronium bromide 0.1mg/kg. Patient was intubated with flexometallic tube no. 36. Continuous monitoring with ECG, SpO_2, $EtCO_2$, NIBP, urine output and temperature was performed.

Surgery was done in prone position. Anaesthesia was maintained with sevoflurane in 50% oxygen and 50% nitrous oxide with injection vecuronium bromide. Pressure-control ventilation adjusted to maintain $EtCO_2$ 25$\pm$2. Inj mannitol (1 gm /kg) was given to control

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intracranial pressure. Other intra-operative drugs given were injection ranitidine, antibiotics, injection dexamethasone and injection phenytoin sodium and injection ondansetron hydrochloride.

Surgery was completed uneventfully within 4 hrs. Total intra-operative blood loss was 400 ml & Urine output was 2500 ml. Total 3500 ml i.v fluids was given as a maintenance and replacement fluid.

The muscle relaxation was reversed with injection neostigmine bromide 0.05mg/kg and injection glycopyrrolate bromide 0.4mg. Patient was extubated and shifted to ICU.

Rest of the clinical course was normal in the post operative period. Patient also got relief from the vomiting & gait disturbance. He was complaining of mild headache which was reduced in intensity. Patient was discharged from the hospital on the 5th post operative day.

DISCUSSION

VHL disease is an autosomal dominant disorder associated with 2nd copy of genes of cell has a mutation and produce faulty VHL protein. That occurs at rates of one case per 36,000 to 45,000 persons.

Renal cell carcinoma and cysts developed in 25-60% of patients and pheochromocytoma in 10-20% of patients[1]. So patient has s/s of hypertension, tachycardia, blurring of vision and syncopal attack. Pancreatic cyst may also present with diabetes. Haemangioblastoma of the retina and the CNS are the most typical lesions found in VHL patient[1]. These patients have vision problem, ataxia, walking difficulties, headache, vomiting and neurological deficits. Polycythemia may also occur in 20% of patients with VHLS[4]. This is due to the production of erythropoietin like substance from hemangioblastoma that increase red cell synthesis & red cell iron turnover without splenomegaly[3].

The retinal lesions known as angiomatosis retinae were described by Von-Hippel in 1904. Then latter on Lindau described the syndrome. Treatment with laser photocoagulation can halt the progress but if untreated, lead to glaucoma and blindness[5].

The experience of anesthetic management of patients with VHLD is limited. The choice of anesthesia and monitoring depends on the type of surgery and extent of pathology[1]. Certain controversies exist in coexistent pheochromocytoma and cerebellar hemangioblastoma. They first planned surgery for cerebellar lesion as CNS symptoms worsens. Pheochromocytoma excision done after stabilization with phenoxybenzamine and nifedipine[2]. Neuroaxial blockade in presence of spinal hemangiblastoma is controversial. So, in the absence of contraindications elective caesarean section under epidural anaesthesia is a choice for management of child birth in patient with VHL disease[5]. However risk related to use of neuraxial anaesthesia in patients with an asymptomatic spinal cord or cerebellar haemangioblastoma should be carefully considered[1].

There are many reasons to screen for VHL disease like[3].

(1) Any patient younger than 50 years of age with CNS haemangioblastoma or any age with multicentric CNS lesion. They should undergo CNS MRI with contrast, ophthalmic examination, abdominal USG and CT scan plain or with contrast and urinary VMA assay.

(2) Any patient born with VHL syndrome should undergo routine CNS, ophthalmic and abdominal examination starting as early as 10 years as and not later than 20 years.

(3) Any patients suspected of VHL syndrome should have genetic analysis for germ-line mutation of the VHL gene.

In the past, the majority of patients with VHL died of complications of the renal cell carcinoma and CNS haemangioblastomas. With improvements in the treatment and diagnosis of VHL, including serial screening and a multidisciplinary approach to management of these patients, their life expectancy has significantly improved[1].

At conclusion, VHL syndrome is a rare disease. A careful evaluation of different system is necessary. Proper preoperative evaluation with suitable use of anesthetic drugs and proper monitoring are necessary for successful outcome. **So, one should investigate for other sites and complication of different organs.**

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CASE REPORT

Ellis-van Creveld Syndrome – Review with Case Report

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KEY WORDS : polydactyly, chondrodysplasia

INTRODUCTION

Ellis-van Creveld syndrome, also called chondroectodermal dysplasia, is a disease complex consisting of bilateral ulnar polydactyly, chondrodysplasia of long bones resulting in disproportionate dwarfism, ectodermal dysplasia affecting principally the nails, teeth and congenital heart defects.

CASE REPORT

A 13 month old male child born out of non-consanguineous marriage presented to Pediatric OPD with complaints of cough, cold, difficulty in breathing and fever since 3 days. He had history of repeated lower respiratory tract infections in the past requiring hospitalization. On examination,the patient had short stature, narrow chest, protuberant abdomen, short distal extremities(Figure 1). He had generalized hypotonia. He had two small peg shaped teeth, bilateral postaxial polydactyly and small dystrophic nails(Figure 2). He also had hypospadias and undescended testis.On systemic examination, the patient was having tachypnoea, with subcostal indrawing. On auscultation, he had bilateral wheeze and tachycardia with systolic grade III murmur. Development quotient was 68%. History of congenital anomaly in the form of peg shaped teeth, short distal limbs, and bilateral upper limb postaxial polydactyly in the elder sister, other two elder siblings had no apparent congenital anomalies.

The patient was admitted for management of respiratory distress. His blood counts, renal and liver function tests were normal. On plain skiagram of chest, bilateral paracardiac pneumonia was present. On skeletal survey, bilateral short radius, ulna, tibia and fibula was present. There were six metacarpals and phalanges (Figure 3). The phalanges of both hands and feet were short and stubby, while spine was normal. On 2D echocardiography, patent ductus arteriosus with left to right shunt with mild mitral regurgitatation and mild pulmonary arterial hypertension was present. Ultrasound of abdomen and karyotyping were normal. The patient had disproportionate short stature, polydactyly, patent ductus arteriosus and short dystrophic nails, on basis of these features clinical diagnosis of Ellis-Van Creveld syndrome was made.

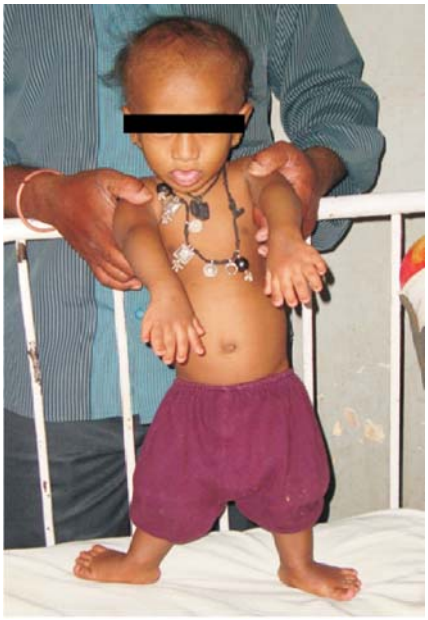

Figure 1 : Showing disproportionate short stature i.e. normal trunk, with symmetrical shortening of distal extremities& bilateral polydactyly.

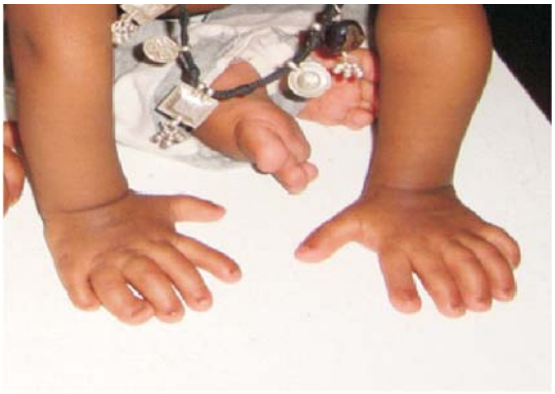

Figure 2 : Small dysplastic nails and bilateral postaxial polydactyly

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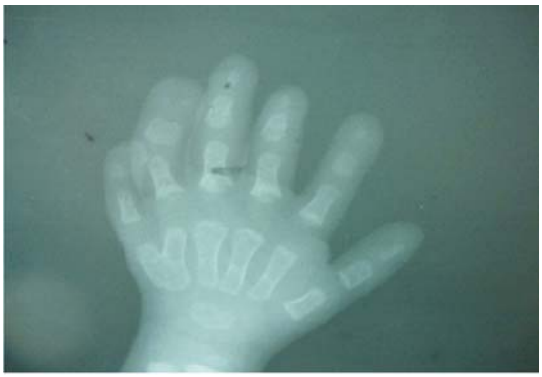

Figure 3 : Showing short stubby 6 metacarpal bone and phalanges.

DISCUSSION

Ellis-van Creveld syndrome is a skeletal dysplasia first described in 1940 by Richard W. Ellis and Simon van Creveld who coined the term "chondro-ectodermal dysplasia".[1,2,3] It is complex genetic disorder which is also called mesoectodermal dysplasia or chondrodystrophy syndrome. It is a rare autosomal recessive disorder[1,2,3] with prevalance rate 1:333,000[4] of the population with equal incidence in males and females, more common in closed ethnic communities as the Amish population of Pennsylvania. Almost half of these patients die during childhood by cardiopulmonary defects.

It is a transmitted in autosomal recessive mode. The EVC1 gene has been mapped to chromosome band 4p16 whose mutations were identified in these patients[1,5]. Mutations in a second gene, called EVC2 also gives rise to the same phenotype of the syndrome. A 991 amino acid protein encoded by EVC1 gene is shown to localize to the base of the primary cilium of chondrocytes, and defective signalling was observed in proliferating chondrocytes, because of this problem Ellis–van Creveld syndrome is considered to be a ciliopathy.[6]

This syndrome is a tetrad of chondrodysplasia, polydactyly, ectodermal involvement and congenital heart defects.[7] Chondrodystrophy means disproportionate dwarfism i.e. normal trunk, with symmetrical shortening of middle and distal extremities[1] (small stature of prenatal onset; average adult height being 119-161 cm).[1,2] Patients also have lumbar lordosis and genu valgum. Polydactyly is a constant finding, usually bilateral and on the ulnar side.[1,2] It is observed in the hands in most cases but in the feet in only 10% of cases. Ectodermal dysplasia (observed in up to 93% of cases) includes hypoplastic, dystrophic, ridged, friable or even absent nails, tooth involvement may include neonatal teeth, hypodontia, partial anodontia, small peg shaped teeth, and delayed eruption, hairs are usually normal but occasionally thin, brittle, hypochromic.[8] Cardiac abnormalities (in 50 %) includes a common atrium (40 %), AV canal defect, ventricular septal defect, atrial septal defect, and patent ductus arteriosus. The cardiac anomaly is the major cause of shortened life expectancy.[2]

Other anomalies which may be present includes musculoskeletal anomalies i.e., a narrow thorax frequently leading to respiratory difficulties, broad hands and feet, and sausage-shaped fingers. Teeth are small, defective, may be peg-shaped. The mucobuccal fold may be absent while the short upper lip is bound down by multiple frenula(lip-tie).Occasionally, there are genitourinary anomalies i.e. hypospadias, epispadias, hypoplastic penis, cryptorchidism, vulvar atresia, focal renal tubular dilation in medullary region, nephrocalcinosis, renal agenesis, and megaureters. Liver and CNS abnormalities may also be present. Thoracic dysplasia leads to respiratory insufficiency and cardiac anomalies lead to death in infancy in 50% of patients.[2,9]

The Weyersacrofacialdysostosis, an autosomal dominant disorder described in 1951 is characterized by variable extremities and facial features. This condition has been found to be associated with EVC and EVC1 mutations that have confirmed that Weyersdysostosis represents the heterozygous expression of the mutation that causes Ellis–van Creveld syndrome.[10,11]

Ellis-van creveld syndrome involves all embryonic tissue layers and is polysymptomatic; on the basis of bilateral postaxial polydactyly, short middle and distal extremities, dysplastic nails and teeth one can suspect the diagnosis of this syndrome and further skiagram and echocardiography will support the diagnosis of this syndrome.

The management of Ellis–van Creveld syndrome is multidisciplinary, includes symptomatic management of respiratory distress,recurrent respiratory infections, and cardiac failure. Dental care, implants and prosthetic rehabilitation and Orthodontic treatment, orthopedic manipulation of bony deformity, cardiac surgery and plastic surgery.

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CASE REPORT

A Rare Case of Idiopathic Avascular Necrosis of Scaphoid

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KEY WORDS : Idiopathic, Avascular, Necrosis, Scaphoid

ABSTRACT

Avascular necrosis of the scaphoid after a fracture is well-documented, but idiopathic avascular necrosis of the scaphoid (**Preiser's Disease**) is rare and **often debilitating condition**. Little is known about etiology of the condition and even less about the best course of management.

Usually the diagnosis is made with the use of plain radiographs, but one should not hesitate to use MRI for both confirming the diagnosis and evaluating the stage of the disease. Current treatment algorithms are not standardized, and many scaphoids degenerate to a point that a salvage procedure is required. We describe a rare case of **Preiser's disease** with **periscaphoid arthritis**.

INTRODUCTION

Avascular necrosis of the carpal bones can affect the lunate [5], the pisiform [8], capitates [10] and the scaphoid. When the whole scaphoid becomes avascular, following a fracture or an injury, this condition has been called Preiser's disease [2] (after Preiser's original article in 1910[9]).

Although avascular necrosis may occur without any known history of injury [3], it may be difficult to exclude the possibility of mild or repetitive trauma [1]. Other known causes of avascular necrosis include steroid therapy [7], chemotherapy [4] and connective tissue diseases such as systemic lupus erythematosus [10] or progressive systemic sclerosis.[6]

CASE REPORT

A fit 52-year-old female working as school servant presented with 14-month history of pain in her dominant left wrist. No history of trauma could be elicited. On examination, swelling was noted in the anatomical snuff box and the dorsum of the wrist at the scapho-lunate junction. The wrist joint was "irritable". X-ray films showed complete avascular necrosis of the proximal half of the scaphoid with a pathological fracture and significant carpal collapse deformity with periscaphoid arthritis (stage 4; Fig 1). At operation, the articular cartilage over the proximal pole was 'soft and unhealthy, but there was no external sign of fracture or of scapho-lunate ligament damage. An osteotomy was carried out through the waist of the scaphoid, the proximal fragment was excised and limited radial styloidectomy was done to relieve radio-carpal impingement. The patient's symptoms were relieved although she did require treatment for an associated De Quervain's syndrome before she was able to return to work. (Fig 2)

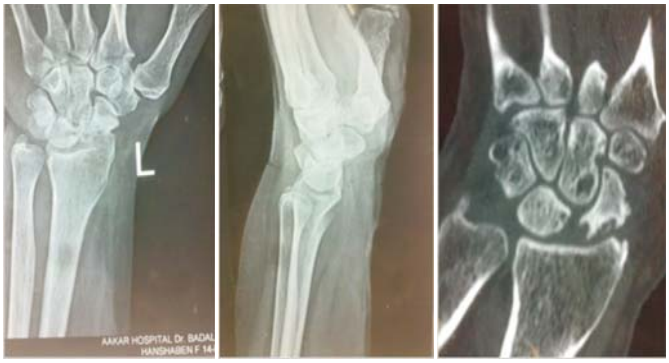

Fig 1 : Preoperative Plain radiograph and CT Scan Images of Left Wrist

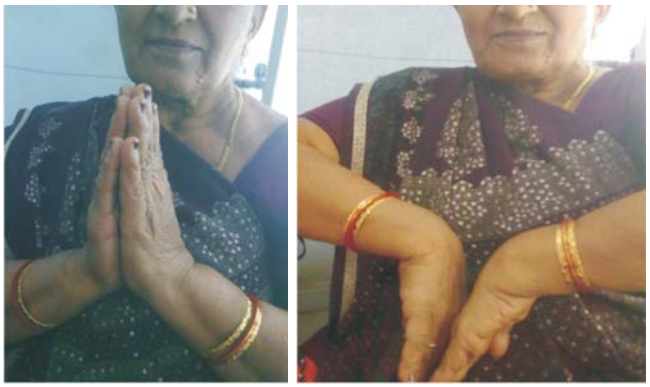

Fig 2 : Post-operative result after one year fairly good range of movement with no pain

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DISCUSSION

Idiopathic avascular necrosis, by definition, occurs in the absence of major trauma or pre-existing fracture, it is well-known that repetitive stress on the wrist can cause damage to the scapho-lunate ligament and this could be sufficient to interfere with the blood supply to the proximal pole of the scaphoid in susceptible patients.

Clinically, the onset of idiopathic avascular necrosis of the proximal pole of the scaphoid is heralded by increasing pain and stiffness of the wrist. Examination shows signs of an "irritable" wrist joint with tendeness and swelling over the dorsum of the wrist due to chronic synovitis. It is hardly surprising that patients also had signs of carpal tunnel syndrome and De Quervain's syndrome, which resolved once the synovitis had settled.

As with Kienbock's disease, idiopathic avascular necrosis of the scaphoid is a progressive condition so that treatment and prognosis depend on the stage of the disease. In the early stages one should consider the possibility of reversing the pathological process. Once the bone has undergone complete avascular necrosis (Stage-3), these changes are almost certainly irreversible so that reconstruction is no longer indicated. If the symptoms are not severe enough to justify a surgical procedure, the patient may benefit from conservative measures.

When surgery is indicated, preferred treatment to date has been a partial silastic,replacement of the scaphoid combined with a local synovectomy. The use of Silicone prosthesis does not preclude the possibility of carrying out partial or total fusion at a later date, should wear become a problem. Similarly, if scaphoid shortening results in symptomatic radio-carpal impingement, the symptoms may be relieved by carrying out a limited radial styloidectomy.

In conclusion, we consider that idiopathic avascular necrosis of the scaphoid is a distinct entity, similar in many ways to Kienbock's disease of the lunate. The prognosis would appear to depend on the stage of the disease, and treatment should be planned accordingly. It appears that the etiology may be related to interference in the extrinsic blood supply to the proximal pole of the scaphoid in susceptible patients. It appears that positive ulnar variance may be significant. These hypotheses warrant further investigation.

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CASE REPORT

Complete Heart Block in Patient of Rheumatoid Arthritis

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KEY WORDS : RA and CHB

ABSTRACT

Heart involvement can be a cause of death in case of RA. [1-3]

A 52 -year-old female patient with a history of RA was admitted to our hospital for dyspnea class II according to NYHA classification, giddiness and palpitation. The electrocardiogram revealed complete heart block whereas the 2D ECHO with DOPPLER showed grade II/IV Mitral Valve regurgitation and no signs of any region wall motion abnormality (RWMA) with LVEF- 68%.The coexistence of rheumatoid arthritis with complete heart block is very uncommon (incidence <0.1%)[4]

It would be interesting to see whether a linkage between the above cardiac lesions with rheumatoid arthritis can be demonstrated. Rarity of association between RA and CHB prompted us to publish this case report as it has never been reported from our country in literature as per best of our knowledge.

CASE REPORT

A 52-year-old female, a known case of Diabetes since 15 years, with a known history of RA was admitted to our hospital with dyspnea NYHA class II, palpitations and giddiness. Rheumatoid arthritis was diagnosed 36 months ago on the basis of clinical and laboratory findings.

The patient was given Methotrexate and NSAIDS [not known to cause CHB]. There wasn't any history of any drug that causes bradyarrhythmia.

On physical examination her heart rate was 42 beats per minute and blood pressure 176/90 mmHg. Auscultation revealed a grade III/VI systolic murmur at the mitral and tricuspid area.

A resting electrocardiogram showed complete heart block [Atrial Rate 100/ min, Ventricular rate 42/min] *(figure 1)*.

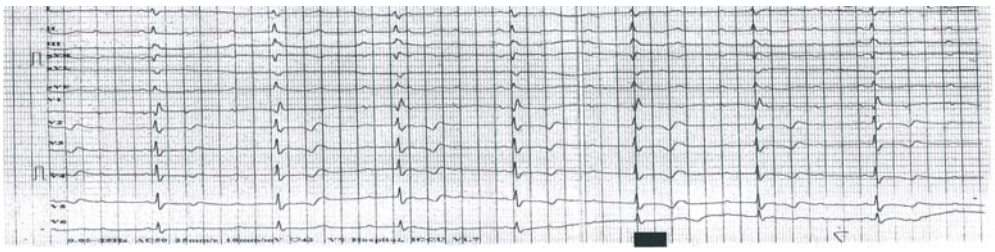
2D echocardiography with color Doppler study demonstrated grade II/IV MR and LVEF 68 %. No other significant finding of ECHO was noted.

The patient had undergone a coronary angiogram to rule out any significant coronary lesion. CAG (coronary angiogram) revealed no significant lesion. A permanent pacemaker (VVI) was implanted as a curative treatment to CHB.

Laboratory findings

➢ Hb- 11.3 gm/dl ➢ WBC count- 10,300/mm^3, ➢ Hematocrit - 39.5%, ➢ platelet count - 1,96,000/mm^3, ➢ urea - 28 mg/dl, ➢ creatinine - 0.6 mg/dl, ➢ SGPT - 21 U/L,	Serum K+ - 4.3 meq/l, Serum calcium - 9.5 mg/dl, Serum phosphorus - 3.5 mg/dl,	RA factor titer - > 64 IU/ml, [0-8] Anti CCP antibody level - > 200 U/ml, [0-5] TSH level- 1.280 microbus/ml

Figure 1



The ECG of the patient showing the complete atrioventricular heart block.

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DISCUSSION

Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown etiology marked by a symmetric, peripheral polyarthritis. It is the most common form of chronic inflammatory arthritis and often results in joint damage and physical disability. As RA is a systemic disease, it may result in a variety of extraarticular manifestations, including fatigue, subcutaneous nodules, lung involvement, peripheral neuropathy, vasculitis, and hematologic abnormalities and also the cardiovascular involvement.[5]

The most frequent site of cardiac involvement in RA is the pericardium.[5]

However, clinical manifestations of pericarditis occur in less than 10%[5] of patients with RA despite the fact that pericardial involvement may be detected in nearly one-half of the these patients by echocardiogram or autopsy studies.

Another clinically important manifestation of RA is Cardiomyopathy[5]. It may result from myocarditis [necrotizing or granulomatous], coronary artery disease, or diastolic dysfunction. This involvement is usually subclinical & asymptomatic and only identified by echocardiography or cardiac MRI. Rarely, rheumatoid nodules or amyloid infiltration is seen in the heart muscle.[5] The most common valvular abnormality that occur in RA is Mitral regurgitation[5] and most of the time, it does not require any further management as it is not of severe variety.[9]

Conduction disturbances are relatively rare (incidence < 0.1%)[4] in the RA population. Primary infiltration by mononuclear cells or rheumatoid nodules could cause conduction disturbances at the sino-atrial or atrioventricular nodes or His-Purkinje system[6,7]. Other potential mechanisms are vasculitis of the arterial supply to conductive tissue, hemorrhage into a rheumatoid nodule or extension of an inflammatory lesion from the aortic or mitral valve[7]. Rarely, these lesions may be due to amyloid deposition[7].

Ahern et al have described CHB in 8 patients with RA and reviewed 20 similar cases previously reported [8]. However complete atrioventricular block is rare in RA and does not respond to anti-inflammatory and immunosuppressive therapy [7].

As the patient had complain of giddiness and palpitation without any other apparent cause and giddiness can be due to CHB[10], so the patient was implanted permanent pacemaker .After PPI patient had no giddiness and palpitations. Patient is under care of physician for control of symptoms of RA.

CONCLUSION

On review of literature, there are very few reports of occurrences of CHB in RA. The association of the above cardiac lesions with rheumatoid arthritis may, however, be a random occurrence. Further studies are necessary to assess whether a true association of the above conditions exist.

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CASE REPORT

Unusual Case Report of Rhizomelic Chindrodysplasia Punctata (RCDP) Radiological findings.

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KEY WORDS : chondrodysplasia punctata, congenital malformation, newborn, skeletal dysplasia

ABSTRACT

RCDP is a rare autosomal recessively inherited skeletal dysplasia with an incidence of 1:1,10,000 births. RCDP is caused by mutations in the PEX7 gene. PEX7 gene is found on chromosome 4 in the 6923.3 locus . RCDP characterized by rhizomelia, ichthyosis, seizures, repeated infections, congenital cataracts and joint contractures.. Radiological features include epiphyseal stippling, metaphyseal abnormalities and clefts in vertebral bodies. We report a case of RCDP in a neonate because of small sample size. RCDP carries a poor prognosis with approximately 60% cases surviving the first year ;very few survive beyond 10 years.

CASE REPORT

A five day old male baby was brought for evaluation of delayed cry and dysmorphic facies. He was delivered at term by spontaneous vaginal delivery. There was no history of any maternal disease or teratogen exposure during the antenatal period. The physical examination showed a weight of 2. 5 kg, a length of 41 cm (<10th centile), and a head circumference of 35 cm (~ 75th centile). The infant had proximal shortening of both upper and lower limbs. He had depressed nasal bridge, dysmorphic facies ,low set ears, flat facial feature and anteverted nares. Opthalmic examination revealed cataract in both eyes. There were no skin lesions . The abdomen was soft , non tender with no organomegaly. A skeletal survey demonstrated multiple anomalies including rhizomelic shortening of the upper and lower extremities. Multiple small punctuate calcific stippling was noted in epiphyses of shoulder, elbow, hip , knee and ankle joints. Metaphyseal flaring was noted in both humerus and femur. (Figure- 1 , 2) Coronal clefting was noted in vertebral bodies. (Figure- 3). Ultrasonography of the head and abdomen were normal. Baseline biochemical tests did not reveal any abnormality.

Based on clinical and radiological findings, a diagnosis of rhizomelic chondrodysplasia punctata was postulated.

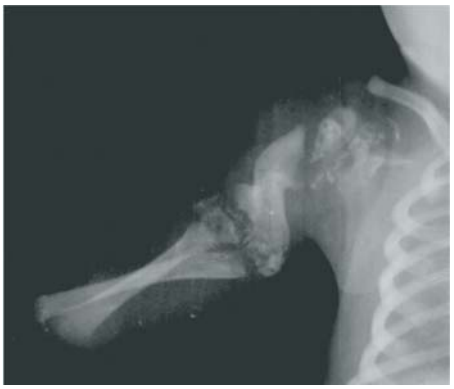

Figure-1 : X –Ray right shoulder with arm with elbow with forearm (Anteroposterior view) shows rhizomelic shortening of humerus with stippled epiphyses and metaphysical widening in shoulder and elbow joints.

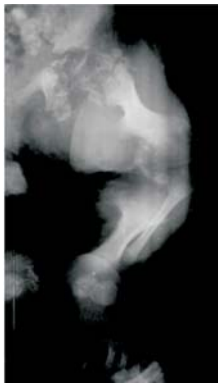

Figure-2 : X-ray left hip with thigh with knee with leg with ankle joint (Anteroposterior view) shows rhizomelic shortening of femur, tibia and fibula with stippled epiphyses and metaphysical widening in hip , knee and ankle joints.

DISCUSSION

RCDP is a rare autosomal recessively inherited skeletal dysplasia with an incidence of 1:1,10,000 births. RCDP is caused by mutations in the PEX7 gene. PEX7 gene is found on chromosome 4 in the 4p16 locus [1]. Rhizomelic chondrodysplasia punctata (RCDP) is a

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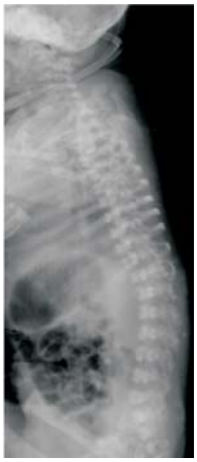

Figure-3 : X-Ray thoraco-lumbar spine lateral view shows coronal clefting of vertebral bodies.

peroxisomal disorder characterized by rhizomelic proximal shortening of the humerus and femur, ichthyosis, ataracts, restricted joint mobility, micrognathia ,flattened nasal bridge, bulbous nose and flattened face appearance [2]. Patients may subsequently develop seizures and severe psychomotor delay. Radiological features include epiphyseal stippling, metaphyseal abnormalities and clefts in vertebral bodies. [3] All these classical radiological findings were present in our case. Other malformations observed in individuals with RCDP include cleft palate, congenital heart disease and ureteropelvic junction obstruction. Most of the affected children develop repeated infections and die within first two years. Death occur in the rhizomelic group due to tracheal stenosis or spinal cord compression usually within the first decade.[4]

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CASE REPORT

Anaesthetic implications in a case of antiphospholipid antibody syndrome for elective caesarean section

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KEY WORDS : Antiphospholipid syndrome (APLS), Pregnancy, thrombocytopenia

ABSTRACT

Antiphospholipid antibody syndrome is an acquired autoimmune disorder characterized by thromboembolic phenomena, thrombocytopenia and bad obstetric history .Here, we report successful anaesthetic management of a case of antiphospholipid syndrome, posted for elective caesarean section

INTRODUCTION

Anti-phospholipid syndrome, originally called anticardiolipin syndrome(Hugh's syndrome), is an acquired autoimmune disorder characterized by the presence of anti-phospholipid antibodies and a chance of arterial and venous thrombosis.[1] APS antibodies are normally present in approximately 5% of population , but clinical presentation of syndrome occurs in 2% of population. Pregnancy itself is a hypercoaguable state. Pregnancy loss is caused by thrombosis of placental vessels and binding of antiphospholipid antibodies to trophoblast cells.[2] This syndrome is associated with recurrent foetal loss, thrombosis, pregnancy induced hypertention, abruptio placenta, intrauterine growth retardation, valvular heart disease and hypothyroidism.[3] The treatment of this syndrome includes low dose aspirin alone or with low molecular weight heparin.[3]

MATERIAL AND METHOD

A 33 year old parturient with diagnosed APL syndrome was referred for planned caesarean section. She was 4th gravida with 3 abortions in her 15 years of active married life. She had past history of cerebrovascular accident 2 years back with right side hemiplegia for which she was hospitalized and given treatment in the form of Enoxaparine, warfarin, valproate, phenytoin, aspirin and atorvastatin and fully recovered after 12 days of treatment .MR venogram showed extensive venous sinus thrombosis of superior sagittal venous sinus, right transverse, right sigmoid and right internal jugular vein sinus. She was advised for APL antibody titre, which showed positive IgG and IgM antiphospholipid antibody and negative anticardiolipin antibody. From above report and clinical criteria, she was diagnosed as a case of APLS. She was advised to continue anticonvulsant and anticoagulant treatment. Diagnostic laparoscopy was done for bad obstetric history and secondary infertility, which was normal. She was advised to stop warfarin and valproate according to obstetrician's advice. Patient switched over to low molecular weight heparin and Aspirin. She conceived after 4 months. Her coagulation profile was monitored throughout pregnancy.

On examination patient has normal vital parameters. Respiratory, central nervous systems and cardiovascular system were normal.

Her routine blood investigations electrocardiogram and 2-D Echo were normal. She was on tab aspirin 75mg OD and inj. Enoxaparin 0.6 mg S.C. BD. Her coagulation profile- PT-test 12.7 sec, (control 13.7). INR 0.9, aPTT 40.4 sec, fibrinogen 5.7 gm/l, platelet count 1.57 lakh/cm^3. Tab aspirin was stopped seven days prior to surgery and last dose of LMWH was taken 12 hr prior surgery.

Written informed consent was taken for high risk of anaesthesia. In the operation theatre a large-bore(18G) intravenous cannula was placed on dorsum of left hand and the patient received antacid prophylaxis in the form of inj. Ranitidine 50mg ,inj ondansetron 4mg intravenously (IV) given. ECG, pulse oximeter and NIBP, urine output were monitored. A 15 degree wedge was given for left uterine displacement. Her vital parameters were PR 90 /min, BP 120/84 mm Hg and RR 20/min. In view of ongoing anticoagulant therapy it was decided to administer general anaesthesia. Premedication, inj.glycopyrrolate 0.2 mg IV was given. Pre-oxygenetation with 100% O_2 for 5 min was done. In Induction, inj. Thiopentone sodium 300mg IV and succinylcholine 100 mg IV was given. The patient was intubated with a 7 mm sized oral cuffed endotracheal tube and ventilated with Bain circuit. . Anaesthesia was maintained with O_2/N_2O at

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50:50, Sevoflurane (0.4-0.8%) and Inj.vecuronium. A healthy male baby was delivered with normal APGAR score. Inj. Methargin 0.2mg IV was given and oxytocin (20 units in 500 ml 5% Dextrose) IV infusion was started. Inj.fentanyl 75µg IV was given. inj bupivacaine 0.25% 20 cc local infiltration was done at surgical site. She was reversed with Inj. Glycopyrrolate 0.4 mg IV and Inj.Neostigmine 3 mg and extubated after adequate recovery and thorough suctioning. She was shifted to post anaesthesia care unit and observed for 24 hr. Intraoperatively her pulse rate and blood pressure were within normal range and a total of 1L of crystalloids were infused and urine output was 300 ml. Her further course in the hospital was uneventful.

DISCUSSION

APLS is defined by the persistent presence of antiphospholipid antibodies in patients with recurrent venous or arterial thromboembolism or pregnancy morbidity.[1] Anti-thrombotic therapy is the mainstay of treatment.[2,3] The reported incidence of APLS in pregnant women is approximately 2%.[10] The diagnostic criteria are clinical as well as laboratory based.

Clinical criteria[4,5,6]

1. Vascular thrombosis: One or more objectively confirmed episodes of arterial, venous or small vessel thrombosis occurring in any tissue or organ
2. One or more unexplained deaths of a morphologically normal foetus at or beyond the 10th week of gestation; or one or more premature births of a morphologically normal neonate before the 34th week of gestation, Three or more unexplained consecutive spontaneous abortions before the 10th week of gestation

Laboratory criteria[4,5,6] are one or more of Lupus anticoagulant, Anticardilipin antibody of IgG or IgM and anti β-2glycoprotien-1 antibody IgG or IgM. Laboratory criteria are positive on two occasion at six week apart are the diagnostic.

APLS is called primary APS when antibodies occur alone and secondary APS is when it is associated with SLE, Rheumatic disease.[1,2,8,9] APLS patients are at high risk to develop thromboembolic phenomena, thrombocytopenia and bad obstetric outcome. There are studies regarding successful pregnancy outcome treated with aspirin and low dose heparin.[5]

Differential diagnosis of APLS with thrombocytopenia includes TTP, Heparin induced thrombocytopenia and DIC. Antithrombotic management can be challenging because even though with normal lab. Reports thromboembolism or bleeding can occur. So the anaesthetic management cannot be decided on lab test reports. Minor alterations in the anticoagulation, infection, and surgical insult may trigger widespread thrombosis. The incidence of thrombosis is highest during perioperative periods. Preoperatively during the withdrawal of heparin, postoperatively during the period of hypercoaguability despite heparin therapy, or before re-establishing adequate anticoagulation because of which we continued anticoagulants as patient had an attack of thrombosis in the past and we managed the case with general anaesthesia.

CONCLUSION

APLS is one of the most commonly acquired hypercoaguable disease. So the mainstay of treatment is antithrombotic therapy. The resources to manage major complications are essential. A successful outcome requires multidisciplinary management in order to prevent thrombotic or bleeding complications and to manage perioperative anticoagulation.

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CASE REPORT

A Rare Case of Severe Aortic Coarctation Amounting to Functional Interruption

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KEY WORDS : Coarctation, Interruption, Stenting

ABSTRACT

Coarctation of the aorta describes the congenital narrowing of any part of the descending thoracic or abdominal aorta. However, it typically refers to narrowing of the proximal thoracic aorta-, at the level of the ductus or ligamentum arteriosum. Coarctation is the third most prevalent form of congenital heart diseases, with an incidence of ~20 to 60 patients per 100,000 live births accounting for 5 to 8% of all congenital heart defects[1,2].

The case under the report was a male patient presented with right side hemiparesis. On examination, a significant blood pressure difference was noted between upper and lower limbs. 2D echo findings suggested severe juxtaductal coarctation of aorta. CT angiography revealed severe arch coarctation amounting to interruption of aortic arch distal to origin of left subclavian artery. Postoperative CT angiography showed correct stent placement and establishment of distal flow.

INTRODUCTION

A spectrum of morphological abnormalities are associated with aortic coarctation from a discrete stenosis distal to the left subclavian artery to a hypoplastic aortic arch and isthmus that typically presents in infancy. Arch hypoplasia occurs in approximately ~25 to 50% cases. In some cases, coarctation is caused by a long tubular stenosis of the descending thoracic aorta. Thoracic aortic coarctation is frequently combined with other congenital defects-, like bicuspid aortic valve, which occurs in 20 to 85% patients[3]. Additional defects may further complicate the approach to patient management.

CASE REPORT

A 16 year old male presented with complain of right side hemiparesis since an age of 5 years and vomiting. On examination: - there was discrepancy in blood pressure of upper and lower limbs with blood pressure of upper limb-170/90 mm Hg and blood pressure of lower limb-120/70 mm Hg. Other routine blood investigations were within normal limits.

2D Echo findings suggested severe juxtaductal coarctation of aorta, severe concentric left ventricular hypertrophy, mild AR. The patient therefore was referred for CT angiography for further evaluation.

CT ANGIOGRAPHY was performed on a 128 slice SOMATOM Definition AS+; (Siemens Healthcare, Forchheim, Germany). The scan range extended from thoracic inlet to the diaphragm. Tube voltage was 120kV, tube current was 80 mAs, pitch was 1.2. The CT data acquisition duration was 2-3 s. CT angiography acquisition with an automated bolus tracking technique was initialised when enhancement in the ascending aorta exceeded 100 HU.

The non-ionic iodinated contrast material (350mg /ml; Omnipaque (Iohexol); GE Healthcare, Shanghai, China) was administered with a dual-chamber mechanical power injector (Medtron, Germany) via a 20-gauge cannula inserted into an antecubital vein (1 ml/kg). After contrast injection, a given mass of saline chaser (half that of the contrast material) was administered at the same rate as the contrast material. Image reconstruction and reformation CT images were reconstructed. These images were reviewed with MIP, SSD and Volume Rendering.

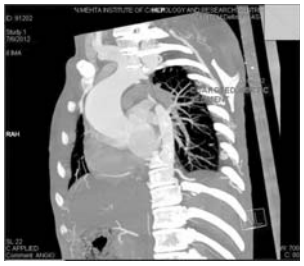

Fig. 1

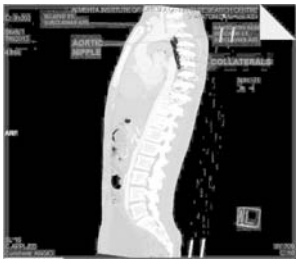

Fig. 2

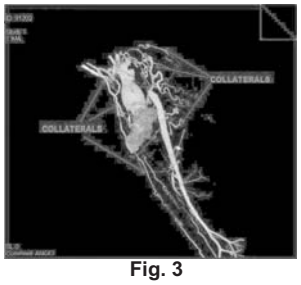

Fig. 3

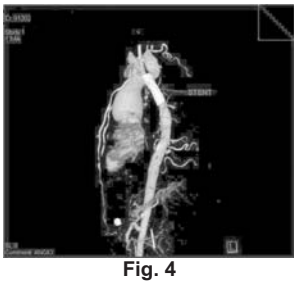

Fig. 4

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CT Findings were – severe aortic coarctation amounting to functional Interruption of aortic arch with involvement of origin of left subclavian artery. The length of coarcted segment was approximately -3.5 cm.

Multiple mediastinal, posterior chest wall, para vertebral and intercostals collaterals bypassing coarctation were seen as described below-

- Dilated right subclavian artery → paravertebral arteries → descending thoracic aorta
- Dilated right internal mammary artery → epigastric arteries → right external iliac artery.
- Celiac trunk → phrenic arteries → epigastric arteries.

Right internal mammary artery was dilated due to increased collateral flow. Left internal mammary artery was not dilated due to involvement of left subclavian artery origin by coarctation.

Inferior rib notching is seen on right side due to intercostals collaterals.

Rest of descending thoracic and abdominal aorta was normal.

OPERATIVE DETAILS

Patient was managed with stent placement in coarcted segment.

Balloon mounted stent (5014) Palmaz (cordis, Jhonson & Jhonson) was self expanded.

Maxi-LD Balloon (cordis, J & J) was inflated at 20 mm Hg for 10 seconds.

No immediate post procedural complications seen.

FOLLOW-UP

Post operative follow-up CT angiography was performed immediate post operatively and after 6 months - which revealed patent stent in situ without any leak[6]. Patient was followed up for two years without any complications.

DISCUSSION

The exact mechanism of native coarctation is not entirely understood. Prenatal ultrasound abnormalities suggest that coarctation may already be present in utero. Substantial evidence suggests that coarctation is part of a more widespread vascular condition. Medial degeneration, with increased collagen and reduced smooth muscle and elastin, has been noted in the aortic wall above and below the coarctation as early as 24 hours postpartum[4]. Associated functional anomalies, including altered baroreceptor activity, reduced arterial reactivity and compliance, and increased arterial stiffness in the precoarctation vasculature, have also been noted. It is likely that these changes contribute to the pathophysiology of hypertension, and simply fixing the mechanical obstruction does not in itself reverse the structural and functional abnormalities in the proximal vasculature, resulting in the likelihood of late hypertension and its consequences.

CLINICAL PRESENTATION

Most cases of coarctation are diagnosed in children, with approximately a third presenting with critical coarctation in infancy. Severe stenosis is unmasked when the ductus arteriosus closes, causing cardiac failure due to the aortic obstruction. If the ductus remains patent, critical stenosis may remain undiagnosed. Less severe degrees of narrowing allow collaterals to become established around the coarctation, and may escape diagnosis until later in childhood. Approximately 20% of patients do not present until adulthood. The usual clinical picture of late presentation in children and adults is one of incidental hypertension. Occasionally, patients present with heart failure, aortic rupture or dissection, infective endocarditis, or stroke[5].

DIAGNOSIS

Despite the advances in prenatal detection of congenital heart defects with fetal echocardiography, the diagnosis of coarctation 'in utero' is notoriously difficult. If antenatal ultrasound is suggestive, careful postnatal follow-up with echocardiography is warranted. Signs in infancy include features of cardiac failure and/or systolic murmur with discrepant arm-to-leg pulses or blood pressures. Clinical examination in children or adults may reveal radio-femoral delay and difference of blood pressure between the upper and lower limbs, in the presence or absence of arm hypertension. There may be palpable collateral vessels around the scapula and evidence of a systolic murmur in the axilla or back.

Routine investigations may give a clue to the diagnosis. Electrocardiography may be normal or show evidence of left ventricular strain or hypertrophy. Chest radiography may demonstrate an enlarged heart, abnormal cardiac contour, and in older children/adults, ascending aortic enlargement and rib notching, caused by collateral vessels. The diagnosis can be confirmed by several techniques including transthoracic echocardiography.

CT offers several advantages over echocardiography, giving an overview of the relevant aortic morphology and anatomical relationships, including the presence of large collateral vessels. Multidetector computed tomographic angiography (MDCT) allows rapid acquisition and high-resolution imaging of the thoracic aorta and its branches, giving excellent anatomical information.

This case is rare as the length of coarcted segment is large - (3.5 cm) with well-established collateral circulation.

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CASE REPORT

Emergency Pancreatico-Duodenectomy (Whipple Procedure) for Blunt Abdominal injury having complete transection of 1st and 3rd part of Duodenum and Neck of Pancreas

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KEY WORDS : Coarctation, Interruption, Stenting

ABSTRACT

Introduction

Blunt abdominal injury having complete transaction of 1st and 3rd part of duodenum and neck of pancreas is a rare injury. The typical mechanism by which this occurs is overstretching of the pancreas and crushing of duodenum across the vertebral column during blunt abdominal trauma. The management of this injury depends on the location and extent of the injury.

Case presentation

14 year old male child presented with blunt abdominal trauma as the h\o of fell down from the 1st floor onto the end of a handlebar of bicycle. He arrived in the emergency room with unstable vital signs. On Ultrasonography there was gross free fluid in peritoneal cavity and 5×4cm hematoma on Rt lobe of liver. An emergency exploratory laparotomy was performed; emergency pacreatico-duodenectomty (Whipple's procedure) was done. The recovery after surgery was completely uneventful.

INTRODUCTION

Injury of the duodenum and pancreas, either single or in combination, pose serious challenge to a treating surgeon. The deep retroperitoneal, protected location of these two organ leads to a low incidence of injury. But when they do get injured, the detection is difficult, management problematic and complication serious. The age old surgical adage: "Duodenum small but deadly, the pancreas not your friend and they are filled not with juices, but with black ingratitude". The most common associated injuries are to the liver, spleen, kidney, stomach, colon, and major blood vessels. Completetransaction of 1st and 3rd part of duodenum and neck of pancreas is even rarer, and very few case reports have been published. Here, we present a case of a 14 year old male patient with a complete transaction of 1st and 3rd part of duodenum and neck of pancreas that was managed successfully by emergency pacreatico-duodenectomty (whipple's procedure).

Case presentation

- 14 year old male child presented with blunt abdominal trauma in emergency with h\o of fell down from the 1st floor onto the end of a handlebar of bicycle. After 3 hour of injury...
- Clinical presentation:-Pulse 120|min, BP 90|70 mmHg. Per abdominal examination there was distention, guarding tenderness present,No any other external injury mark.
- USG abdomen thorex: - 5×4cm hypoechoic lesion in Rt lobe of liver, gross free fluid noted in peritonial cavity which was haemorragic on aspiration.
- After clinical examination and USG report, we planned for exploratory laprotomy

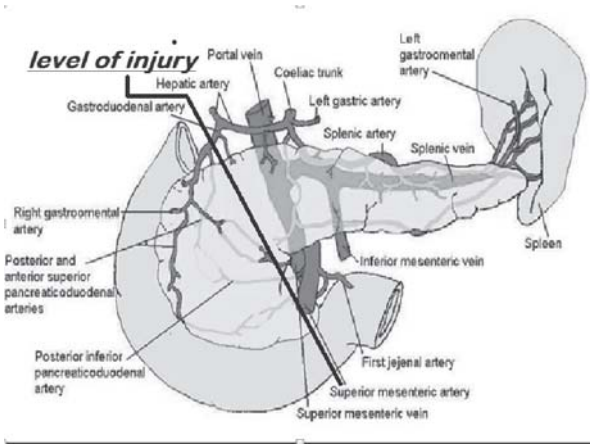

Fig. 1.: Schematic diagram showing level of injury.

Procedures: -Adequate homeostasis achieved and putting gelatin sponge on anterior liver surface, Complete duodenum mobilized with head of pancreas and than remaining part of duodenum dissected out, then 1st part of duodenum closed with silk 2-0 in two layers, Pancreaticogastrostomy in single layer with prolene 3-0

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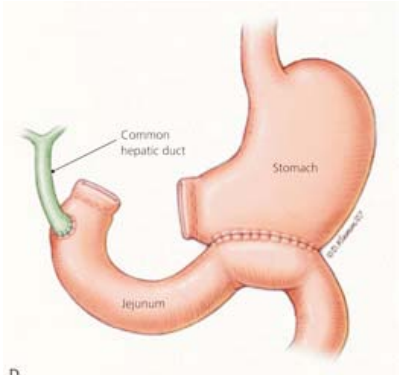

Fig 2. Schematic diagram of PG+CD+GJ

interrupted stitches. Cholecystectomy with Cholydocod-uodenostomy with prolene 3-0 interrupted stitches; Gastro- jejunostomy with silk 2-0 in two layers, Feeding jejunostomy distal to Gastro-jejunostomy was done. Ryles tube and two abdominal drains were kept one at anastomatic site and other in pelvic fossa. Pt was put on elective venti for one day, octreotide was given for seven days after surgery at a dose of 50 µg three times a day as the pancreas was soft and our patient did not have any contraindications for octreotide treatment. On the day after surgery, the indwelling drains contained high levels of amylase (> 25,000 U/l) and lipase (> 80,000 U/l). The high levels decreased to normal serum levels within four days Feeding J was started on 7th POD. Patient was discharged on 17th post operative day with uneventful postoperative course. Upper GI scopy performed at follow up 1 year after his operation revealed that the orifice of distal pancreas at the pancreaticogastrostomy site was patent and blood glucose level was normal.

DISCUSSION

The incidence of pancreatic and duodenal injury is low with pancreatic injuries ranging between 1 to 9% and duodenal injuries 3 to 5% of all abdominal injuries. The penetrating injuries are 3 to 4 times more common than blunt injuries[1,2,3].

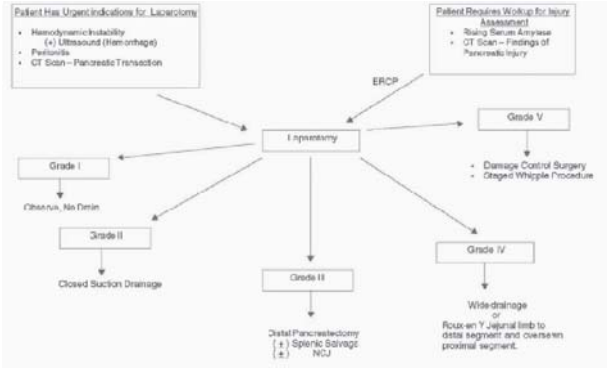

Fig 3. Flowchart of Pancreatic Injury.[1,2.]

The morbidity of duodenal injury is about 30 to 60% and in pancreatic injury 30 to 40%.

The mortality rate in duodenal injury 5 to 30% and in pancreatic injury 9 to 35%. And in combine injury about 20 to 40%[1,2,3.].

The signs of intraabdominal bleeding or peritonitis following bowel injury with intraabdominal contamination usually indicate the necessity for emergency surgery, at which time concomitant blunt pancreatic trauma may be detected.

Preservation of the pancreas, and reconstruction of the pancreatic-intestinal continuity following pancreaticoduodenectomy must be accomplished between the remnant pancreas and the jejunum, as the propensity for leakage and disruption at the site of the pancreaticojejunostomy is a major reason for morbidity and death. Pancreaticogastrostomy (PG) is an alternative method for restoring pancreatic-intestinal continuity after pancreaticoduodenectomy, which has resulted in lowering the operative mortality from 25% to 8%[5,6.]. Furthermore, islet cell concentration in the tail of the pancreas has been shown to be significantly greater than inthe body and head. This method preserves all functioning pancreatic tissue, and therefore avoids the possibility of pancreatic insufficiency and/or diabetes[7].

American Association for the Surgery of Trauma – Organ Injury Scale (AAST-OIS) for duodenum (8).

Grade		Injury description	AIS
I	Hematoma	Involving single portion of the duodenum	2
	Laceration	Partial thickness, no perforation	3
II	Hematoma	Involving more than one portion	2
	Laceration	Disruption < 50 % of circumference	4
III	Laceration	Disruption 50–75 % circumference of D2	4
		Disruption 50–100 % circumference of D1, D3, D4	4
IV	Laceration	Disruption > 75 % circumference of D2	5
		Involving ampulla or distal common bile duct	5
V	Laceration	Massive disruption of duodeno-pancreatic complex	5
	Vascular	Devascularization of duodenum	5

Fig 4. Grades of Duodenal Injury.[1,2.]

Moreover, the procedure is conservative, and the anastomosis is not technically difficult5[5,6,7.].

As the body of the pancreas lies directly posterior to the stomach, it is relatively easy to anastomose the organs under minimal tension, and once the anastomosis is completed, the organs are fixed in juxtaposition[5,6,7.].

Furthermore, gastric acid pH is thought to be unfavourable for proteolytic activity. This lessens the

chance of postoperative pancreatitis, autodigestion with hemorrhage, and abscess formation. On follow-up, spontaneous closure of the orifice on PG with atrophy of the distal pancreas were also identified. In the stomach there is minimal activation of enzymes, the orifice on PG might gradually close without any obstructive symptoms, which could lead to atrophy of the distal pancreas. but still beta cell function is adequate for preventing diabetes mellitus[5,6,7,8].

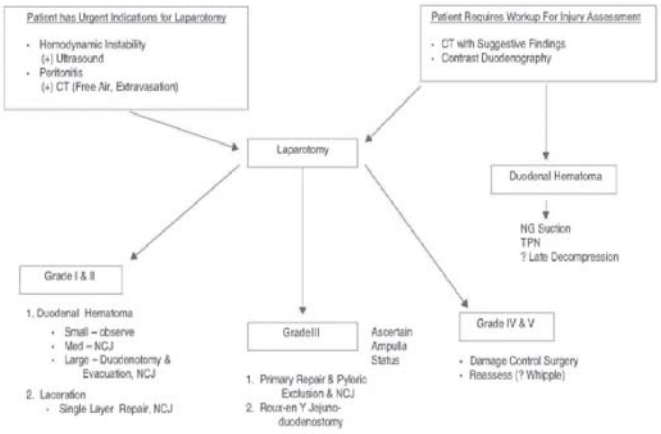

Fig 5. Flowchart of Duodenal Injury.[1,2.]

CONCLUSIONS

- The propensity for leakage and disruption at the site of the pancreaticojejunostomy is a major reason for morbidity and death after pancreaticoduodenal resection. Because it is less prone to leakage and disruption, pancreaticogastrostomy has been reintroduced as a possible alternative to pancreaticojejunostomy.
- PG is a safe and effective procedure for preserving the endocrine function of pediatric patient with critical pancreatic injury

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying image.

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