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Dear Members,

Wishing you all a very happy ending of this winter season.

As you all know that with the ending of one season, other starts. But since last few years, we all witness sudden change of weather in between or some intermittent phase where more than one season exists. Its commonly known as effect of Global Warming. But friends, have you observed similar kind of behavioral patterns among human beings too? That pattern changes frequently. That is known as impact of Globalization.

With the advancement of Information Technology and Social media, any kind of information spreads with jet speed. If information is negative, the speed gets doubled. And that prevails every where. Because that's how the human brain works. That's how we have grown up. But friends, yes, with conscious and continuous efforts, that can be transformed toward positive side. Though it's exhaustive job but in long run, it certainly pays. Our sincere request to medical fraternity friends, looking to present scenario of patient doctor relationship, the way it deteriorates so rapidly, let us have a beginning from our side to improve it.

Certainly we at IMA GSB are witnessing very good impact of advancement of technology by involvement of local branch leaders through social media. There is very good day to day interaction among them all. Which has started bringing them closer to each other; sharing of their local branch activities and many more things to evolve.

Friends, last month GSBIMA president Dr Atul Pandya has took the lead of an unique project with support of Gujarat Psychiatry Association "JI VISH" that is to prevent suicidal cases among students all over Gujarat.

We need your active and affirmative participation in IMA activities. That will certainly boost our morale.

Our heartiest congratulations to Imm. Past President Dr. Chetan Patel for achieving "Best Adjudged State President" award during NATCON-2015, New Delhi.

At the end, our best wishes are always there with all exam going students, particularly 10th & 12th as they are considered as benchmark for their career.

Good bye, Jay IMA, Take Care.

DR. ATUL D. PANDYA  
(President, G.S.B.I.M.A.)

DR. JITENDRA N. PATEL  
(Hon. State Secy. G.S.B.I.M.A.)
Dear friends,

We are thankful to all the central council members of GSB IMA for putting their faith, trust and confidence in us and giving the charge of prestigious Gujarat Medical Journal (GMJ) for this year also. On our side, we promise to see that the faith and trust that is put in us is full filled and for that, we shall try our best. GMJ is entering in its 71 years of publication. We are well aware that in these years GMJ has carved out its name as a journal of research oriented and academic minded people, in the medical field. All the editors in past, have tried their best to give a name and fame to this journal and we are enjoying their fruits. But we are aware, that increases our responsibility also. Moreover, our journal is an Indexed Journal, Indexed in InMed. We shall have to maintain that standard of our journal. We shall have to work hard and will have to be vigilant.

Our country and particularly, Gujarat has entered in the field of medical tourism. People from developed and under developed countries come here for treatment and we provide world best treatment to them at a cheaper rates then that is available in developed countries. Apart from big cities of Gujarat like Ahmedabad, Surat, Vadodra and Rajkot-Bhavnagar, even small centers like Anand and Nadiad provide world class treatment in the field of cardiology and nephrology. Our hospitals and expertise are world class and that pushes the medical tourism in Gujarat far ahead. From our own domestic population also we get large number of patients. This provides opportunities for research to our doctors. Now we have better infrastructure facilities for data collection and access to world data, for comparison. It has provided a big boost to research wok in our state. We appeal our colleagues to send their research articles and papers for publication in GMJ. This will help our other colleagues and also government in handling and controlling certain diseases. Government will also be able to determine where more efforts are required.

In this issue, you will find Original articles, Research articles and Case studies on various subjects. Without making any compromise in our laid down policy and standards, we have made all the efforts 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.

In this issue, you will find Original articles, Research articles and Case studies on various subjects. Moreover, from this issue, we have started a new feature- a new column- Readers’ Forum, where our experienced readers can share their observations and experience with other members and esteemed readers can give their opinion, comments and remarks.

Our sincere thanks to GSB president Dr. Atul D. Pandya and hon. secretary Dr. Jitendra N. Patel for encouragement and suggestions. We are grateful to GSB past presidents Dr Kirtibhai Patel, Dr. Jitubhai Patel and Dr. Mahendrabhai Desai for their guidance and help. Our particular thanks to GMJ ex. editor Dr. Amitbhai Shah and our editorial board member Dr. Chinmay Shah (Bhavnagar) for all sorts of help and guidance that they are providing us time to time.

With regards,

DR. K. R. SANGHAVI
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To study usage of antimicrobials in 150 cases of fever admitted in medicine ward

Dr. Parth Desai*, Dr. Sumit Patel**

*Junior Lecturer, Pharmacology, Smt. NHL Medical College, Ahmedabad  
** Assistant Professor, Pharmacology, GCS Medical College, Ahmedabad

KEY WORDS : Fever, Antimicrobials, Rationality

ABSTRACT

Aim : To study the usage of antimicrobials in patients admitted in the medicine wards.

Methodology : It was a prospective, observational and non-interventional study conducted over a period of 12 months. Information of all the patients included in the study like age, sex, duration of stay, brief medical history, investigations, diagnosis, body temperature, information about medicines given- their dose, frequency, route and duration were recorded from the day of admission till discharge from the medicine wards.

Results : A total of 150 patients were enrolled in the study including 89 (59.33%) males and 61 (40.67%) females. Highest number of patients were affected by diseases of respiratory system (45, 30%) followed by haemopoietic system (35, 23.33%). Lower respiratory tract infections (32, 21.33%) were the most common diagnosis of patients enrolled in the study followed by malaria (31, 20.67%). Antimicrobials (144, 96%) were the most frequently prescribed drugs followed by drugs acting on gastrointestinal system (143, 95.33%), analgesic and anti-inflammatory drugs (141, 94%) and vitamins, minerals & dietary supplements (111, 74%).

Conclusion : Fever is a common symptom with which a patient presents to a physician and is considered inherently noxious by both. The most commonly used antimicrobial was amoxicillin as in 47 (31.33%) patients. Keeping current evidence in mind antimicrobials should be given after assessing the cause of the infection. Further studies are needed at different locations to compare our findings and add to the body of evidence.

INTRODUCTION

Regulation of body temperature requires a delicate balance between the production and loss of heat; the hypothalamus regulates the set point at which body temperature is maintained. Normal human body temperature (normothermia or eusthermia) is a concept that depends upon the place of body at which the measurement is made, the time of day and level of activity of the person. There is no single number that represents a normal or healthy temperature for all people under all circumstances using any place of measurement (1). But nevertheless, according to studies of healthy individuals 18–40 years of age the maximum normal oral temperature is 37.2°C (98.9°F) at 6 A.M. and 37.7°C (99.9°F) at 4 P.M.; these values define the 99th percentile for healthy individuals (2).

Fever has been defined as “a state of elevated core temperature, which is often, but not necessarily, part of the defensive responses of multicellular organisms (host) to the invasion of live (microorganisms) or inanimate matter recognized as pathogenic or alien by the host” (3). The febrile response (of which fever is a component) is a complex physiologic reaction to an infection, tissue damage, inflammation, graft rejection, or malignancy. In general, fever is an elevation of body temperature that exceeds the normal daily variation and occurs in conjunction with an increase in the hypothalamic set point (e.g., from 37°C to 39°C). An A.M. temperature of >37.2°C (>98.9°F) or a P.M. temperature of >37.7°C (>99.9°F) would define a fever (2).

Fever can be due to infectious (e.g. upper respiratory and lower respiratory tract infections, Gastro-Intestinal Infections etc.) or non-infectious (e.g. drug induced, allergic etc.) causes. Many studies done on hospital acquired fever indicate infection as a cause of fever in 37% to 74% of patients, whereas a noninfectious etiology was identified in 3% to 52% (4-10). The most common infectious causes included urinary tract infection, pneumonia, sinusitis, and bloodstream infection (4,7,9,10). The most common noninfectious causes were procedure related (e.g., blood transfusion), malignancies, and ischemic conditions (e.g., myocardial infarction, pulmonary embolism) (4,7,10).

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are used as antipyretics while antibiotics are frequently prescribed in patients suffering from fever due to
infectious causes and sometimes even in non-infectious cases. Out of the three studies describing the use of antibiotics in response to fever\textsuperscript{4,7,9}, in patients determined to have a bacterial cause of fever, antibiotics were prescribed at onset of fever in 66% to 92% of febrile episodes. Rates of antibiotic use for patients with a non-infectious cause of fever ranged from 29% to 55% for a mean duration of 6.6 to 9.6 days\textsuperscript{4,7,9}. Use of antibiotics in fever with non-infectious aetiologies does no good in treating a patient but can certainly increase the chances of Adverse Drug Reactions (ADRs) and emergence of drug resistance.

In most febrile patients, empiric antibiotic therapy should be deferred pending further evaluation\textsuperscript{11}. However, empiric antibiotic therapy is sometimes warranted. Prompt broad-spectrum antimicrobials are indicated for febrile patients who are clinically unstable, even before infection can be documented. These include patients with hemodynamic instability, those with neutropenia (neutrophils < 500/mcL), others who are asplenic (surgically or secondary to sickle cell disease) or immunosuppressed (including individuals taking systemic corticosteroids, azathioprine, cyclosporine, or other immunosuppressive medications), and those who are HIV infected\textsuperscript{11}.

It has been observed that different doctors differ with regard to practice for prescribing antimicrobials in management of patients with fever. So the present study was proposed to collect and analyze information like practice of doctors with regard to usage of antimicrobials in management of fever.

### MATERIALS AND METHODS

A prospective observational study of one year duration was undertaken and total of 150 patients admitted to medicine wards with fever as one of the main complaints were included in the study.

The following inclusion and exclusion criteria were taken in account for selecting the suitable participants for the study and to avoid bias.

#### Criteria for inclusion of participants:

- Patients admitted to either male or female medicine wards with fever as one of the chief complaints.
- Patients of age 18 years and above.
- Patients who stay more than 24 hours in medicine wards

#### Criteria for exclusion of participants:

- Patients who were discharged or transferred to other department within 24 hrs of admission.
- Patients who were uncooperative.
- Patients who were not willing to participate in study.

The patients willing to participate in the study were explained about the purpose and method of the study in the language they understood and only those patients were enrolled, who were willing to give written consent in the informed consent form. Confidentiality in respect to participating patients was maintained at all levels.

#### Collection of data:

Information of all the patients included in the study like age, sex, duration of stay, brief medical history, investigations, diagnosis, information about medicines given - their dose, frequency, route and duration were recorded in case record form from the day of admission till discharge from the medicine wards.

### OBSERVATIONS AND RESULTS

1) **Total number of patients enrolled, grouped according to their sex and age.**

Out of the 150 patients, 89 (59.33%) were male patients and 61 (40.67%) were female patients. Highest number of patients were in the age group of 18-30 years (40, 26.67%) followed by age group of 31-40 years (37, 24.67%), while the least were in age group of 51-60 years (18, 12%).

2) **Diseases / conditions prevalent in patients included in study:**

Most number of patients enrolled in the study were affected due to diseases of respiratory system (45, 30%) followed by diseases affecting haemopoietic system (35, 23.33%). Other systems affected were gastrointestinal system (32, 21.33%), genitourinary system (13, 8.67%) while in 21(14%) patients cause of fever was not diagnosed. The least affected patients were due to diseases affecting central nervous system and musculoskeletal disorders with only 2 patients affected in each of them

3) **Usage of antimicrobials**

Antimicrobials were used in 144 (96%) patients out of the total 150 patients enrolled in the study.

a. **Different antimicrobials used in patients enrolled in the study:**

Most common antimicrobial which was prescribed was amoxicillin (47, 31.33%) singly or in fixed dose combination, followed by metronidazole (33, 22%), artesunate (32, 21.33%) and ceftriaxone (30, 20%). Different cephalosporins including ceftriaxone, cefotaxime, cefixime, cefipime and cefoperazone were prescribed to 66 (44%) patients.
Table I: Antimicrobials used in patients enrolled in the study:

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Antimicrobials</th>
<th>Number of patients n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Metronidazole</td>
<td>33 (22)</td>
</tr>
<tr>
<td>2</td>
<td>Artesunate</td>
<td>32 (21.33)</td>
</tr>
<tr>
<td>3</td>
<td>Ceftriaxone</td>
<td>30 (20)</td>
</tr>
<tr>
<td>4</td>
<td>Amoxicillin</td>
<td>25 (16.67)</td>
</tr>
<tr>
<td>5</td>
<td>Amoxicillin+Clavulanic Acid</td>
<td>22 (14.67)</td>
</tr>
<tr>
<td>6</td>
<td>Ciprofloxacin</td>
<td>20 (13.33)</td>
</tr>
<tr>
<td>7</td>
<td>Cefotaxime</td>
<td>20 (13.33)</td>
</tr>
<tr>
<td>8</td>
<td>Choroquine</td>
<td>19 (12.67)</td>
</tr>
<tr>
<td>9</td>
<td>Levofloxacin</td>
<td>18 (12)</td>
</tr>
<tr>
<td>10</td>
<td>Azithromycin</td>
<td>11 (7.33)</td>
</tr>
<tr>
<td>11</td>
<td>Cefixime</td>
<td>11 (7.33)</td>
</tr>
<tr>
<td>12</td>
<td>Doxycycline</td>
<td>6 (4)</td>
</tr>
<tr>
<td>13</td>
<td>Ofloxacin</td>
<td>6 (4)</td>
</tr>
<tr>
<td>14</td>
<td>Primaquine</td>
<td>5 (3.33)</td>
</tr>
<tr>
<td>15</td>
<td>Albendazole</td>
<td>4 (2.67)</td>
</tr>
<tr>
<td>16</td>
<td>Norfloxacin</td>
<td>3 (2)</td>
</tr>
<tr>
<td>17</td>
<td>Ornidazole</td>
<td>3 (2)</td>
</tr>
<tr>
<td>18</td>
<td>Cefipime</td>
<td>2 (1.33)</td>
</tr>
<tr>
<td>19</td>
<td>Cefoperazone</td>
<td>2 (1.33)</td>
</tr>
<tr>
<td>20</td>
<td>Amikacin</td>
<td>2 (1.33)</td>
</tr>
<tr>
<td>21</td>
<td>Rifaximin</td>
<td>2 (1.33)</td>
</tr>
<tr>
<td>22</td>
<td>Rifampicin</td>
<td>2 (1.33)</td>
</tr>
<tr>
<td>23</td>
<td>Isoniazid</td>
<td>2 (1.33)</td>
</tr>
<tr>
<td>24</td>
<td>Ethambutol</td>
<td>2 (1.33)</td>
</tr>
<tr>
<td>25</td>
<td>Pyrizinamide</td>
<td>2 (1.33)</td>
</tr>
<tr>
<td>26</td>
<td>Cefipime+Subbactam</td>
<td>1 (0.67)</td>
</tr>
<tr>
<td>27</td>
<td>Fluconazole</td>
<td>1 (0.67)</td>
</tr>
<tr>
<td>28</td>
<td>Terbinaine</td>
<td>1 (0.67)</td>
</tr>
<tr>
<td>29</td>
<td>Gentamicin</td>
<td>1 (0.67)</td>
</tr>
<tr>
<td>30</td>
<td>Vancomycin</td>
<td>1 (0.67)</td>
</tr>
<tr>
<td>31</td>
<td>Ertapenem</td>
<td>1 (0.67)</td>
</tr>
<tr>
<td>32</td>
<td>Cloxacillin</td>
<td>1 (0.67)</td>
</tr>
</tbody>
</table>

Figures in parentheses shows percentage out of total patients enrolled in the study

b. Use of antimicrobials simultaneously grouped according to system affected:

Total 68 (47.22%) patients out of the total 144 patients receiving antimicrobials were receiving only 1 antimicrobial while 49 (34.03%) and 27 (18.75%) patients were receiving 2 and 3 or more antimicrobials simultaneously respectively.

Fever is a common morbidity with which a patient presents to a physician. Fever as such should be considered as a sign rather than the disease itself. It can lead to diagnosis of various diseases if intelligently observed and analysed.

Antimicrobials are among the most commonly prescribed drugs on a worldwide basis. But it has been observed that 64% of the total antimicrobial prescribed is either not indicated or inappropriate in terms of drug selection or dosage\(^{(11)}\). In many cases antimicrobials are used without an appropriate bacteriological basis. Not all of these massive uses can be justified. In fact, irrational prescribing of these drugs is known to take place throughout the world. Availability of large number of drugs in the market makes education of prescriber difficult which make the selection of a proper agent intricate and may eventually increase cost and side-effects of drug treatment, bacterial resistance and most importantly patient mortality.

With regard to use of antimicrobials, in this study we found that out of total 150 cases enrolled, 144 (96%) cases received antimicrobials. This shows a high tendency of physicians to prescribe antimicrobials in patients admitted with fever. 14 (9.33%) patients were having a non-infectious etiology, out of which 9 (64.29%) patients suffered from Alcoholic Liver Disease (ALD). Chronic alcohol exposure activates hepatic macrophages producing tumor necrosis factor α (TNF-α), which enter the hypothalamic circulation and stimulates release of local prostaglandins, resetting the hypothalamic thermal setpoint\(^{(11)}\). This factor is responsible for fever in these patients. Out of the 9 patients diagnosed as Alcoholic Liver Disease antimicrobials were prescribed to 8 of them. Being a non-infectious cause of fever it is surprising to observe such prescription rate of antimicrobials. But worthwhile to note is that bacterial infection is a serious and often fatal complication of patients with alcoholic liver disease and can prove fatal either directly or by precipitation of gastrointestinal bleeding, renal failure, or hepatic encephalopathy\(^{(14,15)}\). So antimicrobials were prescribed for prophylaxis and not actually to treat the disease itself.

Out of the total 21 patients of fever of unknown origin, 20 received antimicrobials. Empiric treatment of patient with antimicrobials ideally should be withheld till the diagnosis of the patient is confirmed. But factors like a feeling of obligation for giving quick relief to the patients, natural delay in getting the culture reports and many a times demands of the patient to take injections for quick relief...
and to maintain doctor-patient relationship antimicrobials are prescribed by the physicians\textsuperscript{19}. Lower respiratory tract infections were the most common diagnosis of patients (32, 21.33%) enrolled in this study and antimicrobials were prescribed to all the patients. It is said that excessive use of antimicrobials in this condition will lead to flourishing of resistant microorganisms. But clinicians are probably concerned that if they do not provide adequate antibiotic cover it may potentially harm their patients. Ongoing research into identifying patients likely to benefit from antibiotic treatment and identifying who can safely be managed without antibiotic treatment is an urgent priority. A study done by Winchester CC et. al concluded that antibiotic prescribing on the day of LRTI diagnosis was associated with reductions in hospital admissions and mortality related to respiratory infection. Antibiotics may help to prevent adverse outcomes for some patients with LRTI\textsuperscript{17}. Second most common diagnosis of patients in our study was malaria. 31 (20.67%) patients suffered from malaria out of which 30 were due to P. vivax infection and only 1 due to P. falciparum malaria. National malaria guidelines 2011 suggest using chloroquine in full therapeutic dose of 25 mg/kg divided over three days in all P. vivax cases\textsuperscript{18}. Artemisinin Combination Therapy (ACT) should be given to all confirmed P. falciparum cases found positive by microscopy or Rapid Diagnostic Test (RDT). ACT consists of an artemisinin derivative combined with a long acting antimalarial (amodiaquine, lumeфантрине, mefloquine or sulfadoxине-пириметамине)\textsuperscript{[19]} Out of the total 30 P. vivax cases, 21 (70%) received artesunate. Chloroquine was given to 14 (46.67%) patients with P. vivax infections out of which 4 also received artesunate. This clearly shows excessive prescription of artesunate which should be reserved for P. falciparum cases. Only one case with P. falciparum was noted and artesunate was administered to this patient. A study done to analyse prescription patterns of some urban and rural health facilities found that antimicrobials were prescribed to 69.4% of patients. It is worthwhile to note that in this study majority of patients (78.1%) had fever as one of the main complaints, so the results can be compared with our study. It was also observed in that study, rather than the type of illness, presence of fever showed significant association with higher rate of antimicrobial prescription\textsuperscript{[19]}. A study on patients admitted in ICU found that antimicrobial was prescribed in 83% of total patients enrolled\textsuperscript{[20]}. Out of the total 144 patients who received antimicrobials, 68 (47.22%) patients were receiving only 1 antimicrobial while 76 (52.78%) patients were receiving 2 or more antimicrobials simultaneously. A study conducted in a hospital in Mumbai reported that prescriptions with single antimicrobial agent were 48.7% and those with two or more antimicrobial drugs were 51.3%\textsuperscript{[21]}. These figures are very close to the figures of our study. Another studies carried out in a tertiary care teaching hospital in Bengaluru and Vadodara reports that prescriptions with two or more antimicrobial agents were 78.7% and 71.14% respectively\textsuperscript{[22,23]}. This shows even a higher trend of prescriptions with more than two antimicrobials. **CONCLUSION** Fever is a common symptom with which a patient presents to a physician. There is a wide-spread practice to use antimicrobials empirically. The reason being many-a-time patients are non-affording for costly laboratory investigations and other being the natural delay in getting laboratory reports. So antimicrobials are given empirically based on signs and symptoms of the patient to alleviate their suffering. Newer antibiotics with a broad range of spectrum should be reserved for more serious infections and should not be used in cases where they can be managed by older antimicrobials. A classic example found in this study was of P. vivax malaria which should ideally be treated with chloroquine. But in this study 70% of such cases received artesunate, a drug which should be kept reserved for P. falciparum malaria. A more restrained use of antimicrobials in cases of fever is the need of the hour. **REFERENCES** 1. Mackowiak PA, Wasserman SS, Levine MM. A critical appraisal of 98.6 degrees F, the upper limit of the normal body temperature, and other legacies of Carl Reinhold August Wunderlich. JAMA 268 (12): 1578–80. 2. Dinarello CA, Porat R. Fever and Hyperthermia. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J. Harrison’s Principles of Internal Medicine. 18th ed. USA: The McGraw-Hill Companies, Inc;2012:p:143-7. 3. IUPS Thermal Commission, Glossary of Terms for Thermal Physiology 2nd ed. Pflugers Arch. 1987;410:567-87. 4. Arbo M, Fine MJ, Hanusa BH, Selfcik T, Kapoor WN. Fever of nosocomial origin: etiology, risk factors, and outcomes. Am J Med 1992;95:505–12. 5. Bor DH, Makadon HJ, Friedland G, Dasse P, Komaroff AL, Aronson MD. Fever in hospitalized medical patients: characteristics and significance. J Gen Intern Med 1988;3:119–25.


Colonic interposition in corrosive stricture of esophagus: Experience in 35 patients

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ABSTRACT
Massive ingestion of corrosive agents, accidentally or in a suicidal attempt, results in severe injuries of the upper alimentary tract followed by stricture. The purpose of this retrospective study is to review our experience with colonic interposition in patients with corrosive esophageal strictures, to assess our results and to identify technical factors that may result in an improved outcome. From March 2011 to November 2014, 35 patients of corrosive stricture of esophagus were managed surgically by colonic interposition with (n=07) or without (n=28) esophagectomy. The left colon with transverse colon based on left colic artery and middle colic artery was used in 27 and 6 patients respectively. The right colon with transverse colon based on middle colic artery was used in 2 patients. The peristaltic orientation of graft consisted of isoperistalsis in 29 patients and antiperistalsis in 6 patients. Results of surgery were satisfactory with three postoperative deaths (8.5%) and complications in 10 patients (28.5%). The mean length of stay was 21.7 days with a range of 15 to 35 days. Cervical anastomotic leak was seen in 2 patients (5.7%). It resolved with conservative management in both patients over 2-4 weeks. Reflux was noted in 3 patients (8.5%) who responded to medical management. Redundancy of colon graft was detected in 3 patients (8.5%) in post-operative barium meal study without any symptoms. Esophageal reconstruction or bypass with colonic interposition for corrosive stricture is well accepted and proven definitive management with good results and quality of life.

INTRODUCTION
Massive ingestion of corrosive agents, accidentally or in a suicidal attempt, results in severe injuries of the upper alimentary tract. In case of extensive esophagogastric necrosis, emergency esophagogastrectomy is required to avoid the extension of corrosive lesions to adjacent organs and death. Conservative management of less severe lesions may lead to long or multiple esophageal strictures unsuitable for endoscopic dilation. In both circumstances, reconstructive surgery is necessary to restore digestive continuity.

The first successful esophageal reconstructive procedure was done by Roux in 1907, when he performed an antethoracic (subcutaneous) esophago-jejunoplasty. In 1911, Lexer added a cutanoplasty to the Roux procedure in an attempt to avoid jejunal necrosis. At the same time Kelling and Vuillet first employed the colon for the reconstruction of esophagus. In 1965 Belsey reported good functional results in using the left colon for the esophageal reconstruction. Long-segment colon substitution for the esophagus has been performed since 1964 at the First Surgical University Hospital in Belgrade. The purpose of this retrospective study is to review our experience with colonic interposition in patients with corrosive esophageal strictures; to assess our results and to identify technical factors which may result in an improved outcome.

MATERIALS AND METHODS
From March 2011 to November 2014, total 40 patients of corrosive injury of stomach and esophagus were managed in single surgical units of each Government Medical College, Surat and GMERS Medical College, Valsad. The data were collected from hospital records, records of patients in a unit and follow up case records of patients for the duration mentioned. We have done colonic interposition in 35 patients; gastric pull up in 03 patients in which esophagectomy was done in two patients and 02 patients were managed with only gastrojejunostomy. We included in our retrospective study 35 patients of corrosive esophageal stricture managed by colonic interposition with (n=07) or without (n=28) esophagectomy. The corrosive agents were acids (n=30) and liquid lye (n=05). Ingestion was associated with suicidal intent in 24 (68.5%) patients and accidental in 11 (31.4%) patients. There were 25 female and 10 male patients (sex ratio: 2.5:1), age ranging from 20 years to...
49 years (mean: 29.4 years) and duration after corrosive ingestion was from 3 months to 2 years. Level of all strictures with number of patients and type of procedure employed according to level of stricture was as per given in Table I.

**PRE-OPERATIVE PREPARATIONS**

The decision to perform esophageal reconstruction was made only in psychologically stable patients after careful psychiatric evaluation. All patients had prior feeding jejunostomy. Apart from routine blood and radiological investigations, all patients were subjected to barium swallow. Upper G.I. endoscopy was performed in all patients: (1) to define site, number and length of strictures in esophagus and (2) grading of mucosal injury with condition of rest of the esophagus especially upper one third esophagus, pharynx, and oral cavity. Patients in whom esophagectomy was planned, were subjected to CT thorax. Routine preparation of the colon consisted of antegrade catharsis through tube jejunostomy preceding the operation combined with cleansing of the colon mechanically by means of enemas. Then, tablet neomycin 500 mg and tablet erythromycin base 500 mg per jejunostomy were given every 4 hours preceding 24 hours of operation.

**SURGICAL PROCEDURE OF COLONIC INTERPOSITION**

The operation was carried out through an upper abdominal median incision and a left cervical oblique incision along the medial border of the sternocleidomastoid muscle in 28 patients; and in 7 patients was combined with a right thoracotomy. The cervical esophagus was explored and transected at the level above which esophagus was normal. In case the cervical esophagus was too extensively injured and scarred, hypopharyngocolostomy had to be performed (n=09). Hypopharyngocolostomy includes removal of all scar tissues and construction of a large anastomosis between the pharynx and a bevel shaped long colonic conduit. Sufficient colon segment for conduit was mobilized from mesocolon; middle and left colic arteries were identified and freed respectively, the root of the vessels elected was clamped with bulldog clamps for about 15 minutes. At the same time, the planned ends of conduit were clamped with intestinal clamps and watched. If the segment of the colon appeared normal in color, peristalsis, and pulsations of marginal arteries (especially those in both ends of the segment), it would be transected. The left colon with transverse colon based on left colic artery and middle colic artery was used in 27 and 6 patients respectively. The right colon with transverse colon based on middle colic artery was used in 2 patients. The peristaltic orientation of conduit consisted of isoperistalsis in 29 patients and antiperistalsis in 6 patients (Fig. a, b, c). The substernal tunnel was prepared in 28 patients and colon was brought through posterior mediastinum in 7 patients. A substernal tunnel was formed by blunt instrumental dissection with a simultaneous cervico-abdominal approach; the proximal end of graft was then brought up gently behind the stomach through the gastro-hepatic ligament and was passed on up to the neck through the tunnel. A proximal esophagocolic or hypopharyngocolic anastomosis was performed in sideto side fashion with hand-suturing single-layer technique in 28 patients without esophagectomy. In patients with esophagectomy (n=07), proximally end to side esophagocolic anastomosis and distally side to side cologastric anastomosis was done with stapled ends of colon and stomach with. In patients with supraglottic and subglottic strictures, total laryngectomy with end tracheotomy and only end tracheostomy were done respectively with hypopharyngocolic anastomosis. In 28 patients without esophagectomy, cologastric anastomosis (n=24) was performed over the midportion of the anterior wall of the stomach without extensively injuring the stomach and cologastroduodenostomy was performed in 4 patients. A pyloroplasty was performed in all patients (n=31) except those in whom cologastroduodenostomy (n=4) was done. Mean operative time was 4 hours (range 2.5 to 7 hours). Complimentary procedures included re-establishment of the colonic continuity and a careful closure of the mesocolon to avoid internal hernia. Resection of upper portion of sternum in order to avoid or decrease compression on the proximal colonic conduit at the level of the thoracic inlet was not needed in any patient. Feeding jejunostomy was re-performed in all patients.

**Fig. 1** Preparation of colonic segment with vascular pattern and peristaltic orientation (a) Isoperistaltic right colon graft based on the middle colic artery (MC), (b) Antiperistaltic left colon graft based on the middle colic artery and (c) Isoperistaltic left colon graft based on the left colic artery (LC) and ascending left colic artery (ALC). 1. For anastomosis to the esophagus and 2. For anastomosis to the stomach. SM=Superior Mesenteric artery, IM= Inferior Mesenteric artery, RC= Right Colic artery, IC= Ileocolic artery
Barium swallow studies were routinely carried out to evaluate the patency of the conduit and the condition of the anastomosis 10 days after reconstruction of the esophagus (Fig.II). After discharge from the hospital, patients were monitored in the outpatient clinic. The ability to swallow, body weight, and activity were recorded. The length of follow-up ranged from 1 month to 3 years. Data for the follow-up study were obtained through clinic visits and questionnaires. Complications developed postoperatively or during follow-up were considered operative morbidity and deaths within one month after operation were defined as operative mortality.

RESULTS

Results of surgery were comparable to other studies (Table II) with 03 postoperative deaths (8.5%) and complications in 10 patients (28.5%) as per given in Table III. The mortality was due to sepsis with aspiration pneumonitis in 02 patients during immediate postoperative period. The mean length of stay was 21.7 days with a range of 15 to 35 days. The most commonly postoperative complications were cervical anastomotic leakage in 2 patients (5.7%) and cervical wound infection in same patients (n=2). They resolved with conservative management in both patients over 2-4 weeks. Reflux was noted in 3 patients (8.5%) who responded to medical management. Redundancy of colon graft was detected in 3 patients (8.5%) in postoperative barium meal study without any symptoms. Any of our patients did not develop other possible complications like anastomotic or non-anastomotic stenosis, intestinal obstruction, pneumothorax, ischemic colitis and conduit necrosis.

According to criteria of Hanna and colleagues results were graded as 'good', 'fair' and 'poor. Patients graded 'Good' when they were symptom free, capable of swallowing a regular diet and gaining weight, normal physical activities accordingly. When patients could swallow but with regurgitation and had decrease in daily activities graded as 'Fair'. Those who had dysphagia, regurgitation and aspiration were graded as 'Poor'. In our study 3 patients died postoperatively; more than 90% patients (n=29) had 'Good' result, 3 patients had 'Fair' and none of them had 'Poor' result.

DISCUSSION

Accidental or intentional ingestion of corrosive agents can cause severe destruction of the tissues and organs of the foregut. Acid agents cause more damage to the stomach than to the esophagus. In contrast, an alkaline substance frequently causes esophageal burns and stricture and only occasionally produces gastric injury. In our study 30 patients had ingested acid and 05 had ingested alkaline agents. All patients presented with stricture of both esophagus and variable portion of stomach.

The organs which can be used for esophageal replacement in patients after corrosive injuries are stomach, jejunum and colon. Stomach has disadvantages of long term gastroesophageal reflux, possible ulceration, anastomotic stenosis and progressive dysfunctional propulsion. The stomach is not long enough to re-establish a continuity of esophagus when anastomosis has to be performed in the neck because the diffuse injuries of the esophagus when patients had to undergo partial gastrectomy after corrosive injuries. Jejunal interposition is seldom used because of the difficulty for operation since blood vessels of jejunum are too thin and easier to be affected after anastomosis. Furthermore, the jejunum is fragile to the erosion of acid in long run, so the jejunum should not be the first choice. The colon has number of attributes that make it an excellent option in esophageal replacement bypass. The advantages include its length and usually its excellent blood supply. By virtue of its length, it prevents the exposure of esophageal mucosa to refluxed gastric juice, thereby decreasing the risk of Barrett's metaplasia developing in residual esophagus. The disadvantages of colon interposition include the fact that using the colon also requires it to be preoperatively cleansed, additional operative time for colon mobilization and anastomosis at three sites, rather than one required for the gastric pull up. The durability and long-term function of interposed colon segments were confirmed in study of Wilkins. Three of the patients in his series had segments that were functioning well more than 20 years after operation, and 9 others had transplants that showed good function at 10 to 20 years of follow-up. In our study we used colon as a conduit over stomach because patients included in the study stomach was also injured moderately or severely.

Patients undergoing colon interposition require careful preoperative evaluation. The cardiopulmonary status and
### Table I Choice of procedure according to level of stricture in esophagus

<table>
<thead>
<tr>
<th>Level of stricture</th>
<th>No. of patients</th>
<th>Surgical procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supraglottic</td>
<td>1</td>
<td>Substernal colonic interposition with hypopharyngeocolostomy and total laryngectomy with end tracheostomy</td>
</tr>
<tr>
<td>Subglottic</td>
<td>1</td>
<td>Substernal colonic interposition with hypopharyngeocolostomy and end tracheostomy</td>
</tr>
<tr>
<td>Hypopharyngeal</td>
<td>07</td>
<td>Substernal colonic interposition with hypopharyngeocolostomy</td>
</tr>
<tr>
<td>Cervical esophagus</td>
<td>19</td>
<td>Substernal colonic interposition with esophagocolostomy</td>
</tr>
<tr>
<td>Thoracic esophagus</td>
<td>07</td>
<td>Transthoracic esophagectomy and posterior mediastinal colonic with cervical esophagocolostomy</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td></td>
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### Table II Comparing operative mortality and morbidity with other studies*

<table>
<thead>
<tr>
<th>References</th>
<th>Year of study</th>
<th>No. of patients</th>
<th>Mortality (%)</th>
<th>Morbidity (%)</th>
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<tbody>
<tr>
<td>Wilkins et al⁶</td>
<td>1980</td>
<td>100</td>
<td>09</td>
<td>40</td>
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<tr>
<td>Mansaur et al¹²</td>
<td>1981</td>
<td>40</td>
<td>17.5</td>
<td>10</td>
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<tr>
<td>Cuvet et al³⁰</td>
<td>1987</td>
<td>53</td>
<td>3.8</td>
<td>30</td>
</tr>
<tr>
<td>Cerfolio et al⁸</td>
<td>1995</td>
<td>32</td>
<td>9.4</td>
<td>24</td>
</tr>
<tr>
<td>Our study</td>
<td>2014</td>
<td>35</td>
<td>8.5</td>
<td>28.5</td>
</tr>
</tbody>
</table>

*all studies were of only colonic interposition

### Table III Postoperative complications (n=10)

<table>
<thead>
<tr>
<th>Complications</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical anastomostic leakage and Cervical wound infection</td>
<td>02 (5.7%)</td>
</tr>
<tr>
<td>Aspiration pneumonitis</td>
<td>02 (5.7%)</td>
</tr>
<tr>
<td>Reflux or regurgitation</td>
<td>03 (8.5%)</td>
</tr>
<tr>
<td>Redundancy of colonic conduit</td>
<td>03 (8.5%)</td>
</tr>
</tbody>
</table>
nutritional status should be optimized. Preoperative colonoscopy should be performed before reconstruction in patients aged more than 55 years and in those with a family history of colon cancer to rule out colonic malignancy. In our study colonoscopy was not indicated in any patient. The role of preoperative mesenteric arteriography is controversial. The routine use of this invasive technique seems somewhat excessive, because anatomic variations in the colonic vasculature rarely modify the planned operative procedure in the healthy state dramatically. If the patient has previous lower-extremity claudication or repair of an abdominal aortic aneurysm, mesenteric arteriography is of value in identifying abnormalities of the colonic blood supply, as the inferior mesenteric artery may be occluded. In our study none of the patients required arteriography.

The timing for operation of esophageal replacement after corrosive injury is still controversial. Bassiouy et al. found in rats that collagen deposition peaked during the second week but continued for a long time after corrosive injury of esophagus. Scar retraction began as early as the end of the second week, and lasted for about six months. It took about 6-12 months before full fibrosis stopped to develop after the injury, which showed that the edge of the stricture in the esophagus might not be confirmed until then. A too earlier operation, when the scar has not completely formed, may promote the risk of anastomotic stenosis. So, it is believed that the chance of successful surgical management is greater if the operation is carried out at least six months after the injury. Although it was reported that esophageal replacement could be performed even 2-3 months after injury, but many conditions must be met and the mucosa in the pharynx must be normal. In our study 33 patients we performed operation 6 months after injury and in 3 patients between 3 and 6 months.

Choice of segment of colon depends on the blood supply of the particular segment to be used. Marginal colic arterial anomalies and cut off are more often seen on right side (5-70%) and most of the anatomic variations of the collateral circulation (54%) are between the right and the middle colic artery. Most of the colonic conduit necrosis occur due to a poor venous drainage that could easily be overlooked during the operation because its evaluation is much more difficult than the evaluation of arterial supply. The left colon is preferable over right colon or ileocolic segment of colon for interposition because the diameter of the left colon is smaller and less prone to dilatation, its constant vascular supply pattern and comparatively less variation than right colon. Left colon is positioned usually in antiperistaltic fashion but it has several drawbacks, that it may cause inflammation of the anastomosis, and affect the healing process. In our study, leakage of cervical anastomosis occurred in 2 cases in the antiperistaltic anastomosis group, which was much higher than the isoperistaltic group. Moreover reflux (n=03) was also a problem in antiperistaltic group. These pointssuggest a possible role of reversed peristalsis in contributing towards postoperative complications. Experimental studies showed that the isoperistaltic colon has a reasonable reservoir function and clearance is completed by peristaltic activity that prevents regurgitation and aspiration. Posterior mediastinal approach (esophageal bed) is the best approach because it is more direct and the shortest route for replacement of esophagus and therefore less likelihood for kinking or twisting of conduit. Substernal placement is the most preferred approach as it is easier to prepare tunnel, cosmetically looks good, and less problems of obstruction or kinkingas compared to antethoracic or subcutaneous route. In our study majority (28 out of 35) patients were operated upon without esophageal replacement, so we used substernal route in those patients. Patients in whom we performed esophagectomy (n=07), we used esophageal bed for colon graft.

It is generally believed that corrosively changed esophagus has a high risk of developing malignancy. According to literature, the incidence of carcinoma developed on corrosively scarred esophagus after a period of 40-50 years from caustic ingestion is about 4%. This factor relates only to patients whose esophagus had been constantly exposed to the thermal and chemical effects of food. If the reconstruction performed 6-12 months after the caustic ingestion and the esophagus is excluded from the passage of food, the risk of developing malignancy is becoming irrelevant. The risk of serious complications is higher during esophagectomy immediately after surgery due to inflammation and scarring of esophagus induced by previous dilatations. Esophagectomy is considered only in the presence of complete, nondraining intrathoracic strictures to avoid the development of esophageal mucocele. The other indication can be when the reconstruction is performed decades after the caustic ingestion, due to the malignant potential. In our study we removed esophagus in 7 patients, out of which 6 patients had nondraining intrathoracic strictures and one patient presented two years after corrosive ingestion.

Esophageal replacement by colon has major morbidity and mortality. Morbidity after colonic interposition includes specific problems related to the dysfunction of the colonic substitute and general complications common to major abdominal procedures. Both conditions may lead to secondary functional failure, loss of the colonic conduit, and patient's death. In accordance with other reports, we found anastomotic stenosis, redundancy, and reflux the most common indications for revision surgery. In the literature, rates of stricture formation after colonic
interposition range between 3% and 58%, and are thought to be higher after reconstruction for corrosive injury than for other conditions. In our study none of the patient developed anastomotic or non-anastomotic stricture and stenosis. Colonic redundancy is the second most common mechanical complication that required surgical correction. Passive dilatation of the colon under the negative intrathoracic pressure above any point of partial obstruction and the excessive lengths of the graft compared with its vascular pedicle are the main mechanisms involved in the genesis of colonic redundancy. Opening of the thoracic inlet, widening of the diaphragmatic hiatus, measurement of the conduit to create a straight course and confection of a wide, well vascularized distal colonic Anastomosis have been proposed to prevent redundancy. The rate of asymptomatic redundancy after colon interposition varies between 3% - 25%, although all patients probably develop some degree of redundancy in the long-term. Asymptomatic redundancy occurred in 3 patients (8.5%) in this study. Reflux has been reported in 8% to 15% of colon interposition patients. Concomitant destruction of the upper esophageal sphincter and anisoperistaltic colon interposition for corrosive stricture is well accepted and ischemic conduit necrosis are major causes of mortality. In our series, mortality was 8.5% (n=3), all 3 patients died due to sepsis; out of which 2 patients had aspiration pneumonitis. There was no ischemic conduit necrosis. Mortality and morbidity are comparable to those of other studies.

CONCLUSION

Esophageal reconstruction or bypass with colonic interposition for corrosive stricture is well accepted and proven definitive management with good results and quality of life. Left colonic segment is preferred for interposition in isoperistaltic fashion. Although posterior mediastinal route is the shortest to place colon but require surgical correction. Passive dilatation of the colon under the negative intrathoracic pressure above any point of partial obstruction and the excessive lengths of the graft compared with its vascular pedicle are the main mechanisms involved in the genesis of colonic redundancy. Opening of the thoracic inlet, widening of the diaphragmatic hiatus, measurement of the conduit to create a straight course and confection of a wide, well vascularized distal colonic Anastomosis have been proposed to prevent redundancy. The rate of asymptomatic redundancy after colon interposition varies between 3% - 25%, although all patients probably develop some degree of redundancy in the long-term. Asymptomatic redundancy occurred in 3 patients (8.5%) in this study. Reflux has been reported in 8% to 15% of colon interposition patients. Concomitant destruction of the upper esophageal sphincter and anisoperistaltic colon interposition for corrosive stricture is well accepted and ischemic conduit necrosis are major causes of mortality. In our series, mortality was 8.5% (n=3), all 3 patients died due to sepsis; out of which 2 patients had aspiration pneumonitis. There was no ischemic conduit necrosis. Mortality and morbidity are comparable to those of other studies.

REFERENCES


5. Yong Han, Qing-Shu Cheng, Xiao-Fei Li, Xiao-Ping Wang; Surgical management of esophageal strictures after caustic burns: A 30 years of experience ; World J Gastroenterol 2004;10(19):2846-2849.


Results of Platelet Rich Plasma Therapy in early stages of Osteoarthritis Knee

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KEY WORDS : Autologous PRP, Osteoarthritis knee

ABSTRACT

Introduction : Osteoarthritis of knee is a most common form of arthritis causing degeneration of articular cartilage and subchondral bone.

Osteoarthritis of knee is a most common form of arthritis spread rampantly today. Platelet-rich plasma injections aim to promote cartilage repair and relieve osteoarthritic symptoms, potentially delaying the need for joint replacement surgery. Objective : To investigate the therapeutic potential of administration of platelet-rich plasma (PRP) examining its effects on progression of early stages of osteoarthritis of knee.

Methods: Methodology : A case series study of 50 patients was carried out. Results were analyzed on the basis of following scores: (1) WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) (2) KSS(Knee Society Score) (3) VAS(Visual Analogue Scale) Results : No severe adverse events were observed. Statistically significantly better results in the Western Ontario and McMaster Universities Osteoarthritis Index and KSS and VAS scorings were recorded in a group of patients who received PRP injections after a 3- and 6-mo follow-up. Conclusions : Our preliminary findings support the application of autologous PRP as an effective and safe method in the treatment of the initial stages of knee osteoarthritis. Further studies are needed to confirm these results and to investigate the persistence of the beneficial effects observed.

INTRODUCTION

Osteoarthritis of knee is a most common form of arthritis causing degeneration of articular cartilage and subchondral bone.

PRP was first developed in the 1970s and first used in Italy in 1987 in an open heart surgery procedure. PRP therapy began gaining popularity in the mid 1990s. It has since been applied to many different medical fields such as cosmetic surgery, dentistry, sports medicine and pain management. It is a simple, low-cost and minimally invasive method that provides a natural concentrate of autologous blood growth factors (GFs) that can be used to enhance tissue regeneration. Platelet-rich plasma injections aim to promote cartilage repair and relieve osteoarthritic symptoms, potentially delaying the need for joint replacement surgery. Platelets produce growth factors that are thought to stimulate chondrocyte proliferation, leading to cartilage repair. The efficacy of certain growth factors in healing various injuries and the concentrations of these growth factors found within PRP are the theoretical basis for the use of PRP in tissue repair.[1] The platelets collected in PRP are activated by the addition of thrombin and calcium chloride, which induces the release of the mentioned factors from alpha granules. Human osteoarthritic chondrocytes exposed to platelet-rich plasma demonstrated less interleukin-1β-induced inhibition of collagen 2 and aggrecan gene expression, and diminished nuclear factor-B activation, which are pathways involved in osteoarthritis pathogenesis.

AIMS AND OBJECTIVES

To determine the effectiveness of intra-articular PRP injections in active patients with knee OA and to evaluate clinical outcomes in patients with and without previous surgical treatment for cartilage lesions.

MATERIALS AND METHODS

• Study Design: Case series.
• Inclusion criteria:
  - 40-60 years of age
  - Early stages of kellgren grade 1-2 of osteoarthritis knee
• Exclusion Criteria:
  - Patients who have received any intraarticular therapies
  - Have undergone any previous surgical intervention for cartilage regeneration
  - Patients having rheumatoid arthritis.
Fifty patients with knee OA were followed for a minimum of 6 months. All were treated with 3 intra-articular injections of autologous PRP. All the patients received a 6-mL platelet-rich plasma injection using every week. Multiple evaluative scores were collected at pretreatment and at 6 months posttreatment. The required sample of patients was determined beforehand by using statistical power analysis.

- Methods

Clinically, patients were assessed for pain, deformity, range of motion, activity level and functional capabilities preoperatively. Functional assessment was done by using KSS and WOMAC score and VAS score. Radiological assessment was done in form of AP, lateral x-rays.

**OBSERVATIONS AND RESULTS**

No severe adverse events were observed. Statistically significantly better results in the Western Ontario and McMaster Universities Osteoarthritis Index and VAS scores were recorded in a group of patients who received PRP injections after a 3- and 6-mo follow-up. They showed many improvements including reduced pain after knee movement and at rest. Cartilage assessment was limited because of the small sample size. The majority of the patients expressed a favorable outcome at 6 months after treatment.

- Knee Society Score:

In 1989, The Knee Society Clinical Rating System was developed to rate both the knee prosthesis function and patients' functional abilities after total knee arthroplasty. The system is subdivided into a knee score that rates only the knee joint itself and a functional score that rates the patient's ability to walk and climb stairs. The Knee Society has proposed this new rating system to be simple but more exacting and more objective. The rating is divided into separate knee and patient function scores. Thus, increasing age or a medical condition will not affect the knee score.

Knee society functional scores were improved from 36.4 to 55.10 at 3 months and 59.1 at 6 months of follow up.

<table>
<thead>
<tr>
<th>Score</th>
<th>0(months)</th>
<th>3(months)</th>
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<tr>
<td>&lt;50</td>
<td>40</td>
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<td>50-65</td>
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Figure 3: Showing KSS Score at 3 and 6 months

- WOMAC Score:

The WOMAC is one of the most widely utilized self-report measures of lower extremity symptoms and function. It is used to assess pain, stiffness, and physical function in patients with hip and/or knee osteoarthritis. The WOMAC consists of 24 items divided into 3 subscales: pain, stiffness and physical function. The mean WOMAC scores were 10.18, 3.12, 36.56, and 49.86, respectively, and at follow-up after 3 months were 5.00, 2.10, 20.08, and 27.18, and after 6 months were 4.50, 2.09, 18.50 and 25.09 respectively, showing significant improvement.

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Vas Score:
The visual analogue scale or visual analog scale (VAS) is a psychometric response scale which can be used in questionnaires. It is a measurement instrument for subjective characteristics or attitudes that cannot be directly measured. When responding to a VAS item, respondents specify their level of agreement to a statement by indicating a position along a continuous line between two end-points.

Patients showed improvement from mean score of 7 to 5.5 and 4.9 at 3 months and 6 months of follow up respectively.

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<th>VAS Score</th>
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<td>6—10</td>
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DISCUSSION
The mean age of patients in our study was 59.15. The disease process was found to be more common in females and age group of 50-60.

PRP has been used in surgeries to promote cell regeneration since 1987. Although blood is mainly a liquid (called plasma), it also contains small solid components (red cells, white cells, and platelets.) The platelets are best known for their importance in clotting blood. However, platelets also contain hundreds of proteins called growth factors which are very important in the healing of injuries.

PRP is plasma with many more platelets than what is typically found in blood. The concentration of platelets — and, thereby, the concentration of growth factors — can be 5 to 10 times greater (or richer) than usual. To develop a PRP preparation, blood must first be drawn from a patient. The platelets are separated from other blood cells and their concentration is increased during a process called centrifugation. Then the increased concentration of platelets is combined with the remaining blood. Two spins are performed to remove rbc's and wbc's from the sample. The upper portion of the volume that is composed mostly of PPP (platelet-poor plasma) is removed. Pellets are homogenized in lower 1/3rd (5 ml of plasma) to create the PRP (Platelet-Rich Plasma).

Spakova et al study results- On average, a 4.5-fold increase in platelet concentration was obtained in the PRP group. No severe adverse events were observed. Statistically significantly better results in the Western Ontario and McMaster Universities Osteoarthritis Index and Numeric Rating Scale scores were recorded in a group of patients who received PRP injections after a 3- and 6-mo follow-up.

Elizvato et al studies- Only minor adverse events were detected in some patients, such as mild pain and effusion after the injections, in particular in the PRP group, where a significantly higher post-injective pain reaction was observed (p=0.039). At the follow-up evaluations, both groups presented a clinical improvement but the comparison between the two groups showed statistically significant difference in all scores evaluated. A trend favorable for the PRP group was only found in patients with low grade articular degeneration (Kellgren-Lawrence score up to 2).

All studies included in this assessment reported short-term improvements in function and a decrease in pain scores; however this effect did not appear to be sustained over a long period of time. The procedure appears to be safe, with the only adverse event reported being short-term pain following injection due to inflammation.

CONCLUSION
Our preliminary findings support the application of autologous PRP as an effective and safe method in the treatment of the initial stages of knee osteoarthritis. Further studies are needed to confirm these results and to investigate the persistence of the beneficial effects observed. Better results were achieved in younger and more active patients with a low degree of cartilage degeneration.

Although there is some evidence that PRP injections provide some symptomatic relief, there is no evidence that PRP injections alters the natural progression of OA. Randomised controlled trials using a comparator are needed to demonstrate the effectiveness of PRP treatment of OA of the knee.
ABSTRACT
Foreign body in paediatric airway requires early intervention to prevent serious consequences. This is a retrospective analysis of 69 cases of rigid bronchoscopy for suspected foreign body in tracheobronchial tree at New Civil Hospital Surat. In this series 85.5% of patients were below 3 years of age. Positive history of foreign body ingestion was present in 70% patients. All patients were given general anaesthesia with controlled ventilation. Definite foreign body was removed in 87% of patients, amongst them 89% were vegetable foreign body. Two patients require preprocedure and two require postprocedure tracheostomy. It is concluded that excellent cooperation and communication between the airway specialists are essential for successful outcome of the procedure.

INTRODUCTION
Foreign body aspiration in tracheobronchial tree is a leading cause of accidental death in children under one year of age. Early removal of foreign body is essential to prevent permanent lung damage like bronchitis, pneumonia & collapse. Compromise of the lumen of the paediatric airway whether by pathology like foreign body or edema or by instrumentation may drastically reduce the flow of gas and there by gas exchange. Here the oxygenation is not the only problem but removal of carbon dioxide is also an important concern. The foreign body can act as check valve resulting into varying degree of air trapping distal to it.

Rigid bronchoscopy for extraction of foreign body in children provides better quality of image & larger channel for removal of the foreign body, thick & copious secretion & bleeding from the airway.1, 2 A successful management of these cases requires mutual respect, cooperation & communication between endoscopist and anaesthesiologist keeping in mind that patient’s safety is of prime importance.

Reduced perioperative mortality and morbidity of bronchoscopy during these days is due to improved equipment, safer drugs and adequate monitoring. Knowledgeable team of specialists involved in management paediatric airway further reduces the risk associated with it.

MATERIAL & METHOD
This retrospective analysis included 69 children who underwent bronchoscopy at New Civil Hospital Surat over the period of four years for suspected foreign body ingestion.

TECHNIQUE OF ANAESTHESIA
All the cases were undertaken as emergency cases. In preoperative holding area thorough history was taken and examination was done. Signs of respiratory distress like tachypnea, intercostals in drawing, use of accessory muscles of respiration were noted. Probable location of the foreign body was discussed with endoscopist keeping in view of respiratory examination and X ray findings. Patients' relatives were explained about the need of the procedure and associated risk and high risk consent was obtained. Relatives were also explained that tracheostomy may be required during procedure or after the procedure and consent for it was also attained. General anaesthesia was given to all patients for bronchoscopy. The patients were preoxygenated for 3-5 minutes and intravenous line was secured. Perioperative monitoring included precordial stethoscope, pulse oximetry & ECG. All the patients were premedicated with Inj. Glycopyrrolate 0.008 mg/kg IV., Inj. Hydrocortisone 2 mg/kg and Inj. Dexamethasone 0.2 mg/kg were also given prior to bronchoscopy as there action starts after 20 -30 minutes. Anaesthesia

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was induced with Inj. Ketamine hydrochloride 2 mg/kg IV followed by Inj. Succinylcholine 1.5 mg/kg. IPPV was given with 100% O2 and Halothane (1 to3%). Endoscopist was allowed to proceed with the bronchoscopy.

The bronchoscope used was rigid bronchoscope made up of solid metal tube. Distal open end had side holes for ventilation of another lung while removing foreign body from main stem bronchus of opposite lung. Proximal end had two ports and attachment for light source. One port was for procedure like viewing, introduction of forcep for grasping foreign body and suction tube. The side port was for oxygenation. Ventilation was continued by connecting the modified Jackson Rees circuit to side port of the bronchoscope. Positive pressure ventilation was given intermittently by bringing the bronchoscope back above carina and occluding the open end. In between this oxygenation was continued by apneic ventilation by delivering continuous oxygen flow of 10 liter/ min with Jackson ree's circuit attached to it.\(^8\)

Anaesthesia was maintained during the procedure with O2, halothane, intermittent ketamine & succinylcholine as & when required. In-between the procedure and when SpO2 fell below 85% the bronchoscope was brought at carina and both the lungs were ventilated by occluding the proximal end of the scope by thumb of endoscopist. The experience of the anaesthesiologist helps him to decide when to interrupt the procedure for oxygenation of the patient but again with the aim that the endoscopist remove the foreign body the earliest. Once the foreign body was grasped with the forceps IPPV was withheld till the bronchoscope along with the forceps holding the foreign body were taken out from the larynx. If the attempt was not successful after oxygenating the patient the same procedure was repeated. Once the foreign body was removed IPPV with mask was given and endoscopist reinserted the bronchoscope to make sure that there were no additional fragments and to suck accumulated secretion & pus if present. While withdrawing the bronchoscope 4% lignocaine was instilled through it at subglottic region limiting the dose up to 4 mg/kg. Check laryngoscopy was done to look for pieces of foreign body in hypopharynx and oropharynx. After that child was allowed to breathe O2 through facemask until awake. Five patients endotracheal intubation was required & IPPV with 100% O2 was given. Suction through endotracheal tube was also done in them. Once airway reflexes had returned and child was awake the endotracheal tube was removed.

All the patients were given oxygen and kept under observation inside the operation theatre for about 20-30 minutes. The endoscopist was asked to stay in operation theatre with bronchoscope and treacheostomy tray during this period. Patients were shifted to recovery room where they received humidified O2 for minimum four hours.

**OBSERVATIONS AND RESULTS**

The data of all 69 cases was analyzed and the results were described as under.

Most of the patients (85.5%) were between the age group of 11/2 months to 3 years. Almost 80% patients were male and 20% were female. History of fever was present in half of them (52%) whereas history of cough was present in 75% patients. 46% patients had history of breathlessness and only 3% presented with stridor. Definite history of foreign body ingestion was present in 70% of patients. In remaining 30% it was suspected, as they presented with cough, fever, and breathlessness. Duration of history ranged from 5 hours to as long as two months but majority of them presented within two days of symptoms.

Bronchoscopy was positive in 60 (87%) cases and negative in 9 (13%) cases. Vegetable foreign body was found in 87% patients whereas, 10% patient had nonvegetable foreign body. Two patients had secretion as cause of obstruction. Various types of foreign body like tamarind seed, groundnut, betalnut, sitafal seed, peanut, chana, coconut, rice grain, chalk, plastic toy etc.were found. The commonest amongst them was groundnut and it was found in 25 out of 60 positive bronchoscopy. The most common site from which foreign body was removed was right main stem bronchus (51%) followed by left main stem bronchus (26%). Nine patients had foreign body in trachea and 2 had it at carina.

Two patients required preprocedure and two patients required postprocedure tracheostomy. Two patients had pre procedure severe hypoxia (SpO2 < 60%) and bradycardia an situation of impending cardiorespiratory arrest .They were resuscitated and preprocedure tracheostomy was done as foreign body was just in subglottic region causing airway obstruction and hypoxia. After tracheostomy foreign body was removed successful y. The Complications during the bronchoscopy noted were bradycardia in 2 patients, cyanosis in 2 patients, and severe hypoxia in two patients. Two patients develop post procedure upper airway edema causing significant airway obstruction. For these two they required post procedure tracheostomy.

**DISCUSSION**

Removal of foreign body from the tracheobronchial tree has been a challenge to the anaesthesiologist as there is compromised ventilation due to presence of foreign body and secretion in the airway, along with instrumentation of the airway. The diagnosis of foreign body in tracheobronchial tree is made either by history of foreign body ingestion or history of fever, cough, breathlessness, wheezing or choking etc.. As noted by others (Dr. Raju
Gandhi et al.) in this study also most of the patients were below three years of age. They had put forward the theory that habit of putting things in mouth in absence of molar teeth make them susceptible to foreign body ingestion. 3 In this series history of foreign body ingestion was present in 52% of the patients. In Agrawal et al study 65% patients had positive history of foreign body ingestion. 4 The foreign body was found in 89% patients in main stem bronchus by Dr. Agrawal et al and 77% in this study. They found vegetable foreign body in 95% patients which is similar to our finding (87%). The commonest foreign body was areca nut and pea nut in their series and groundnut in ours and Dr. Raju Gandhi et al study. This is owed to the prevailing habit of eating groundnuts in Gujarat.

Vegetable foreign body is more troublesome because it expands with moisture 2 and fragment into multiple small pieces. Oil containing objects such as peanut, groundnut produce chemical inflammation. 6 There are chances of fragmentation, which can precipitate the dreaded complication of foreign body impaction in both main stem bronchi. 4 The commonest site for foreign body location was right main stem bronchus (51%) in this group of patients. Shivkumar et. al. and Dr. Raju Gandhi et al also had similar observations. 5,3

PRINCIPLES OF ANESTHETIC MANAGEMENT OF BRONCHOSCOPY ARE: 7

(1) Adequate oxygenation and ventilation.

(2) A still patient whose airway reflexes are sufficiently suppressed so, there is no coughing laryngospasm, bronchospasm or breath holding during the procedure.

(3) Protection of the airway from the aspiration of gastric content and trauma.

(4) A rapid return of consciousness and airway reflexes following the procedure.

There is not a single anaesthetic technique that can satisfy all these requirements. Before deciding the technique of anaesthesia it is important to have an idea about the probable location and type of foreign body. Fortunately very rarely anaesthetist needs to anaesthetize patient with foreign body in larynx or upper trachea. Either active cough removes it or deep inspiration pushes it down in bronchus and in unfortunate situation patient is severely hypoxic to reach hospital. 7

In spontaneous ventilation technique patient is allowed to breathe spontaneously after induction of anaesthesia. Considering airway obstruction, which can get worsen during induction, spontaneous respiration has advantage that degree of obstruction can be easily assessed. As this technique maintains patient’s respiratory efforts, it does not require IPPV which can push foreign body deep further in small airway making it difficult to remove. If bronchoscope remains deep in one of the bronchus for longer time, patient is likely to become hypercarbic and inadequately anaesthetized. 1 Rapidly moving cord may dislodge the foreign body from the forceps and fall into previously patent bronchus 5 at a time when other bronchus is still obstructed by inflammatory response and secretions. Sometimes there is difficulty in removing foreign body through moving cords. Emergence from anaesthesia is slower and patient might remain sedated with suppressed airway reflexes.

The technique, which was used in patients of this series, was intravenous induction, neuromuscular paralysis with succinylcholine. Induction of anaesthesia was done with ketamine in this series. Propofol is also good alternative for induction of anaesthesia. Short duration and lack of analgesic effect are the limitation of propofol when compared with ketamine. Inhalation induction may take longer time as already pulmonary gas exchange is reduced due to foreign body in airway. IPPV can be done through the side arm of the ventilating bronchoscope or venturi. Sevoflurane might be an alternative to halothane.

| Table I  Distribution of the age of the patients |
| Age (yrs) | No of patients | % of patients |
| 0 - 3     | 59             | 85.53%        |
| 4 - 7     | 4              | 5.79%         |
| 8 - 11    | 4              | 5.79%         |
| >11       | 2              | 2.89%         |

| Table II  History of foreign ingestion |
| History of foreign Body ingestion | No of patients | % of patients |
| Present                      | 48             | 69.57%        |
| Absent                       | 21             | 30.43%        |

| Table III  Result of bronchoscopy |
| No. of patients | % of patients |
| Positive        | 60             | 87%           |
| Negative        | 9              | 13%           |

| Table IV  Type of foreign body |
| Type of Foreign body | No of Patients N=60 | % of Patients |
| Vegetable           | 52             | 87%           |
| Non vegetable       | 6              | 10%           |
| secretion           | 2              | 3%            |
as inhalation agent. The advantage of halothane is that it is better bronchodilator than sevoflurane and halothane can maintain depth of anaesthesia during the airway instrumentation as during this period patient is hardly receiving inhalation anaesthetic agent. The major disadvantage of the technique used in this case series is that IPPV may push foreign body further deep making the removal more difficult. This was reduced by gentle ventilation with hand at low airway pressure.

The advantage of this technique is that it provides sufficiently relaxed patient, which shortens the duration of the procedure. The recovery after procedure is faster with active reflexes.¹

The venturi technique allows continuous ventilation without intermittent period of apnea to permit instrumentation. But it has shortcomings like the amount of room air entrained dilutes O₂ through jet, making inspired O₂ less and variable leading more chances of hypoxemia to the patient.¹

Instrumentation of the airway may produce mucosal swelling which can cause difficulty in breathing in postoperative period. Humidified O₂, nebulized racemic epinephrine and prophylactic use of steroids are the techniques to minimize and treat it.¹,²,⁴ Rarely patient may require endotracheal intubation or tracheostomy to maintain the patency of the airway. In this study five patient required endotracheal intubation for ten to fifteen minutes and two patients required post procedural tracheostomy to maintain adequate ventilation.

Intravenous induction with ketamine and neuromuscular paralysis provide satisfactory condition for removal of foreign body. The most important element of any technique is skill and attentiveness of the airway specialist the anaesthesiologists and the endoscopists.

ACKNOWLEDGEMENT

We would like to acknowledge the efforts of dept of ENT surgery New Civil Hospital Surat who were the endoscopist for these patients, in successful management of all these cases. We accept that the role of staff member of anaesthesia dept Dr. P. V. Vaidya (Ex Associate prof.) Dr. Bansari Kantharia (Additional Prof.) Dr. Ravindra Gandhi (Ex Associate prof.) Dr. Malti Pandya (Ex Assistant Prof.) Dr. Harsha Patel (Additional Prof.) in giving anaesthesia to above mentioned patients.

REFERENCES


Clinical Profile of Acute Flaccid Paralysis in Paediatric Population

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*Professor & Head of Unit, **Assistant Professor, ***Fellow in Paediatrics Critical Care
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KEY WORDS : Acute flaccid paralysis, Guillian Barre Syndrome, electrophysiological study.

ABSTRACT
Aim : To study the clinical profile of acute flaccid paralysis in paediatric age group and to evaluate role of electromyography and nerve conduction velocity study. Methods : The present study was conducted at civil hospital, Ahmedabad. All paediatric patients less than 12 years of age who presented with weakness and hypotonia in any part of body of acute onset (less than 4 weeks) with areflexia were studied in detail. They were subjected to appropriate investigations including EMG-NCV study. Result: Majority of the patients- 75 (83.33%) with AFP had Guillian Barre syndrome. The most common variety was the ascending type seen in 62 (82.7%) patients. On nerve conduction study , majority of patients (45.55%) showed changes of AIDP. Intravenous immunoglobulin and methylprednisolone were the main treatment modality used. There was a greater recovery in disability in patients of AIDP as compared to other types of polyneuropathy. Conclusion: The findings of our study indicate that Guillian Barre Syndrome contributes the most to cases of Acute Flaccid Paralysis. AIDP is the most common variety of GBS seen with the best prognosis.

INTRODUCTION
A case of acute flaccid paralysis is defined as 'any child aged less than 15 years who has acute onset of flaccid paralysis for which no obvious cause (like trauma or electrolyte imbalance) is found'.

Common causes of AFP in our country included poliomyelitis, GBS, transverse myelitis and traumatic myelitis. AFP in children has been the focus of polio eradication initiative of the world health organisation. As India is now declared polio free, more cases of GBS are being detected due to thorough implementation of AFP surveillance programme by the government.

Acute flaccid paralysis can be diagnosed on the basis of clinical judgement and supportive investigations. With the help of mechanical ventilation and IVIG, there has been a considerable reduction in mortality.

MATERIAL AND METHOD
The present study was conducted in the paediatric department of civil hospital, Ahmedabad over a period of 2 years from August 2010 to September 2012.

All pediatric patients less than 12 years of age who presented with weakness and hypotonia in any part of the body of acute onset (less than 4 weeks) with areflexia were included.

OBSERVATION
There were a total of 90 cases of Acute Flaccid Paralysis during the study period. AFP cases accounted for 0.91% of the hospital admissions. Out of the total 90 patients, 75 patients (83.33%) had Guillian Barre Syndrome, 4 each (4.44%) had Diphtheric polyneuritis and Spinal Muscular Atrophy, 3 patients (3.33%) had myopathy and there was 1 case each (1.11%) of Transverse myelitis and...
Hereditary Sensory motor neuropathy. Out of the 75 patients of GBS, 51 patients (68%) were in age group of 3-9 years, 33.3% of patients were in age group of 3-6 years. This is comparable with a study by Arun Agarwal et al which showed that 37.4% of patients of GBS were in the age group of 3-6 years. The study by Arun Agarwal et al also showed that GBS accounted for 78.5% of cases of AFP. Out of 75 patients of GBS, 43 were male and 32 were female with a M:F ratio of 1.34:1, which is comparable with a study by R. korinthenberg which showed a M:F ratio of 1.26:1.

Out of all cases of GBS, 54.7% cases were found in months of July to October. Ameer Ahmed et al also demonstrated maximum incidence (46.5%) of GBS during months of July to October.

At the time of presentation, the most common complaint was weakness of limbs, seen in all (100%) patients. 59 patients (65%) had quadriaparesis, 29 patients (32.2%) had paraparesis and 2 patients (2.22%) had monoparesis. 21 patients (23.33%) had respiratory distress on presentation. 12 patients (13.3%) had complaint of difficulty in swallowing. Our study showed that maximum patients- 29 (38.6%) had grade 4 disability according to scale of Hughes and colleagues. 61.34% of the patients presented to the hospital within 72 hours of weakness and mean days of duration of weakness before admission was 6.01 days which is comparable with study of Roshanlal Koul et al which showed a mean duration of weakness of 8.5 days. Out of total patients of GBS, majority- 62 (82.7%) had ascending variety of paralysis. 9 patients (12%) had descending variety, 3 patients (4%) had Miller Fisher Syndrome and 1 patient (1.33%) had pharyngo-cervico-bronchial variety of GBS. The most common preceding illness was respiratory infection, seen in 33 (36.7%) cases. Out of total patients, 54.4% were fully immunized, 23.3% were partially immunized and 16.67% were unimmunized and immunization details were not available for 5.5% patients. Autonomic disturbances were seen in 53.33% of patients. 41.11% of patients had albumin cytological dissociation and mean protein value was 132 mg/dl. Electrophysiological study was done in all patients which revealed acute inflammatory demyelinating polyneuropathy (AIDP) in 45.55% of patients, acute motor axonal neuropathy (AMAN) in 13.33% patients, acute sensory motor axonal neuropathy (AMSAN) in 6.66% patients, pure sensory neuropathy in 2.22% patients, myopathy in 3.33% patients and anterior horn cell defect in 4.44% patients.

Out of total 90 stool samples sent, stool culture was negative in 84 (93.33%) cases and non polio enterovirus (NPEV) was isolated in 6 (6.67%) cases. Out of total cases of GBS, IVIG was given in 36.67%, methyl prednisolone was given in 36.67%, methyl prednisolone was given in 43.33% cases and plasmapharesis was done in 1.11% cases. Ventilator support was required in 21.33% cases. The mortality rate in the present study was 8.88%. On 60 days follow up, 37 patients (41.11%) had complete recovery, 18 patients (20%) had grade 1-2 disability, 14 patients (15.55%) had grade 3 disability and 6 (6.67%) had grade 4-5 disability. 7 patients were lost to follow up. Significant improvement was noted in disability at 60 days follow up in patients diagnosed as AIDP as compared to other types of polyneuropathy. (p<0.005)

If IVIG was given within 72 hours of admission, there was a significant decrease in mortality. (p<0.005)
Acute flaccid paralysis means paralysis of acute onset with flaccidity of affected limbs. Case definition of 'AFP' goes as – "Any child aged less than 15 years who has acute onset of flaccid paralysis for which no obvious cause (trauma or electrolyte imbalance) is found.1 Common causes of AFP are infectious causes like poliomyelitis, campylobacter, coxsachie, echovirus, etc; immunological like Guillain Barre Syndrome and Transverse Myelitis; traumatic causes like traumatic neuritis; toxin mediated like diptheria, botulism, etc and other rare entities like drug induced, organic matter, metal or pesticide induced. GBS is the most common cause of AFP in our country.

AFP in children has come to focus due to polio eradication initiative by WHO. All over the world, poliomyelitis cases have decreased by over 99%. Since 1988, from an estimated 3,50,000 cases then to 406 cases in 2013. In 2014, only 3 countries-Afghanistan, Nigeria and Pakistan remain polio endemic, down from 125 in 19887. India, along with 10 other countries in South East Asia Region was declared polio free (3 years of zero confirmed cases due to indigenous wild virus) by WHO certification process.

Guillian Barre Syndrome is an acute, demyelinating, inflammatory polyradiculopathy which is of rapidly progressive type. It occurs in all age groups but rarer below 1 year, with incidence of 0.4-0.7 cases per 1,00,000 population with slight male preponderance. In approximately 65% cases, precedent infections causes like campylobacter (most common), mycoplasma, influenza, coxsachie, immunization history or lymphoma is elicited. It is mediated by immunological dysfunction where antibodies act and destroy indigenous neural component- GM1 gangliosides. The variants include AIDP, AMAN, AMSAN, ASAN, Miller Fischer, congenital, pandysautonomia and overlap syndrome. Asbury's8 clinical essential diagnostic criteria include areflexia, course less than 4 weeks, weakness of more than or equal to 2 limbs and exclusion of other causes.

Characteristic CSF picture reveals albumino-cytological dissociation with NCV picture revealing conduction block, prolonged distal latency and F waves. Hughes disability grading scale9 helps in management of GBS cases, with supportive management required in grade 1-2 and specific therapy like IVIG or plasmapharesis followed by neurorehabilitation later. Steroids contrary to general belief, prolongs recovery.9

Poliomyelitis was the major cause of AFP prior to eradication era. Poliovirus, belonging to enteroviridae family has three serotypes, with humans being only reservoir. Route of transmission is feco-oral, less commonly droplet infection, with faeces being main reservoir. The myriad of clinical presentations seen are due to cell destruction in anterior horn and brain stem

### Table 1: Age incidence and etiology

<table>
<thead>
<tr>
<th>Etiology</th>
<th>≤ 3 years</th>
<th>≤ 6 years</th>
<th>≤ 9 years</th>
<th>≤ 12 years</th>
<th>Total no. of patients (n=90)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guillain Barre syndrome</td>
<td>9 (12%)</td>
<td>28 (37.33%)</td>
<td>23 (30.66%)</td>
<td>15 (20%)</td>
<td>75 (83.33%)</td>
</tr>
<tr>
<td>Transverse myelitis</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1 (1.11%)</td>
</tr>
<tr>
<td>Post diphtheric polyneuritis</td>
<td>-</td>
<td>2 (50%)</td>
<td>2 (50%)</td>
<td>-</td>
<td>4 (4.44%)</td>
</tr>
<tr>
<td>Traumatic neuritis</td>
<td>2 (100%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2 (2.2%)</td>
</tr>
<tr>
<td>Spinal muscular atrophy</td>
<td>4 (100%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4 (4.44%)</td>
</tr>
<tr>
<td>Myopathy</td>
<td>2 (66.66%)</td>
<td>1 (33.33%)</td>
<td>-</td>
<td>-</td>
<td>3 (3.33%)</td>
</tr>
<tr>
<td>HSMN</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1 (1.11%)</td>
<td>1 (1.11%)</td>
</tr>
<tr>
<td>Total</td>
<td>17 (19%)</td>
<td>31 (33.3%)</td>
<td>26 (28.9%)</td>
<td>16 (17.8%)</td>
<td>90 (100%)</td>
</tr>
</tbody>
</table>

Out of 90 patients of AFP cases, majority 75(83.33%) patients had GBS.
Out of 75 patients of GBS cases, majority 51(68%) patients were in age groups of 3-9 years.
Table 2: Immunization status

<table>
<thead>
<tr>
<th>Immunization</th>
<th>No. of patients (n=90)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unimmunized</td>
<td>15</td>
<td>16.67%</td>
</tr>
<tr>
<td>Partially immunized</td>
<td>21</td>
<td>23.3%</td>
</tr>
<tr>
<td>Completely immunized</td>
<td>49</td>
<td>54.44%</td>
</tr>
<tr>
<td>Not known</td>
<td>5</td>
<td>5.5%</td>
</tr>
</tbody>
</table>

Out of 90 patients, 54.4% of the patients were fully immunized.

Table 3: Sex incidence

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Male</th>
<th>Female</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guillain Barre syndrome</td>
<td>43</td>
<td>32</td>
<td>1.34:1</td>
</tr>
<tr>
<td>Transverse myelitis</td>
<td>1</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Post diphtheric polineuritis</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Traumatic neuritis</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Spinal muscular atrophy</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Myopathy</td>
<td>1</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>HSMN</td>
<td>1</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td>39</td>
<td>1.31:1</td>
</tr>
</tbody>
</table>

Out of total 90 patients, 51 were male and 39 were female. Male to female ratio was 1.31:1.

Table 4: Variants of Guillain Barre syndrome

<table>
<thead>
<tr>
<th>Variants</th>
<th>No. of patients (n=75)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending variety</td>
<td>62</td>
<td>82.7%</td>
</tr>
<tr>
<td>Descending variety</td>
<td>9</td>
<td>12%</td>
</tr>
<tr>
<td>Miller fisher syndrome</td>
<td>3</td>
<td>4%</td>
</tr>
<tr>
<td>Pharyngo-cervico-brachial variety</td>
<td>1</td>
<td>1.33%</td>
</tr>
</tbody>
</table>

Out of total 75 patients of GBS, majority 62(82.7%) presented with ascending variety of paralysis.

which may manifest as either – asymptomatic illness (90-95% patients). Abortive illness (4-8%), non paralytic (1%) and <1% paralytic polio being either spinal, bulbar or paralytic polio encephalitis. Clinical diagnosis is confirmed by virus isolation from stool or pharynx. Silent, abortive and non paralytic forms require supportive management and paralytic form requires strict bed rest, physiotherapy and rehabilitation with prevention of complications. Prevention strategies lie on immunization only.

Transverse myelitis, other cause of AFP is a demyelinating disease of spinal cord mediated by either
cell mediated autoimmune response, vasculitis or direct viral invasion. Characteristic clinical features are flaccid muscle paralysis, sensory level and sensory system affected with sphincter disturbances. Spontaneous recovery occurs and is complete in 60% of patients. Steroids are used in its treatment.

Traumatic neuritis caused by injections commonly given in gluteal region may lead to AFP. Illness is accompanied by pain with absent of diminished ankle jerk followed by sequel in form of atrophy seen later though not as severe as polio.

AFP thus is a broad clinical entity with an array of diagnostic possibilities. An acute and early diagnosis, detection and management of bulbar and respiratory weakness, evaluation for cardiovascular instability and suspecting spinal cord lesions are mainstay of effective management of AFP. Long term follow up and management is required to prevent complications.

REFERENCES

2. Arun Agarwal, J N Behera; study of institutional AFP cases with reference to national polio eradication programme.
4. Ameer Ahmad; Abdul Rehman; Bahwal Victoria hospital Bahawalpur; one year surveillance data of acute flaccid paralysis, Pak J medi. Sci. June 2007; 23(3): 308-12
Relaprotomy : Etiopathological factors and decision making.

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Associate professor, Professor, Professor and Head of Department, Resident Doctor,
Department of General Surgery, V. S General Hospital & GCS Medical College, Ahmedabad.

KEY WORDS: Ondemandrelaprotomy, multiple factors, mortality

ABSTRACT

Introduction: The decision for relaprotomy is frequently challenging when faced with a critically ill patient with nonspecific signs and symptoms. The objective of this study is to identify preoperative, intraoperative and postoperative factors that may predict the need for relaprotomy. Material and Method: Planned relaprotomy and relaprotomy on demand are two frequently employed surgical treatment strategies for patients with previous abdominal surgeries. Here a prospective study of ondemandrelaprotomy patients during September 2009 to August 2012 is presented. Total 44 patients were included. Results: Incidence of Relaprotomy: 3.65 %, Male: female ratio: 2.6:1, Age group: 15 to 60 years with mean age 40.22 years, Rate of relaprotomy in emergency primary laparotomy: 4.7 %, Rate of relaprotomy in planned primary laparotomy: 2.83%, Mortality in our study was 20.45 %. Conclusion: ClinicalAcumen and Multiple factors need to be considered for making relaprotomy decision.

What is Relaprotomy?

Relaprotomy term has Greek origin: re-repeated, Laparastomach, Tomie-cut up i.e. a repeated exploratory operation of the stomach cavity. So relaprotomy means repeated opening of abdominal cavity.

The planned relaprotomy strategy requires a decision to be made during the primary laparotomy. Example: in some secondary peritonitis cases, relaprotomies are performed every 1-3 days until no residual infection is found. The ondemandrelaprotomy strategy is based on doing arelaprotomias and when required. Example: after the primary laparotomy for peritonitisonly when patient’s condition deteriorates or fails to improve, then decision for relaprotomy is taken.

Indications for Relaprotomy: 15 patients were operated for faecal fistula (34.09 %), 12 patients were operated for intestinal obstruction (27.27 %), 9 patients were operated for intraperitoneal abscess (20.45 %), 6 patients were operated for burst abdomen (13.63 %), 2 patients were operated for necrotizing pancreatitis (4.54 %)

The mean duration between primary and relaprotomy was 10+/−7.56 days and mean duration of hospitalization was 30+/−12.5 days.

Study:

This was an observational prospective study conducted at Sheth V.S. General Hospital, Ahmedabad, Gujarat.

Ethical clearance was taken. Patients who underwent abdominal surgeries from September 2009 to August 2012 were studied. Out of 1150 patients of primary laparotomy, 44 patients needed relaprotomies (3.65 %)

Exclusion criteria: all trauma cases, damage control surgeries, cases with an initially laparoscopic procedures which were followed by planned laprotomies or laprotomies during colostomy or ileostomy closure, Second look or check laprotomies which aim to check the revascularization in cases after acute mesenteric ischemia and/or in oncological procedures

Classification:

1) According to the time of first operation
   1.1 Early – through the period of patients hospitalization
   1.2 Late

2) According to the purpose of doing relaprotomy
   2.1 Healing – by radical or palliative character
   2.2 Diagnostically-controlled

3) According to the kind of the complication, relaprotomy in
   3.1 Postoperative peritonitis
   3.2 Intestinal obstruction that existed consequently from uncured inflammation in the abdominal cavity and/or retro peritoneum
3.3 stomach bleeding or gastrointestinal bleeding
3.4 other reasons

4) According to the reasons that causes the complication
   4.1 qualification mistakes that causes inadequately diagnostic and tactic behaviour
   4.2 organizational mistakes

<table>
<thead>
<tr>
<th>Indications for primary laparotomy which required relaparotomy</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perforative peritonitis</td>
<td>23</td>
</tr>
<tr>
<td>Intestinal obstruction</td>
<td>14</td>
</tr>
<tr>
<td>Necrotizing pancreatitis</td>
<td>1</td>
</tr>
<tr>
<td>Hydatid disease of liver</td>
<td>2</td>
</tr>
<tr>
<td>Obstructive jaundice</td>
<td>2</td>
</tr>
<tr>
<td>Others/Unknown cause(operated outside)</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Operative Procedures done in primary laparotomy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Resection and Anastomosis</td>
<td>11</td>
</tr>
<tr>
<td>Primary closure of perforation</td>
<td>18</td>
</tr>
<tr>
<td>Exploratory laparotomy with adhesiolysis</td>
<td>7</td>
</tr>
<tr>
<td>Appendicectomy</td>
<td>3</td>
</tr>
<tr>
<td>Hydatid cyst removal</td>
<td>2</td>
</tr>
<tr>
<td>Hepatobiliary surgery</td>
<td>2</td>
</tr>
<tr>
<td>Pancreatic surgery</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sites of primary Lapotomy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Gastrointestinal Tract</td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>Survived</td>
</tr>
<tr>
<td>--------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Stomach</td>
<td>2</td>
</tr>
<tr>
<td>Duodenum</td>
<td>1</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>1</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1</td>
</tr>
<tr>
<td>Liver</td>
<td>1</td>
</tr>
<tr>
<td>Lower Gastrointestinal Tract</td>
<td></td>
</tr>
<tr>
<td>Small bowel</td>
<td>15</td>
</tr>
<tr>
<td>Appendix</td>
<td>5</td>
</tr>
<tr>
<td>Colon</td>
<td>8</td>
</tr>
<tr>
<td>Rectosigmoid</td>
<td>1</td>
</tr>
<tr>
<td>Multiple site</td>
<td>3</td>
</tr>
<tr>
<td>Obstetrics-Gynecology</td>
<td>2</td>
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**Blood investigations:**

<table>
<thead>
<tr>
<th>Hemoglobin</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-9</td>
<td>12</td>
</tr>
<tr>
<td>10-12</td>
<td>17</td>
</tr>
<tr>
<td>&gt;12</td>
<td>15</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>White Blood cell count</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;11000</td>
<td>13</td>
</tr>
<tr>
<td>11000-15000</td>
<td>17</td>
</tr>
<tr>
<td>15000-20000</td>
<td>8</td>
</tr>
<tr>
<td>&gt;20000</td>
<td>6</td>
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<table>
<thead>
<tr>
<th>Serum Albumin</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5-5.5</td>
<td>12</td>
</tr>
<tr>
<td>3-3.5</td>
<td>15</td>
</tr>
<tr>
<td>&lt;3</td>
<td>17</td>
</tr>
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</table>

**Ultra sonography findings**

<table>
<thead>
<tr>
<th>Ultra sonography findings</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilated bowel loops with mild to moderate free fluid</td>
<td>17</td>
</tr>
<tr>
<td>Minimal interbowel free fluid with internal echoes</td>
<td>15</td>
</tr>
<tr>
<td>Moderate free fluid in pelvic region with echoes</td>
<td>5</td>
</tr>
<tr>
<td>No Abnormality Detected</td>
<td>7</td>
</tr>
</tbody>
</table>

**Indications for relaparotomy due to complications in postoperative period**

<table>
<thead>
<tr>
<th>No.</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>Faecal fistula</td>
</tr>
<tr>
<td>9</td>
<td>Intrapertitoneal abscess</td>
</tr>
<tr>
<td>12</td>
<td>Intestinal obstruction</td>
</tr>
<tr>
<td>6</td>
<td>Burst abdomen</td>
</tr>
<tr>
<td>2</td>
<td>Necrotizing pancreatitis</td>
</tr>
</tbody>
</table>

**Days after primary laparotomy**

<table>
<thead>
<tr>
<th>Days</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>26</td>
</tr>
<tr>
<td>10-20</td>
<td>8</td>
</tr>
<tr>
<td>20-30</td>
<td>6</td>
</tr>
<tr>
<td>1 month to 2 months</td>
<td>4</td>
</tr>
</tbody>
</table>

**Post-operative Radiological investigations after primary laparotomy:**

1) In 12 cases Abdominal X-ray standing were suggestive of multiple air fluid levels, 10 showed free gas under diaphragm and 22 cases showed normal abdominal x-ray standing.

2) Ultra sonography findings

3) Computerized Tomography scan : 4 cases needed Computerized Tomography scan for Relaparotomy, out of which 2 showed intraperitoneal abscess and 2 showed anastomatic leak.

**Summary of Results : In our study**

- Perforative peritonitis was the main indication of primary laparotomy in our study requiring relaparotomy followed by intestinal obstruction. Operative procedures like Resection anastomosis and primary closure of perforations were needed in most of the patients.

- Lower Gastrointestinal cases required more reexploration than Upper Gastrointestinal cases. Even mortality was more in Lower Gastrointestinal cases.

- Most of the patients had anemia, leukocytosis and hypoproteinemia (hypoalbuminemia).

- Basic radiological investigations were needed in all patients. Some required detail investigations like Computerized Tomography scan.

- Maximum cases required reexploration within the first 10 days.

- Fecal fistula (anastomatic leak, bowel necrosis etc.) and intestinal obstruction were main indications for relaparotomy.

**OUTCOME:**

Out of 44 patients, 34 patients recovered and were discharged, 9 patients died. 5 patients had died due to septicaemia with Multiorgan Dysfunction Syndrome. 2 patients died of pulmonary complications with cardiorespiratory arrest, 2 patients died of uremia and hepatorenal shutdown, and 1 patient took Discharge Against Medical Advice and did not come for follow up.
DISCUSSION

Studies done about ondemand relaparotomy and planned relaparotomy showed that there is no statistically significant difference in morbidity and mortality but ondemand relaparotomy group have substantial reductions in number of relaparotomies, health care utilization and medical costs. So we have considered all the Ondemandrelaparotomy cases for our study.

The rate of relaparotomies in our study is 3.65 % which is consistent with the rates of 1-4.4% reported in literature.

Clinical decision making aided by other blood and radiological investigations were most helpful in deciding for relaparotomy.

Timely relaparotomy is valuable in the identification and treatment of complications following abdominal surgery.

Symptoms in postoperative period like abdominal pain, copious-seropurulent discharge from primary laparotomy wound, vomiting, constipation, obstipation, abdominal distention should be investigated further.

On examination of patient other than vitals, abdominal findings like abdominal distention, generalized tenderness, hypo or hyperperistaltic bowel sounds, fecal or purulent content of drainage fluid may indicate need for relaparotomy.

The parameters which lead to the suspicion of anastomatic leak are tachycardia (heart rate >100 beats/minute), fever (body temperature >100 degree F), local or generalized peritoneal reaction during physical examination, leucocytosis (>11000 White Blood Cell Count/cu mm), prolonged paralytic ileus (>2 days) as demonstrated by signs during physical examination along with the other investigations which were required.

Indications requiring Relaparotomies are similar everywhere and our indications matched with numerous other studies of which leading causes are fecal fistula, intestinal obstruction, and intraperitoneal abscess.

As most of the cases of primary laparotomy was done in the emergency, we had no time to prepare bowel. However broad spectrum antibiotic coverage was done, thorough peritoneal lavage and all aseptic measures were taken. Hand Sewn anastomosis was done in most cases as indicated. Primary perforation suturing was done when required.

Raised temperature, tachycardia, tachypnoea, with or without hypotension suggests to look for septicaemia. Poor nourishment and anemia suggest poor immune response. Diabetes mellitus, Jaundice along with the other comorbid conditions are other precipitating factors which can lead to relaparotomy.

In relaparotomy patients, we had the blood investigations available like Blood pH, serum electrolytes, Renal function test, Liver Function Test, Complete Blood Count, serum proteins which were not always available in primary laparotomy in emergency conditions. The necessary corrections were made in relaparotomies. Again the facilities for ventilation were made available beforehand. Opinion of physicians, anesthetists, other superspecialists could be availed and their expert advice could be followed.

In our study, 65.90 % patients had anemia, 70.45 % patients had leucocytosis and 72.72 % had hypoalbuminemia.

The mean duration between primary laparotomy and relaparotomy was 10+/−7.56 days and mean duration of hospitalization was 30+/−12.5 days.

In our study, relaparotomies for lower GastroIntestinal surgeries carry higher mortality.

Mortality in our study was 20.45 % of which the main causes were septicaemia with Multi Organ Dysfunction Syndrome, pulmonary complications, hepatorenal shutdown. All of them required ventilator and ionotropic support.

Clinical acumen forms the basis to decide for Relaparotomy in majority of the cases. Multiple factors are responsible to consider for relaparotomy which are anemia, septicaemia, hypoproteinemia, and complications from primary laparotomy like fecal fistula, intestinal obstruction, intraperitoneal abscess and burst abdomen.

Multiple factors may lead to Relaparotomy which is beyond the hands of a clinician yet a vigilant, vigorous and timely management could help reduce the rate of relaparotomies.

CONCLUSION

Clinical acumen forms the basis to decide for Relaparotomy in majority of the cases. Multiple factors are responsible to consider for relaparotomy which are anemia, septicaemia, hypoproteinemia, and complications from primary laparotomy like fecal fistula, intestinal obstruction, intraperitoneal abscess and burst abdomen.

Multiple factors may lead to Relaparotomy which is beyond the hands of a clinician yet a vigilant, vigorous and timely management could help reduce the rate of relaparotomies.

REFERENCES

1. Trakia journal of sciences Vol 8.No.1 Pg 87-90,2010
3. JAMA,August 22/29,2007-vol 298, no.8


17. Cheadle WG, Spain DA: The continuing challenge of intraabdominal infection. AMJ surgery 2003, 186: 15S-22S.


A cadaveric study of presence of rarely occurring but normal anatomical variant of anterior chest wall - The Rectus Sternalis Muscle

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KEY WORDS : Pectoral region, Embalmed cadaver, Rectus Sternalis

ABSTRACT

Introduction: Rectus Sternalis muscle is a very rare anatomical variant of the anterior chest wall musculature. Though regularly present in lower animals, it is occasionally detected in humans. Presence of Rectus Sternalis muscle may cause alterations in the electrocardiogram or confuse a routine mammography. If found accidentally in mammography, CT scan or MRI studies, it must be documented in a patient's medical records and the patient must be informed of the fact. It can be used in microvascular anastomosis and as a pedicle flap for reconstructive surgery of breast, head, neck, and the anterior chest wall. Rectus Sternalis muscle is often misdiagnosed for many of the benign and malignant anterior chest wall lesions and tumors. 

Aims & Objectives: To spread knowledge to prevent diagnostic errors and complications in surgeries of the pectoral region. 

Material and Methods: 48 embalmed and preserved cadavers were studied to know the presence of Rectus Sternalis muscle in Pectoral region in dissection hall of Anatomy Department, Government Medical College, Surat, Gujarat, during routine dissections of MBBS course during 2009-15. 

Observation and Result: Rectus Sternalis muscle was found bilaterally in anterior chest wall, superficial to Pectoralis Major Muscle only in two cadavers. It was found as a vertical strip of muscle in the anterior chest wall musculature. The incidence of Rectus Sternalis thus found is 4.16 % in this study. 

Conclusion: Knowledge of Rectus Sternalis is important for interventional and diagnostic procedures which are related to this region.

INTRODUCTION

The rectus sternalis muscle which is also known as the Sternalis Rectus thoracis, Episternalis, Muscularis sternalis, Para sternalis and the Presternalis2,3. It is a very rare anatomical variant of the anterior chest wall musculature. Rectus Sternalis muscle though occasionally detected in humans it is regularly present in lower animals. It was first ever demonstrated by Carbollius in 1604. Later on Dupuy in 1726 gave the first formal description of this muscle. Since then, many cases with Rectus Sternalis muscle have been reported. It is a superficial vertical strip, which is sternal or parasternal in position, lies superficially and perpendicular to the pectoralis major muscle. Origin of the muscle is usually from the upper sternum and the infraclavicular region. While the insertions range from the abdominal external oblique muscle aponeurosis to the pectoral fascia, lower ribs, costal cartilages, rectus abdominis muscle sheath.4,5 Rectus Sternalis is twice as often unilateral as it is bilateral; there is a great variation in height, width and thickness6 with its almost equal occurrence in genders from 5-8%. One school of thoughts believes that Sternalis muscle is derived from neighboring muscles, such as pectoralis major, rectus abdominis, sternocleidomastoid, panniculus carnosus and external oblique.

Rectus Sternalis muscle is a very rare anatomical variant of the anterior chest wall musculature. Though regularly present in lower animals, it is occasionally detected in humans. This muscle is well documented and familiar to anatomists but quite unknown among clinicians and radiologists1. To minimize the risks of surgical complications, thorough knowledge of anatomical variants of the rectus sternalis with its clinical significance is needed. If the clinicians are unaware of this muscle variant, it may lead to undesirable changes in prognosis of patient's diseases and their conditions. If rectus sternalis muscle is present it may cause alterations in the electrocardiogram7 or confuse a routine mammography7. If found accidentally in mammography, CT scan and / or MRI studies, it must be documented in a patient's medical records and the patient must be informed of the fact, for during reconstructive surgery of the breast, head and neck, and the anterior chest wall it can be used as a pedicle flap or flap for micro vascular anastomosis.
Many of the benign and malignant anterior chest wall lesions and tumors have turned out to be nothing but the misdiagnosis of the presence of the rectus sternalis muscle. To prevent diagnostic errors and complications in surgeries of the pectoral region, knowledge of anatomical and embryological details of this rare rectus sternalis muscle is very important.

**MATERIAL AND METHOD:**

Time duration: August 2009 to August 2015

Sample size: 48 cadavers

Place: Dissection hall, Anatomy Department, Government Medical College, Surat, Gujarat

Method: Routine dissection of the pectoral region was done to find the incidence, occurrence, anatomical variations of the rectus sternalis muscle. Details of the muscle found were taken along with photographs when found during dissection.

**RESULT**

During routine dissection of the pectoral region, on one of the formalin fixed male cadavers this rare rectus sternalis muscle was found. Similarly on one of the female cadavers a pair of rectus sternalis was found, too. Thus out of the entire sample size of 48 we found a bilateral rectus sternalis muscle only in two cadavers. No unilateral rectus sternalis was found. Two straps like flattened muscles, on either hemithorax, were found lying superficial to the pectoralis major muscle and the pectoral fascia.

Cadaver 1:

The right side:

Origin: sternal origin of the right sternocleidomastoid muscle, and the upper segment of the right pectoralis major. Few fibers arising from the sternal origin of the left sternocleidomastoid muscle

Insertion: Some fibers near the level of xiphisternal joint, close to the origin of right rectus abdominis muscle and external oblique aponeurosis. Other fibres of Rectus Sternalis were in continuity with fibres of pectoralis major muscles.

The left side:

Origin: sternal origin of the left sternocleidomastoid muscle, and the upper segment of the left pectoralis major.

Insertion: The muscle gradually inserted onto the left 5th-7th costal cartilages and costochondral junction, on the left sternocostal arch and pectoralis major muscle.

Cadaver 2:

Origin: Parasternal origins, from the right and left sternocleidomastoid muscles respectively, and upper segments of the pectoralis muscles.

Insertion: at the level of the xiphisternal joint, the fibers of both the rectus sternalis muscle ended near the origin of the rectus abdominis muscle in continuity with the...
pectoralis muscles and merging in the external oblique aponeurosis.

**DISCUSSION:**

The bilateral sternalis muscle is found in less than 1.7% while the unilateral manifestation has been reported to be present in 4.5% of subjects. The occurrence of sternalis muscle has many racial and regional variations 4-7% in white population, 8.4% in black population, 11% in Asian population, 1% in Taiwanese population and 9.3% in Turkish population. In Indian population, its incidence is 5-8% equal in both genders.

In our current study we found that the occurrence of this unique muscle is 4.16%, with an equal incidence of occurrence in both the genders. Also we found bilateral occurrence of the muscle dominating in our study unlike the standards where occurrence of unilateral sternalis is much common.

In the male cadaver we found that the rectus sternalis muscle was of Type: F (As per classification by Raikos et al.)

Description:
On the right side the lower 5cm fleshy and flat ribbon like end was attached to superficial surface of right pectoralis major muscle by fascia.
On the left side the lower 2.5cm fleshy and flat ribbon like end was attached to superficial surface of left pectoralis major muscle by fascia.

While on the female cadaver we found it to be of Type: E (As per classification by Raikos et al.)

Description: on either side the lower ends ended as fleshy flat ribbons of 3-4 cm ending as it attached themselves to the superficial fascias of the pectoralis muscles on their respective sides.

One theory postulates the embryological origin of sternalis muscle, stating that it is a derivative of the hypaxial myotomes / dermomyotomes from which the ventral and lateral body wall muscles of thorax and abdomen are developed. Also that it originates from the adjacent muscles or their blastemas, like the sternocleidomastoid, rectus abdominis, and panniculus carnosus muscle sheet, abdominal external oblique muscle or from the ventrolateral part of the diaphragm. Other school of thoughts support that the muscle develops either from the rectus abdominis sheath or from pectoralis major due to a defect in the muscle patterning. Especially, in the latter case, the defective precursor migration of the prepectoral mass which gives rise to the pectoralis major and minor muscles may also contribute to the sternalis muscle development, while mechanical disturbances may lead to atypical clockwise rotation of the muscle fibers.

In Gray’s anatomy this muscle is described as a superficial vertical slip, or slips which ascend from lower costal cartilages and the rectus sheath to blend with sternocleidomastoid muscle or to attach to the upper sternum or costal cartilages. In the present cadaveric study, the latter view held stronger, since the muscle had a tendinous upper part and a lower fleshy belly. Different studies have come to different conclusions, varying on the race, region and the built of sample size taken into consideration. So we can conclude that origin and insertion of this rare muscle has humongous variations and that it is yet a matter of debate till date.

According to Sarikcioglu L et al., it is a composite type of muscle.

The views regarding its innervations also vary with different authors. As it was quite difficult to save the tiny nerves while removal of the fascia from the muscle, in our particular study we could not establish any firm grounds regarding the innervations of rectus sternalis muscle. As per different authors it may be supplied by ventral tips of hypomere, twigs of pectoral nerve, anterior cutaneous branches of intercostal nerves, external or internal thoracic nerves. In our study the nerve supply was from the anterior cutaneous branches of the intercostal nerves. However we propose that the innervations of the rectus sternalis muscle depends on the topographical location and function of the particular and individual muscle.

The function of this muscle is still a mystery. With no confirmed documented data as to what exactly does this muscle do or how it acts upon. Yet there are views as in to it may be acting in elevation of lower chest as an accessory muscle or it may be taking part in movements of the shoulder joint.

Though rare to find, the rectus sternalis muscle is but a normal anatomical variant of the anterior chest wall. Thus its knowledge becomes mandatory for every clinician, especially for surgeon, plastic surgeon and radiologist to avoid misdiagnosis.

**CONCLUSION:**

Quite unknown to most clinicians, and yet very well known to all anatomists this rare and normal anatomical variant of the anterior chest wall without any precise function, origin or teleology is having an important role in reconstructive surgery as muscle flaps for head & neck, breast and the anterior chest wall region.
REFERENCES:


Analysis of Fixed-dose Drug Combinations (FDCs) available at various pharmacy stores of western India

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KEY WORDS : Fixed-dose Drug Combinations (FDCs), Rationality, Essential Medicine List

ABSTRACT

Aim: To study the prevailing scenario of fixed-dose drug combinations available in pharmacy stores.

Methodology: This was an observational, analytical and cross sectional study and was conducted at the department of Pharmacology, S.B.K.S MI&RC, Sumandeep Vidhyapeeth, Piparia, Vadodara. This study involved analysis of currently available FDCs in four pharmacy shops of Vadodara, for essentiality and rationality. Information about number of drugs, number of FDCs, number of ingredients in FDCs, category of FDCs, essentiality and rationality of FDCs was collected.

Results: Around 60% FDCs in each pharmacy shop were irrational. Significantly lower number of drugs and FDCs were present in Store B while significantly higher numbers of rational FDCs were present in Store C. In all four pharmacy stores more than 75% of FDCs contained only two or three ingredients.

Conclusion: India has 4th largest pharmaceutical industry in the world and also significant drug use problems. In India, irrational FDCs are freely available and also prescribed by physicians. There is a concern regarding the production, prescription, and use of irrational FDCs. Considering the enormous use of drugs in Indian population, it is high time that pharmaceutical companies, health care professionals and regulatory authorities join hands and prescribe guidelines for the manufacture and sale of FDCs.

INTRODUCTION

A drug is defined as “any substance or product that is used or intended to be used to modify or explore physiological systems or pathological states for the benefits of the recipient” (1). The primary aim of the therapy is to treat, prevent, suppress or cure any disease with effective and safer drugs (2). India with population of 120 crore plus people is a second largest country in the world and has 4th largest pharmaceutical industry (3). At the same time India is the country with significant disease burden and drug use related problems. A patient may suffer from chronic or multiple diseases at the same time which requires the use of more than one drug (polypharmacy) for treatment. However, polypharmacy may increase the complexity of drug therapy, risk of adverse events, cost of therapy and poor patient compliance (4). Many Fixed-dose Drug Combination (FDCs) are developed and prescribed to solve some of these disadvantages associated with polypharmacy. A FDC is defined as “a formulation of two or more active ingredients combined in a single dosage form in fixed doses” (5). Use of FDCs is associated with many advantages like synergistic or additive action and increased efficacy (e.g., cotrimoxazole – combination of sulfamethoxazole and trimethoprim), reduced side effects (e.g., levodopa with carbidopa), reduced pill burden as well as cost and better patient compliance (e.g. anti tubercular drug combinations, anti retroviral drug combinations). There is a concern regarding the irrational production, prescription, and use of irrational FDCs. Considering the enormous use of drugs in Indian population, it is high time that pharmaceutical companies, health care professionals and regulatory authorities join hands and prescribe guidelines for the manufacture and sale of FDCs (6).

During the last decade, more than one-third of all the new drug products introduced worldwide were FDCs (6). In European countries like Spain, the use of FDCs was found to be up to 56% of total medicines prescribed. (7) There are more than 80,000 formulations available in the Indian market either as single drug formulation or as FDCs (6). In 2008, estimated FDC market in India was
been utilized in the present study, viz-

Various studies (11-16) conducted globally have identified rationality criteria to analyze FDCs, which have been utilized in the present study, viz-:

Parliamentary standing committee on health and family welfare noted in its fifty-ninth report (May 2012) on the functioning of the central drugs standard control organisation (CDSCO) of India that some State Drug Authorities have issued manufacturing licenses for a very large number of FDCs without prior clearance from CDSCO (10). Therefore, it is need of an hour to evaluate the existing community use of FDCs in Indian market. However, few studies are conducted in India with this focus. The present study was conducted in a large tertiary care teaching hospital in western part of India. Four different busy pharmacy stores of the city were studied to find out the community use of FDCs.

MATERIAL AND METHOD:

This was an observational, analytical and cross sectional study and was conducted from November 2010 to May 2012, over a period of 18 months, at the department of Pharmacology, affiliated to a 1250 bedded hospital in western part of India. The study included gathering data from four pharmacy stores, two (store A and B) out of which were operating from campus of two tertiary care teaching hospitals attached to medical colleges and other two (store C and D) pharmacy stores operating from two tertiary care trust hospitals. A written permission from the responsible authority of all the pharmacy stores was obtained before initiating collection of any data and information.

An inventory of existing medicines in the pharmacy stores on the day of study had been made. All the formulations available in pharmacy stores were counted. FDCs from among the available formulations had been segregated and analyzed. While doing so, FDCs containing ayurvedic or herbal products or any other medicines belonging to health care system other than modern medicine were excluded. The number of FDCs was expressed as percentage of total formulations available in the respective pharmacy stores on a given day. FDCs were categorized according to their action on body system into fourteen different groups. Each FDC was further analyzed to find out the details about numbers of ingredients in the given FDC.

There are no uniform worldwide acceptable criteria or uniform principles to judge rationality of FDCs. Neither there is any national regulatory guideline of India in place. Various studies (11-16) conducted globally have identified rationality criteria to analyze FDCs, which have been utilized in the present study, viz-:

1. Active pharmaceutical ingredient (API) of the combination should preferably be in the 17th model list of essential medicines (WHO EML 2011) or in 3rd the national list of essential medicines (NLEM) of India
2. Combination should have advantage of established evidence of efficacy and safety over single compounds administered separately
3. Overall cost of the combination should preferably be less than the combined cost of the individual components.
4. Dose & proportion of each API present in FDC should be appropriate for its intended use
5. The pharmacokinetic (PK) properties of individual drugs should be matching
6. Individual drugs should have different mechanism or/and site of action.

The majority of these criteria are recommended by WHO. Each FDC was evaluated with respect to the above mentioned criteria and categorised into one of the following three categories:

A. Rational FDCs:
FDCs which matched exactly with those given in either EML of WHO or NLEM of India were considered rational. Those FDCs which contained either a substitute of essential medicine or other identical drug from the group and met the above six criteria were also considered as rational. E.g: FDC of ampicillin with sulbactam is though not listed in either of the above two lists, it was considered rational since amoxicillin is a substitute of clavulanic acid (beta lactamase inhibitor) and this FDC meets all the above five criteria.

B. Semirational FDCs:
All those FDCs which did not match with FDCs listed in either EML of WHO or NLEM of India but still demonstrated a synergistic or additive pharmacodynamic profile and at the same time did not have the potential to cause any increase in adverse effects were considered semi rational, even though they were not strictly meeting pharmacokinetics or cost criteria. E.g: the combination of two diuretics (spironolactone plus frusemide) are not listed in either EML or NLEM of India, but still demonstrated a synergistic or additive pharmacodynamic profile.

C. Irrational FDCs:
When a FDC was not found to serve any PD or PK advantage, or did not have additive or synergistic effect or was shown to have the potential of causing enhanced adverse effects, it was considered as irrational FDC.
irrespective of purported advantages of cost or convenience. In other words, all those FDCs which could not be rated as rational or semirational were accorded the status of irrational FDCs. E.g: paracetamol plus ibuprofen, ciprofloxacin plus tinidazole, cough mixtures containing combinations of antitussives, antihistaminics, expectorants etc.

Result:

Information in respect of drugs available from four pharmacy outlets was analysed to find the number of drugs having single ingredient or available as FDCs in each pharmacy stores as shown in table 1. Number of FDCs available as percentage of total drugs in each shop was expressed as percentage of total drugs in respective shop. The pharmacy store A not only stocked the highest number of drugs (2082) but also had the highest percentage (34.20) of drugs available as FDCs. This was followed by store D (1890 drugs, 29.15% FDCs) and store C (741 drugs, 28.74% FDCs). Store B had the lowest number of drugs (516) with significantly higher number of single ingredient drugs (78.10%, p<0.0001) and significantly lower number of FDCs (21.90%, p<0.0001) (Table 1).

<table>
<thead>
<tr>
<th>Category of drugs</th>
<th>Pharmacy stores</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A, n (%)</td>
</tr>
<tr>
<td>Single ingredients</td>
<td>1370 (65.80)</td>
</tr>
<tr>
<td>FDCs</td>
<td>712 (34.20)</td>
</tr>
<tr>
<td>Total</td>
<td>2082 (100)</td>
</tr>
</tbody>
</table>

In all four pharmacy stores more than 75% of FDCs contained only two or three ingredients, the highest being in store A and the lowest in store C. However there was no significant difference in this regard in any shop. Only store C had significantly higher number of FDCs (3.76%, p=0.04) containing seven ingredients (Table 2).

<table>
<thead>
<tr>
<th>Number of ingredients</th>
<th>Pharmacy stores</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A, n (%)</td>
</tr>
<tr>
<td>2</td>
<td>480 (67.42)</td>
</tr>
<tr>
<td>3</td>
<td>110 (15.45)</td>
</tr>
<tr>
<td></td>
<td>590 (82.87)</td>
</tr>
<tr>
<td>4</td>
<td>44 (7.99)</td>
</tr>
<tr>
<td>5</td>
<td>20 (2.81)</td>
</tr>
<tr>
<td>6</td>
<td>11 (1.54)</td>
</tr>
<tr>
<td>7</td>
<td>11 (1.54)</td>
</tr>
<tr>
<td>8</td>
<td>9 (1.26)</td>
</tr>
<tr>
<td>&gt;8</td>
<td>27 (3.79)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>712 (100)</td>
</tr>
</tbody>
</table>

FDCs pertaining to cardiovascular system were significantly more in store D (10.34%, p<0.001) and significantly less in store C (1.88%, p<0.001). There was a significant difference (p=0.0002) in the number of FDCs in category of antimicrobials, the highest being 25.35% in store C and the lowest (11.50%) in store B. Significantly more number (18.58%, p<0.01) of FDCs for skin conditions was in store B, the least being in store C (6.57%). A little more than 7% of FDCs for eye disorders were available at store B which is significantly more (p=0.007) than in any other stores and the lowest number of ophthalmic FDCs (0.47%) was found in store C. A similar situation was prevailing with regard to FDCs for ear nose and throat conditions. Significantly more number (2.65%, p=0.003) was available from store B as compared to only 0.47% in store C. Nearly one third (30.99%) FDCs in the category of nutritional products was found in store C which was significantly more (p=0.01) than in other stores. The number of such products was the least (19.47%) in store B (Table 3).
Table 3: FDC categories based on action on body system in pharmacy stores

<table>
<thead>
<tr>
<th>Category of FDCs</th>
<th>Store A</th>
<th>Store B</th>
<th>Store C</th>
<th>Store D</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular system</td>
<td>66(9.27)</td>
<td>07(6.19)</td>
<td>4(1.88)</td>
<td>57(10.34)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Musculoskeletal system</td>
<td>70(9.83)</td>
<td>06(5.31)</td>
<td>16(7.51)</td>
<td>57(10.34)</td>
<td>0.28</td>
</tr>
<tr>
<td>Antimicrobials</td>
<td>117(16.43)</td>
<td>13(11.50)</td>
<td>54(25.35)</td>
<td>67(12.16)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>29(4.07)</td>
<td>03(2.65)</td>
<td>3(1.41)</td>
<td>19(3.45)</td>
<td>0.29</td>
</tr>
<tr>
<td>Gastrointestinal system</td>
<td>29(4.07)</td>
<td>06(5.31)</td>
<td>11(5.16)</td>
<td>34(6.17)</td>
<td>0.41</td>
</tr>
<tr>
<td>Genitourinary system</td>
<td>7(0.98)</td>
<td>01(0.88)</td>
<td>3(1.41)</td>
<td>14(2.50)</td>
<td>0.15</td>
</tr>
<tr>
<td>Respiratory system</td>
<td>95(13.34)</td>
<td>14(12.39)</td>
<td>33(15.50)</td>
<td>51(9.26)</td>
<td>0.06</td>
</tr>
<tr>
<td>Skin</td>
<td>73(10.25)</td>
<td>21(18.58)</td>
<td>14(6.57)</td>
<td>60(10.89)</td>
<td>0.01</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>19(2.67)</td>
<td>08(7.08)</td>
<td>1(0.47)</td>
<td>15(2.72)</td>
<td>0.007</td>
</tr>
<tr>
<td>Ear nose and throat</td>
<td>2(0.28)</td>
<td>03(2.65)</td>
<td>1(0.47)</td>
<td>1(0.18)</td>
<td>0.003</td>
</tr>
<tr>
<td>Endocrine system</td>
<td>41(5.76)</td>
<td>07(6.19)</td>
<td>6(2.82)</td>
<td>39(18.30)</td>
<td>0.16</td>
</tr>
<tr>
<td>Nutritional products</td>
<td>149(20.93)</td>
<td>22(19.47)</td>
<td>66(30.99)</td>
<td>116(21.05)</td>
<td>0.01</td>
</tr>
<tr>
<td>Drugs related to Metabolism</td>
<td>6(0.84)</td>
<td>00</td>
<td>0</td>
<td>8(1.45)</td>
<td>0.17</td>
</tr>
<tr>
<td>Miscellaneous FDCs</td>
<td>9(1.26)</td>
<td>02(1.77)</td>
<td>1(0.47)</td>
<td>13(2.36)</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>712</strong></td>
<td><strong>113</strong></td>
<td><strong>213</strong></td>
<td><strong>551</strong></td>
<td></td>
</tr>
</tbody>
</table>

Of the total 213 FDCs in store C, only 47 (22.07%) and 48 (22.54%) were matching those in WHO EML and NLEM respectively. However these were the highest and significantly more than in store D (6.9%, p<0.001 and 9.26% p=0.0003) in WHO EML and NLEM respectively. The same pattern was maintained and a significantly more (p=0.0005) number of FDCs (15.02%) from store C was found to be matching those in both WHO EML and NLEM. The least number of such FDCs common to both lists was only 5.63% in store D. A little less than 90% (89.66%) FDCs from store D neither matched the ones in WHO EML nor NLEM. The lowest number of such FDCs was 70.42% in store C which was significantly less (p<0.0001). However a maximum number of FDCs (712) was available in store A whereas the lowest number (113) was in store B (Table 4).

Table 4: Matching of FDCs in all pharmacy stores with that of WHO EML and NLEM

<table>
<thead>
<tr>
<th>Drug list</th>
<th>Store A, n(%)</th>
<th>Store B, n(%)</th>
<th>Store C, n(%)</th>
<th>Store D, n(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO EML</td>
<td>88 (12.36)</td>
<td>10(8.85)</td>
<td>47(22.07)</td>
<td>38(6.90)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>NLEM</td>
<td>98 (13.76)</td>
<td>16(14.16)</td>
<td>48(22.54)</td>
<td>51(9.26)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Both WHO EML and NLEM</td>
<td>67(9.41)</td>
<td>09(7.96)</td>
<td>32(15.02)</td>
<td>31(5.63)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Neither WHOEML nor NLEM</td>
<td>593(83.29)</td>
<td>96 (84.96)</td>
<td>150 (70.42)</td>
<td>494(89.66)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>712</strong></td>
<td><strong>113</strong></td>
<td><strong>213</strong></td>
<td><strong>551</strong></td>
<td></td>
</tr>
</tbody>
</table>

Almost 30% of FDCs in store C were found to be rational against only about 10% FDCs in store D and this difference was significant (p<0.0001). Semirational FDCs were significantly higher (26.55%, p<0.0001) in store B than only 9.39% of store C. With regard to irrational FDCs there was no significant difference (p=0.46) in number of FDCs in all four pharmacy stores. This figure hovered around 60% in each shop (Table 5).
Table 5: Status of FDCs in pharmacy stores

<table>
<thead>
<tr>
<th>Status of FDCs</th>
<th>Store A, n(%)</th>
<th>Store B, n(%)</th>
<th>Store C, n(%)</th>
<th>Store D, n(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RATIONAL</td>
<td>119(16.71)</td>
<td>17(15.04)</td>
<td>63(29.58)</td>
<td>57(10.34)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SEMIRATIONAL</td>
<td>163(22.89)</td>
<td>30(26.55)</td>
<td>20(9.39)</td>
<td>140(25.41)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IRRATIONAL</td>
<td>430(60.39)</td>
<td>66(58.41)</td>
<td>130(61.03)</td>
<td>354(64.25)</td>
<td>0.46</td>
</tr>
<tr>
<td>TOTAL</td>
<td>712 (100)</td>
<td>113 (100)</td>
<td>213 (100)</td>
<td>551 (100)</td>
<td></td>
</tr>
</tbody>
</table>

**DISCUSSION:**

The rationality of a fixed dose combination is one of the most controversial and debatable issues in today’s clinical practice. The Indian laws have not been properly defined to grant marketing approvals for the FDCs by state or central drug controlling authorities. Therefore, the state drug controlling authorities have continuously been approving various FDCs, lacking any pharmacodynamic or pharmacokinetic advantages and acceptable rationale (17).

We focused on examining the actual scenario of marketing, and hence indirectly indicating their use, by studying the drugs and FDCs available in four pharmacy stores. Two of the studied pharmacy stores were operating in large tertiary care teaching hospitals, attached to medical collages, one of the state government and the other run by a private charitable trust. The other two stores operated from medium sized charitable hospitals, of which one is primarily catering to children. Analysis of availability of drugs and FDCs in these pharmacy stores showed that store B had a significantly less number of drugs (516) and FDCs (113) as compared to the other stores (Table 1). This is a good sign that a pharmacy shop located in the campus of a tertiary care teaching hospital has so much less number of drugs and even FDCs. As against this, the pharmacy shop in store A, another tertiary care teaching hospital had highest number of drugs (2082) and FDCs (712). This worked out to be more than four times of the total drugs and more than six times of FDCs in store B. With regard to rational FDCs, it was found that store C topped the list with 29.58% rational FDCs and store B topped the list of semirational FDCs with 26.55%. Though not significant, store B had the lowest number of irrational FDCs (66) as against the highest number of irrational FDCs in store A (430). However, the highest percentage of irrational FDCs was found to be in store D (Table 5). The overall percent of irrational FDCs in four pharmacy stores ranged from about 58% to 64% (Table 5). Therefore there is scope for all four pharmacy stores to reduce the number of medicines, decrease the percentage of FDCs and eliminate the number of irrational FDCs to the extent possible. Availability of a large number of FDCs, many of which are irrational and often harmful, demands serious thinking and action on part of the policy makers, producers and prescribers.

This situation has arisen probably because the pharmaceutical industry in India has been manufacturing and marketing FDCs which are non essential, often irrational and sometimes harmful to the recipients (18). Probably the pharmaceutical industry is driven more by profit than by patient interest. Responding to the pressure for newer products, marketing heads of pharmaceutical companies used to invent combinations of two or more drugs, often launched without an assessment of their therapeutic benefits. Questions may arise why do physicians prescribe irrational combinations? Why the regulatory authorities do approve these irrational FDCs? There are more questions than answers regarding irrational FDCs (19). In a study done by Gulati et al, over 70 dangerous FDCs are being sold in India under more than 1,000 brand names (20). The prescribers can help resolve the situation by consciously not prescribing such FDCs and the drug control authorities by not granting permission for such FDCs. Medical experts worldwide have expressed serious concerns over the increased marketing of drug combinations by pharmaceutical companies, particularly in the developing countries. Considering the enormous use of drugs in Indian population, it is the high time that pharmaceutical companies, health care professionals and regulatory authorities join hands and prescribe guidelines for the manufacture and sale of FDCs. It is the need of the hour that hospitals should constitute drugs and therapeutics review committees to promote rational prescription of FDCs.

The major strength of the present study is that to the best of our knowledge this is a first effort on such a large scale to analyse the scenario of FDCs available in our setup. On the flip side, the study had some inherent limitations as well like short duration of study and limited number of pharmacy stores included in the study. Although this cannot be called the perfect study in the true sense as
actual number and percentage of drugs and FDCs could not be arrived at. However the findings of the study are likely to be very close to the real figures. The second limitation of the study is that we could not include the privately run pharmacy stores (not attached to any hospital) in the analysis.

REFERENCES

10. Department-related parliamentary standing committee on health and family welfare, 59th report on the functioning of the central drugs standard control organisation (cdsco) rajya sabha secretariat, new delhi ,may, 2012
12. Why some leading drugs in the Indian market should not be sold but are still sold, FDCs of ampicillin and cloxacillin: A lay person's guide to medicines, locost, vadodara, 2006:154
Histopathological Evaluation of Eyelid Lesions

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KEY WORDS: Eyelid lesions, Histopathology

ABSTRACT

Background: Eyelid pathology is of growing importance whose early diagnosis saves the visual system. The study aimed at to find out the proportion of eyelid lesions with respect to age, sex, location and histopathological type & to correlate our results with other similar studies. Materials and methods: A total 230 surgical specimens of eyelid lesions were studied from March-2008 to April-2014. Clinical & histopathological analysis was done. Results: The mean age of patients studied was 41.02 years with the highest number of cases in the age group of 31-40 years (17.39%) & the lowest number of cases in the age group more than 80 years (0.86%). Male preponderance was observed (57.82%). Right upper eyelid was the most commonly involved site (40%). Benign lesions were more common than malignant lesions (69.56% vs. 30.44%). Amongst the benign eyelid lesions, nevus was the commonest lesion (17.5%); while amongst the malignant eyelid lesions, squamous cell carcinoma was the commonest (34.28%). Conclusion: All surgically excised eyelid lesions should always be subjected to histopathological examination to establish correct diagnosis & for further management.

INTRODUCTION

Eyelids are beautiful curtains provided by nature to protect the eyeballs. If we compare with any other organ of our body, they have maximum variety of tissues per unit weight.1 Eyelids are therefore affected by variety of lesions. They may be epithelial, adnexal, vascular, neural, histiocytic, melanocytic or inflammatory in origin. Moreover, eyelids are also affected by different systemic diseases.2 The definite histopathological diagnosis of these lesions is crucial to their proper management.

AIMS & OBJECTIVES

The study was carried out with the following aims & objectives:

1. To know the proportion of eyelid lesions with respect to age, sex, location and histopathological type.
2. To study the morphology of various eyelid lesions & to analyze various subtypes.
3. To correlate our results with other similar studies.

MATERIALS & METHODS

A total 230 surgical specimens of eyelid lesions obtained from Ophthalmology institute affiliated to the NHL Municipal Medical College, Ahmedabad were studied over a period of six years; from March 2008 to April 2014. A detailed history of each patient regarding age, sex, chief complaints, & other relevant findings was obtained. Biopsies were fixed in 10% formalin. Each specimen was grossly examined for its size, shape, appearance and consistency. Tissues were processed by routine paraffin embedding technique & stained with Hematoxylin & Eosin stain. Special stains such as PAS stain & Z-N stain were performed whenever required. Histopathological evaluation was done & final diagnosis was given. Statistical analysis was done.

RESULTS & OBSERVATIONS

The mean age of patients studied was 41.02 years. The highest rate of eyelid lesions was observed in the age group of 31-40 years (17.39%) & the lowest rate of eyelid lesions was found in the age group more than 80 years (0.86%). Males were found to be affected more than females (57.82% vs. 42.18%).
Table - I : Age & sex distribution of eyelid lesions

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>No. of cases (%)</th>
<th>Male (%)</th>
<th>Female (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>d•10</td>
<td>11 (4.78%)</td>
<td>5 (2.17%)</td>
<td>6 (2.6%)</td>
</tr>
<tr>
<td>11-20</td>
<td>36 (15.65%)</td>
<td>21 (9.13%)</td>
<td>15 (6.52%)</td>
</tr>
<tr>
<td>21-30</td>
<td>38 (16.52%)</td>
<td>23 (10%)</td>
<td>15 (6.52%)</td>
</tr>
<tr>
<td>31-40</td>
<td>40 (17.39%)</td>
<td>23 (10%)</td>
<td>17 (7.39%)</td>
</tr>
<tr>
<td>41-50</td>
<td>24 (10.43%)</td>
<td>12 (5.21%)</td>
<td>12 (5.21%)</td>
</tr>
<tr>
<td>51-60</td>
<td>35 (15.21%)</td>
<td>21 (9.1%)</td>
<td>14 (6.08%)</td>
</tr>
<tr>
<td>61-70</td>
<td>32 (13.91%)</td>
<td>19 (8.26%)</td>
<td>13 (5.65%)</td>
</tr>
<tr>
<td>71-80</td>
<td>12 (5.21%)</td>
<td>7 (3.04%)</td>
<td>5 (2.17%)</td>
</tr>
<tr>
<td>&gt;80</td>
<td>2 (0.86%)</td>
<td>2 (0.86%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Total</td>
<td>230 (100%)</td>
<td>133 (57.82%)</td>
<td>97 (42.18%)</td>
</tr>
</tbody>
</table>

Eyelid lesions were more common in upper eyelids (66%) as compared to the lower eyelids (34%); with right upper eyelid being the most commonly involved site (Figure-I).

Figure : Site distribution of eyelid lesions

Benign lesions were more common (69.56%) than malignant lesions (30.44%). Benign lesions were common in children and adults with no specific sex predilection; whereas malignant lesions were common after 60 years of age with male preponderance (50/70 cases, 71.4%). Amongst the benign eyelid lesions, nevus was the commonest lesion; followed by epidermal cyst, dermoid cyst and hemangioma (Table-II).

Table-II: Distribution of benign eyelid lesions

<table>
<thead>
<tr>
<th>Benign Lesions</th>
<th>No. of Cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemangioma</td>
<td>19 (11.875)</td>
</tr>
<tr>
<td>Seborheic Keratosis</td>
<td>4 (2.5)</td>
</tr>
<tr>
<td>Epidermal Cyst</td>
<td>26 (16.25)</td>
</tr>
<tr>
<td>Infections</td>
<td>5 (3.125)</td>
</tr>
<tr>
<td>Oncocercasiosis (01)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Cysticercosis (01)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Molluscum Contagiosum(02)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Hydatid cyst (01)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Dermoid cyst</td>
<td>22 (13.75)</td>
</tr>
<tr>
<td>Granuloma Pyogenicum</td>
<td>13 (8.125)</td>
</tr>
<tr>
<td>Nevus</td>
<td>28 (17.5)</td>
</tr>
<tr>
<td>Compound Nevus (14)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Intradermal Nevus (12)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Junctional Nevus (02)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Dermolipoma</td>
<td>9 (5.625)</td>
</tr>
<tr>
<td>Inverted Follicular Keratosis</td>
<td>1 (0.625)</td>
</tr>
<tr>
<td>Chalazion</td>
<td>6 (3.75)</td>
</tr>
<tr>
<td>Epidermal Inclusion Cyst</td>
<td>5 (3.125)</td>
</tr>
<tr>
<td>Wart</td>
<td>7 (4.375)</td>
</tr>
<tr>
<td>Inflammation</td>
<td>3 (1.875)</td>
</tr>
<tr>
<td>Eccrine Hidrocystoma</td>
<td>1 (0.625)</td>
</tr>
<tr>
<td>Choristoma</td>
<td>2 (1.25)</td>
</tr>
<tr>
<td>Neurofibromatosis</td>
<td>4 (2.5)</td>
</tr>
<tr>
<td>Schwannoma</td>
<td>1 (0.625)</td>
</tr>
<tr>
<td>Actinic Keratosis</td>
<td>1 (0.625)</td>
</tr>
<tr>
<td>Xanthelasma</td>
<td>2 (1.25)</td>
</tr>
<tr>
<td>Sudoriferous Cyst</td>
<td>1 (0.625)</td>
</tr>
<tr>
<td>Total benign lesions</td>
<td>160 (100)</td>
</tr>
</tbody>
</table>
Amongst the malignant eyelid lesions, frequency of squamous cell carcinoma was the highest, followed by sebaceous cell carcinoma and basal cell carcinoma (Figure-II). Squamous cell carcinoma & Basal cell carcinoma were more common in lower eyelid (20/24 & 17/19 cases respectively); while sebaceous cell carcinoma was more common in upper eyelid (17/21 cases). All the cases of squamous cell carcinoma showed moderate differentiation. Evidence of perineurial invasion was found in 3/24 cases (12.5%). Cases of Sebaceous cell carcinoma revealed well to moderate degree of differentiation with typical sebaceous features. Pagetoid spread to the overlying skin was observed in 3/21 cases (14.28%). We noted ulcerated growth in 11/19 cases (57.9%) of basal cell carcinoma. Other malignant tumours observed were lymphoma, malignant melanoma & malignant spindle cell tumour.

Figure-II : Distribution of malignant eyelid tumours

Diseases originating in the eyelid are commonly encountered by the clinician and thus a common source of material submitted to the pathologist. As eyelid encompasses wide range of tissues, it is subjected to diversity of lesions.

In our study, the mean age of patients was 41.02 years. In the San Francisco study, in a study performed in County Hospital of Oradea & in the study of Hiroshi Toshiba et al, the mean age of patients was 60.1 yrs, 49.5 yrs & 47.8 yrs respectively. Males were found to be affected more than females (57.82% vs. 42.18%) in our study; just like the study performed in County Hospital of Oradea (54.9% vs. 45.1%). Contradictory to these findings, in the San Francisco study, females were affected more frequently than males (53% vs. 46.8%).

In the present study, benign lesions were more common than malignant lesions. Similar results are observed in some studies.

### Table-III: Comparison of benign and malignant eyelid lesions in different studies

<table>
<thead>
<tr>
<th>Name Of Study</th>
<th>Benign lesions</th>
<th>Malignant lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>San Francisco study</td>
<td>75.9%</td>
<td>24.1%</td>
</tr>
<tr>
<td>County Hospital</td>
<td>45.8%</td>
<td>54.2%</td>
</tr>
<tr>
<td>Obata H et al</td>
<td>73%</td>
<td>27%</td>
</tr>
<tr>
<td>Abdi U et al</td>
<td>58.90%</td>
<td>41.10%</td>
</tr>
<tr>
<td>Tesliuk GC et al</td>
<td>82.6%</td>
<td>17.4%</td>
</tr>
<tr>
<td>Chauhan SC et al</td>
<td>79%</td>
<td>21%</td>
</tr>
<tr>
<td>Present study</td>
<td>69.56%</td>
<td>30.44%</td>
</tr>
</tbody>
</table>

### Table-IV: The most common benign eyelid lesions in different studies

<table>
<thead>
<tr>
<th>Name of Study</th>
<th>Most common benign lesion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>San Francisco study</td>
<td>Seborrhoeic keratosis (19.7%)</td>
</tr>
<tr>
<td>County Hospital of Oradea</td>
<td>Squamous papilloma (17.83%)</td>
</tr>
<tr>
<td>Obata H et al</td>
<td>Nevocellular nevi (21.9%)</td>
</tr>
<tr>
<td>Abdi U et al</td>
<td>Vascular tumour (21.3%)</td>
</tr>
<tr>
<td>Chauhan et al</td>
<td>Dermoid cyst (21%)</td>
</tr>
<tr>
<td>Shastry Srikanth</td>
<td>Nevus (15.39%)</td>
</tr>
<tr>
<td>Fzarhat et al</td>
<td>Epidermal inclusion cyst (26.67%)</td>
</tr>
<tr>
<td>Present study</td>
<td>Nevus (17.5%)</td>
</tr>
</tbody>
</table>
Comparative analysis of common eyelid malignancies in different studies is shown in Table-V. Squamous cell carcinoma was the commonest malignancy observed in the present study; which is contradictory finding with many other studies which showed basal cell carcinoma as the predominant type. Ramya et al. revealed sebaceous cell carcinoma as the predominant type; while Obata H et al. reported equal frequency of basal cell carcinoma & sebaceous cell carcinoma, with not a single case of squamous cell carcinoma. This emphasizes the impact of environmental, racial & geographic factors in the occurrence of malignant eyelid tumours.

### Table-V : Comparison of eyelid malignancies in different studies

<table>
<thead>
<tr>
<th>Type of Eyelid malignancy</th>
<th>San Francisco study (%)</th>
<th>County Hospital of Oradea (%)</th>
<th>Obata H et al (%)</th>
<th>Abdi U et al (%)</th>
<th>Jahagirdar SS et al (%)</th>
<th>Wang JK et al (%)</th>
<th>Ramya BS et al (%)</th>
<th>Present study (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal cell carcinoma</td>
<td>71.8</td>
<td>72.55</td>
<td>37.5</td>
<td>38.8</td>
<td>44%</td>
<td>62.2</td>
<td>26.8</td>
<td>27.14</td>
</tr>
<tr>
<td>Sebaceous cell carcinoma</td>
<td>7.3</td>
<td>1.96</td>
<td>37.5</td>
<td>27.1</td>
<td>37</td>
<td>23.6</td>
<td>41.4</td>
<td>30</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>9.7</td>
<td>19.61</td>
<td>-</td>
<td>22.4</td>
<td>16</td>
<td>8.7</td>
<td>21.9</td>
<td>34.28</td>
</tr>
<tr>
<td>Others</td>
<td>11.2</td>
<td>5.88</td>
<td>25</td>
<td>11.7</td>
<td>3</td>
<td>5.5</td>
<td>9.6</td>
<td>8.57</td>
</tr>
</tbody>
</table>

Basal cell carcinomas account for approximately 90% of all eyelid malignancies in the United States, and they more commonly develop on the lower eyelid. In the Western hemisphere, squamous cell carcinomas account for 9% of all malignancies in the eyelid; the lower eyelid is more commonly affected. Although sebaceous cell carcinoma rarely arises from the skin in other parts of the body, it is an important neoplasm of the eyelids, where it accounts for approximately 1% to 3% of the malignant epithelial lesions of the eyelid in the United States. This tumor most often originates in the upper eyelid, but the lower eyelid is involved in about one-third of cases. In approximately 10% of cases, the tumor apparently begins multicentrically.

Many of eyelid squamous cell carcinomas are well differentiated or moderately differentiated. One of the special ways for tumor dissemination is represented by perineurial invasion, which we reported in 3/24 (12.5%) cases. Sebaceous carcinoma is an aggressive malignant neoplasm. Features indicative of a poor prognosis are orbital or vascular invasion, involvement of both eyelids, poor differentiation, multicentric origin, large size, a highly infiltrative pattern, and pagetoid spread. Several studies indicate that when basal cell carcinomas of the eyelid are excised under frozen-section control of the surgical margins of resection, the rate of tumor recurrence is significantly reduced.

### CONCLUSION

The study concluded that, eyelid is a heterogeneous tissue; hence we tend to see a variety of lesions, both benign & malignant. A histopathological examination of all surgical specimens of eyelid lesions is absolutely mandatory to come to a definitive diagnosis and for further management of patients.

### REFERENCES:


Recent updates in management of triple negative breast cancer (TNBC)

Dr. Meena J. Shah
Associate Professor, Government Medical College & New Civil Hospital, Surat

KEY WORDS: triple negative breast cancer, chemotherapy, neoadjuvant

ABSTRACT

Triple negative breast cancer (TNBC) is heterogenous disease entity notorious for its poor prognosis and its aggressive nature. Systemic treatment for TNBC (negative for the expression of estrogen receptor and progesterone receptor and HER2 amplification) has been limited to chemotherapy options. TNBCs show variable response to chemotherapy. Most and particularly the basal-like subtype, are aggressive, responding initially to chemotherapy but then relapsing with early visceral metastases. The nature of its biological specificity, which is similar to basal like cancer, tumors arising in BRCA 1 mutation carriers and claudin low cancers, is currently being explored in hopes of finding the targets for novel biologic and chemotherapeutic agents. There is no consensus regarding the use of newer targeted therapies in routine practice. Ongoing clinical trials are testing the efficacy, tolerability and safety of novel treatments in TNBC patients and the results are eagerly awaited. In this review, we aim to give broad overview of disease as well as emerging new chemotherapy and targeted therapy and their performance in clinical trials to date in the neoadjuvant, adjuvant, and metastatic setting.

OVERVIEW

Triple negative breast cancer (TNBC) is defined clinically by the absence of estrogen receptor (ER), progesterone receptor (PgR), and HER2/neu overexpression and encompasses a molecularly diverse group of diseases. It is further divided into six subtypes based on their GEP. They are basal like 1, basal like 2, immunomodulatory, mesenchymal, mesenchymal stem like and luminal androgen receptor. TNBC is one of the most aggressive types of cancer and accounts for approximately 7%–20% of all breast cancers. Most TNBC are basal cell cancer and basal cancers are usually triple negative. It is often high-grade and some women with TNBC have a BRCA1 gene fault. This gene is inherited from a parent and can cause breast cancer to run in families. Most breast cancers caused by BRCA1 are triple negative. Women diagnosed with TNBC are four times more likely to have that cancer spread, or metastasize to vital organs within five years than patients with other types of cancer. The death rate for TNBC is higher only in the first three years following diagnosis. That risk will depend on the stage and grade of the cancer as well as the patient’s response to treatment. Although there’s a higher chance that the cancer will come back within 5 years compared to the ‘positive’ tumors, once that hurdle is cleared then the chances of survival are roughly similar. Without targets, women with TNBC do not benefit from hormonal therapy or trastuzumab, and are left with chemotherapy as their only option. So the best treatment usually involves a gruelling combination of surgery, radiotherapy and chemotherapy. Researchers know that there are still many challenges to treating it as each person may have unique genetic and molecular features. Since chemotherapy-resistant TNBC carries a particularly poor prognosis, the identification of the mechanism of chemoresistance and therapeutic advances are critical. There is therefore a particularly strong rationale for clinical research in this setting. This review is focused on opportunities for developing new approaches for filling the current void in an effective treatment for TNBC patients.

Risk factors

TNBC is more common in African and Hispanic American women than white American women. Researchers are not sure why this is. Overall, breast cancer is actually less common in African American women than in white American women. Black women and women who develop breast cancer under the age of 40 are more likely to have TNBC. An increased risk of TNBC has been shown in premenopausal women. Compared with luminal tumors, TNBC are more likely to arise among women with a younger age at menarche, higher parity, younger age at full-term pregnancy, shorter duration of breast-feeding, use of medication that suppresses lactation, higher body mass index and waist-to-hip ratio, and metabolic syndrome. Most women with triple negative breast cancer don’t have a strong history of breast cancer in their family (hereditary breast cancer. Studies taking a converse approach, looking at patients with TNBC but without a significant familial breast cancer
risk, found that 11%–29% of that population under 50 are BRCA-1 mutation carriers. It has been suggested recently that for women under the age of 50 who are diagnosed with TNBC, BRCA mutation testing is a cost-effective strategy and should be integrated into genetic testing guidelines.

Table-I: Therapeutic agents under investigation in TNBC

<table>
<thead>
<tr>
<th>Therapeutic target/rationale</th>
<th>Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA damage and repair</td>
<td>Platinum agents, PARP inhibitors trabectedin (DNA binding agent)</td>
</tr>
<tr>
<td>Microtubule inhibition</td>
<td>Ixabepilone, eribulin</td>
</tr>
<tr>
<td>Antiangiogenesis</td>
<td>Bevacizumab, sunitinib</td>
</tr>
<tr>
<td>EGFR targeting (Mab &amp; TKI)</td>
<td>Cetuximab, panitumumab, erlotinib, gefitinib</td>
</tr>
<tr>
<td>Src and abl targeting</td>
<td>Dasatinib</td>
</tr>
<tr>
<td>mTOR targeting</td>
<td>Temsirolimus, everolimus, deforolimus</td>
</tr>
<tr>
<td>IGF-1R targeting</td>
<td>Cixutumumab, ganitumab, figitumumab, linsitinib,</td>
</tr>
<tr>
<td>AR inhibition</td>
<td>Enzalutamide</td>
</tr>
</tbody>
</table>

PARP = polyadenosine diphosphate (ADP-ribose polymerase; EGFR = epidermal growth factor receptor; mTOR = mammalian target of rapamycin; Mab=monoclonal antibodies, TKI=tyrosine kinase inhibitor, IGF-1R=insulin like growth factor receptor 1, AR=androgen receptor

Table-II: Studies of adjuvant and neoadjuvant therapy in TNBC

<table>
<thead>
<tr>
<th>Study</th>
<th>No. Pts</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>GEICAM 9805 study(^9)</td>
<td></td>
<td>TAC is more effective than FAC in adjuvant treatment of high risk node negative breast cancer.</td>
</tr>
<tr>
<td>BCIRG 001 study(^10)</td>
<td></td>
<td>TAC is more effective than FAC in adjuvant treatment of node positive TNBC.</td>
</tr>
<tr>
<td>GeparTrio study reported by Huober et al (2TAC f/b either 4 or 6 more TAC in responders or 4 TAC Vs capacetabine plus vinorelbine in nonresponders (^11,12))</td>
<td></td>
<td>In nonresponders, pCR rates less than 10% in both treatment groups.</td>
</tr>
<tr>
<td>NSABP protocol B-40 evaluated addition of capecetabine or gemcitabine to docetaxel f/b AC Vs docetaxel alone</td>
<td>1206</td>
<td>Didn't improve pCR 29.7% and 39.8% respectively Vs 32.7%.</td>
</tr>
<tr>
<td>MD Anderson Cancer Center study evaluated response to neoadjuvant therapy in TNBC and nonTNBC(^13)</td>
<td>1108</td>
<td>Higher pCR rates 22% in TNBC Vs 11% in nonTNBC, 3 yr progression free survival (PFS) (63% vs 76) and 3 yr overall survival OS (74% vs 89%) decreased in TNBCs if no pCR, similar survival rates (94% and 98%) in TNBC and nonTNBC if pCR.</td>
</tr>
<tr>
<td>Retrospective study reported by Von Minckwitz et al (pts treated with neoadjuvant therapy) (^14)</td>
<td>435</td>
<td>PCR 21.6% Vs 8.1% in ER- tumors (TNBC) compared with ER+ tumors, 5 yr OS higher in TNBC than nonTNBC (90% Vs 52%).</td>
</tr>
<tr>
<td>NSABP B-27 trial (4 AC 3 wkly Vs 4 AC f/b 4 docetaxel and subsequent surgery or 4 AC f/b surgery and then 4 adj docetaxel (^15,16))</td>
<td>2411</td>
<td>Addition of docetaxel doubled pCR from 12.9% to 14.4% in each AC arm to 26.1% AC-D arm. Better DFS (disease free survival) and OS in pts who achieved pCR.</td>
</tr>
<tr>
<td>GeparDuo trial (4 preop doxorubicin and docetaxel or 4 AC f/b 4 docetaxel)</td>
<td>913</td>
<td>TNBC achieved significantly higher pCR than ER+ (22.8% Vs 6.2%).</td>
</tr>
</tbody>
</table>
Locoregional treatment of TNBC

Considerations for choosing locoregional treatment for TNBC are same as those with other infiltrating ductal carcinoma. Breast conservation surgery with post operative radiation remains to be the choice of treatment for women with T1 and some T2 TNBC. Women with large TNBC may still be the candidates for conservation surgery as studies suggest that TNBC are extremely sensitive to neoadjuvant chemotherapy. Preliminary data implying a relative radioresistance for TNBC do not imply radiation omission because radiation provides an absolute locoregional risk reduction. At present, the integration of subtypes in locoregional management decisions is still in its infancy. For those who test positive for BRCA1 and BRCA2 mutations are frequently advised to undergo bilateral mastectomy, especially if they are young. At the other end of the response spectrum questions are beginning to be asked as to whether a subset of TNBCs who achieve pCR (pathologically complete response) do not require the full complement of local treatments (completion node dissection and/or extensive locoregional radiation). The consideration to withhold definitive surgery from any patient who achieves such a clinical or radiological response to neoadjuvant chemotherapy is certainly premature at this time considering that our current tools for assessing response to neoadjuvant chemotherapy are very insensitive to microscopic but clinically relevant residual disease.

Systemic treatment

The standard chemotherapy treatment for TNBC is usually a combination of chemotherapy drugs anthracycline (doxorubicin or epirubicin) and taxane (paclitaxel or docetaxel). TNBC appears to be sensitive to neoadjuvant (preoperative) or adjuvant (postoperative) chemotherapy and patients who achieve a pathologic complete response (pCR) after neoadjuvant chemotherapy in particular have good overall longterm outcome(1,2). Because the only current systemic treatment for TNBC is chemotherapy and for some women, TNBC doesn't respond well to chemotherapy — this is where the challenge comes in for oncologists and new strategies are needed. If the cancer returns, taxanes may be used again or other drugs that have been shown to be effective. Recent interest has focused on several classes of chemotherapeutic agents and targeted agents whose mechanism of action target molecular defects of TNBC. Early research in America suggests that having platinum containing chemotherapy such as cisplatin or carboplatin before surgery works better than other treatments. The theory is that these particular tumors are defective in the way in which they repair damaged DNA. Neoadjuvant chemotherapy studies have reported higher response rates in TNBC than non-TNBC. Tissue analysis in the neoadjuvant setting is also an important research tool for the identification of chemotherapy resistance mechanisms and new therapeutic targets. Strategies to optimize the response to existing chemotherapy treatments (eg, dose-dense or metronomic schedules) have the potential to consolidate chemosensitivity in TNBC.

There is no preferred treatment for the first-line metastatic setting. Although individual agents (antracyclines, taxanes, antimetabolites and other microtubule inhibitors) are recommended, given the often aggressive nature of TNBC and the presence of extensive visceral disease, the use of a combination of drugs, rather than a single agent, is often advocated.

Newer treatment approaches

Several therapeutic agents (alternative chemotherapy and targeted therapy) under investigation in TNBC are listed in Table-I. TNBC is prevalent among carriers of BRCA1 and BRCA2 mutations. DNA damaging agents

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**Table-III: Neoadjuvant trials evaluating platinum agents**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alba et al.(19) (EC followed by Docetaxel versus EC followed by Docetaxel plus Carboplatin)</td>
<td>94</td>
<td>pCR: addition of platinum agents didn’t improve pCR 35% Vs 30%</td>
</tr>
<tr>
<td>Silver et al.(20) (Cisplatin neoadjuvant 4 cis-p preop f/b surgery then adj CT&amp;/or radiation)</td>
<td>28</td>
<td>pCR 21%, overall response rate 64% (both complete response (CR) and partial response (PR))</td>
</tr>
<tr>
<td>Sirohi et al.(21) (efficacy of neoadj Cisplatin in TNBC Vs non TNBC)</td>
<td>62</td>
<td>Clinical response rates, TNBC 88% and nonTNBC 51%. Survival worse in TNBC</td>
</tr>
<tr>
<td>GeparSixto study (addition of Carboplatin to neoadj chemotherapy in TNBC and HER2 +)</td>
<td></td>
<td>Improvement in pCR from 37.9% to 58.7% with addition of carboplatin in TNBC group but not in HER2+</td>
</tr>
</tbody>
</table>
such as platinum salts (cisplatin and carboplatin) bind directly to and cross-link DNA and are likely to lead to irreversible collapse of DNA repair and achieve desirable therapeutic results. The expression of P63/P73 proteins expressed in about 33% of TNBC patients might be potential biomarker indicating platinum sensitivity of tumor. Another type of chemotherapy researchers are looking into is Epothilones (ixabepilone and eribulin). They target the cancer cell's ability to grow and divide. Ixabepilone, have a low susceptibility to mechanisms causing drug resistance, holding a theoretical advantage over taxanes. Ixabepilone-sensitivity may be correlated with the tumor expression of high beta-III tubulin (a type of tubulin highly expressed in TNBC, basal-like, and HER2+ tumors, and a marker of taxane-resistance) and inversely related to ER expression levels. Ixabepilone was approved by the US FDA in 2007 for the treatment of patients with locally advanced or metastatic breast cancer in combination with capecitabine (Xeloda) after failure of an anthracycline and a taxane and as monotherapy after failure of an anthracycline, a taxane, and capecitabine(17,18).

**Clinical trials of systemic chemotherapy and targeted therapy**

Conventional chemotherapy remains the basis of TNBC treatment according to the majority of national and international guidelines including National Comprehensive Cancer Network (NCCN)(6), St Gallen(7), and European Society of Molecular Oncology (ESMO)(8). TNBC has shown to have a better response to taxane-containing regimens than to chemotherapy without taxanes and to have a significantly better response rate to neoadjuvant taxane treatment. Whether they prove more effective in TNBC patients in the adjuvant setting than other breast cancer subtypes is questionable. Today, neoadjuvant therapy is also increasingly viewed as a platform for testing novel therapies as response in some breast cancer subtypes to neoadjuvant treatment is linked with the long-term outcome. Several studies of neoadjuvant and adjuvant chemotherapy are listed in Table-II. The epothilone, ixabepilone, has shown improved pCR rates in ER/PR-negative tumours compared with tumours positive for hormone receptors in a neoadjuvant trial (17). Ixabepilone is currently being evaluated in a neoadjuvant trial in TNBC, in combination with the anti-epidermal growth factor receptor (EGFR) monoclonal antibody cetuximab. In addition, the phase III TITAN trial is comparing the efficacy of every-3-week ixabepilone and weekly paclitaxel (following standard doxorubicin/cyclophosphamide therapy) in the adjuvant setting in patients with TNBC(19). Treatment with eribulin mesylate (Halaven) improved overall survival (OS) of patients with triple-negative and HER2-negative metastatic breast cancer compared with standard chemotherapies, according to a presentation at the 2014 National Cancer Research Institute Conference in Liverpool. In November 2010, the FDA approved eribulin as a treatment for patients with metastatic breast cancer following the administration of at least 2 regimens with an anthracycline and a taxane. This approval was based on data from the EMBRACE trial, which demonstrated a statistically significant improvement in OS for patients receiving eribulin compared with physician’s choice of therapy. Platinum agents have been renewed interest in TNBC. Several neoadjuvant trials evaluating platinum agents in TNBC patients are listed in Table-III. Multiple other small studies have also evaluated neoadjuvant platinum-based therapy in patients with TNBC with varying results (22,23). Platinum agents have also been evaluated in patients with metastatic TNBC. The Triple Negative Trial (TNT) is for women whose breast cancer has come back or spread after treatment. The TNT trial is trying to find out if the chemotherapy drug carboplatin is better at slowing down the growth of triple negative breast cancer than docetaxel (Taxotere). While current data provides insufficient evidence for the routine use of platinum-based therapy in patients with TNBC, several ongoing prospective studies will help define the role of these agents in the treatment of this subset of patients. Retrospective analysis of 106 patients with metastatic breast cancer who received taxane/platinum chemotherapy as first- or second-line treatment, overall response rate (ORR) did not differ significantly between those with TNBC (37.5%) and those with HER2-positive (35.7%) or HR-positive (41.4%) disease. Two large randomized phase III studies established the efficacy of ixabepilone added to capecitabine treatment in patients with metastatic breast cancer resistant to or pretreated with anthracyclines and taxanes. The Cancer and Leukemia Group B (CALGB) 40603 is evaluating the addition of carboplatin and/or bevacizumab to standard chemotherapy in the neoadjuvant setting for TNBC. All these data reveal an important clinical feature of TNBC: patients initial response to therapy is a crucial step in their treatment, and achieving a complete response is a major determining factor in their long-term survival. Thus, TNBC in particular requires initial therapies capable of eradicating the disease. Differences in prognosis between TNBC and non-TNBC disease appear to be related to differences in recurrence patterns. Patients with TNBC who respond to chemotherapy and experience 3–5 years without disease recurrence tend to survive without recurrence. In GeparQuinto trial all patients received EC followed by docetaxel. Patients were randomized to receive bevacizumab or no additional therapy. Those who did not respond to EC were then randomly assigned to paclitaxel with or without everolimus. Among 663 patients with TNBC, the pCR rates were 27.9% in the no bevacizumab group and 39.3% in the group that received chemotherapy plus bevacizumab. These findings were not confirmed in the other large neoadjuvant study, NSABP B-40(90). Bevacizumab plus chemotherapy led to an increase in toxicity in both clinical trials, most notably
hypertension. Given these differences, it is premature to speculate that adding bevacizumab to chemotherapy will benefit all patients with TNBC. In the phase III ECOG 2100 trial of bevacizumab plus paclitaxel as first-line therapy for 772 patients with metastatic breast cancer, a subgroup analysis evaluated the benefit in women with TNBC (n = 233). In this subgroup, adding bevacizumab to paclitaxel significantly prolonged PFS compared with paclitaxel alone (8.8 months vs 4.6 months). In a TNBC subgroup analysis (n = 577) of a single arm phase III study in which bevacizumab was added to chemotherapy of the oncologist's choice (n = 2,251 total), previously untreated patients with metastatic TNBC achieved an ORR of 47%, time to disease progression of 7.2 months, and median OS of 19.5 months. It should be noted that the FDA approval of bevacizumab in breast cancer, including TNBC, has been withdrawn, although it is still available in Europe. This was based on the bulk of the evidence showing that current data do not support efficacy, and demonstrate increased toxicity. Other antiangiogenic agents, including the anti-VEGFR tyrosine kinase inhibitors, sunitinib and sorafenib, are currently being investigated in the neoadjuvant setting; sunitinib with paclitaxel/carboplatin and sorafenib in combination with cisplatin followed by paclitaxel for early-stage TNBC. Olaparib has been investigated in patients with advanced TNBC with or without BRCA-associated breast cancer with mixed results. Other neoadjuvant studies include the SOLTI NEOPARP, which investigates ipirubicin, was later disapproved, plus paclitaxel versus paclitaxel alone as neoadjuvant treatment in TNBC patients and I-SPY 2, which employs an adaptive trial design. A subset of TNBC patients on this trial will receive paclitaxel with or without veliparib in the neoadjuvant setting. A neoadjuvant trial investigating erlotinib (which specifically inhibits the EGFR tyrosine kinase) together with chemotherapy is currently ongoing.

CONCLUSION

Women with TNBC have a higher likelihood of relapse and a poorer prognosis than women with some other intrinsic subtypes. The lack of drug-targetable receptors on TNBC tumours has made improving the available interventions in TNBC an area of important medical need. Optimal management of TNBC patients requires understanding of molecular subgroups and possible use of combinations of conventional and novel targeted agents. The routine use of neoadjuvant anthracycline/taxane combinations in TNBC is currently being supplemented by ongoing investigations of their use with other types of agent. However, neoadjuvant therapy that maximize the rate of pCR currently offer the best treatment approach for TNBC. Several novel strategies are undergoing clinical evaluation in the setting of TNBC, including the epothilone ixabepilone and biologic agents targeting such pathways as angiogenesis (via VEGF), proliferation signaling (via tyrosine kinases and mTOR), and DNA repair (directly via PARP 1 or indirectly via DNA binding). Currently, the mainstay of treatment in the neoadjuvant, adjuvant, and first-line metastatic setting remains the use of anthracycline, alkylating agents, anti-metabolites, and taxane-based chemotherapy. The addition of carboplatin in the neoadjuvant treatment of TNBC improved pCR; the role of bevacizumab, however, is not established due to conflicting data.

REFERENCES


Perineal Endometriosis following vaginal hysterectomy

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KEY WORDS : Perineal endometriosis, Scar endometriosis

INTRODUCTION

Endometriosis is defined as “the presence of functioning endometrial tissue in an anatomical location other than the uterine cavity”. It is the aberrant presence of uterine mucosa in locations outside of the uterus, which is under the influence of ovarian hormones. Common ectopic sites for uterine mucosa include the ovaries, uterine suspensory ligament, recto vaginal septum and pelvic peritoneum. Extra pelvic sites includes the lung, spleen, gallbladder, stomach and kidney. In a 1999 review by Honore, the incidence of scar endometriosis was noted to be 3.5% after the incision of the gravid uterus. The reported incidence after cesarean section ranges from 0.03-0.45%, being about 1% for mid trimester abortion. The episiotomy scar is fairly rare site for endometriosis. The reported incidence of episiotomy scar endometriosis is 0.06%. Most perineal endometriosis occur after vaginal delivery with perineal tearing or episiotomy. Perineal endometriosis without perineal trauma is rare. Vaginal, vulvar or perineal scar endometriosis can occur after operation for prolapse, extirpation of Bartholin’s gland and after vaginal hysterectomy. The best treatment of choice of scar endometriosis is wide surgical excision.

CASE REPORT

A 28-year-old patient presented pain and swelling over left side of perineum 3 cm lateral to fourchette for three months; the pain was refractory to oral analgesia. The pain was cyclical and progressive. She had also complaints of severe dyspareunia for 3 months. There was bleeding from mass for 2-3 days at every 15 days interval for 3 months. Episiotomy scar was 1 cm medial to mass. Sphincter function was good. The patient had no personal or family history of endometriosis. She had two vaginal births, the first one in 2005 with episiotomy and another one in 2010 without episiotomy. She had undergone vaginal hysterectomy before one year due to dysfunctional uterine bleeding. Her general condition was satisfactory, with Pulse-80/min, BP-110/70mmHg. During physical examination, a firm nodule measuring 2 × 3 cm was palpated 3 cm away from fourchette on left side of perineum 1 cm lateral to the episiotomy scar. Transvaginal ultrasound showed normal left ovary, right ovary not visualized due to loaded bowel, uterus was absent (history of hysterectomy). Trans-perineal ultrasound was performed, which demonstrated a heterogeneous echogenic mass of 23 × 20 × 17 mm in size on left side of perineum lateral to episiotomy scar. Diagnosis of perineal endometriosis following vaginal hysterectomy was made.

The patient was operated on under spinal anesthesia. Diamond shape incision was kept surrounding the nodule, 1 cm away on each side of it. (Fig 1) Nodule was resected from surrounding area, taking care of anal sphinctor as it was uninvolved. (Fig 1) Wide excision of perineal area including the previous episiotomy scar was done. (Fig 2) Reconstruction of the perineal muscles were performed with chromic catgut no 1-0, mattress sutures in two layers. Vaginal mucosa was sutured with chromic catgut no 1-0, mattress sutures. Perineal skin was sutured with silk 2-0, mattress sutures. Postoperative course was uneventful; the patient was discharged after four days. The patient showed no signs of recurrence even six months after surgical treatment.

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Histologic examination revealed endometrial tissue with signs of past bleeding and recent outbreaks, endometrial glands lined by cuboidal epithelial cells, surrounded by endometrial stroma and hemorrhagic areas without evidence of malignancy.

Pollack et al\(^2\) reported one of the first perineal endometriosis case without perineal trauma in 1990. Endometriosis is known as the "Disease of Theories" because no one is absolutely sure why this tissue begins to grow in the wrong places. Several theories exist for the development of endometriosis - metaplasia, retrograde menstruation, venous and lymphatic metastasis and mechanical transposition.\(^3,4\)

Perineal trauma, especially perineal tearing or episiotomy during vaginal delivery, can result in perineal endometriosis. The etiology of this type of endometriosis is that endometrial tissue in the perineal area during parturition or instrumentation causes perineal endometriosis. Therefore, perineal endometriosis with perineal trauma can be explained by theory of transplantation.\(^3,4\) Mechanical transplantation of viable endometrial cells to open episiotomy scars and subsequent cell growth occurs at the healing phase of wound.

In present case, perineal endometriosis developed after vaginal hysterectomy. Neither uterus was bisected or morcellated while removal nor schuchard's incision was kept on perineum during vaginal hysterectomy. Endometrium may have been disseminated by lymphatic system, because there are much lymphatic communication in the uterus, cervix, vagina and perineum. Endometrial tissue can pass through these lymphatic ducts or venous route and result in perineal endometriosis. In other words, perineal endometriosis without perineal trauma is believed to be associated with multiple factors, especially benign lymphatic metastasis.\(^3,4\)

Three typical characteristics of perineal endometriosis caused by perineal trauma include:

1. Past perineal tearing or episiotomy during vaginal delivery
2. Atender nodule or mass at the perineal lesion
3. Progressive and cyclical perineal pain

If these three criteria are confirmed, the diagnostic accuracy is 100%.\(^1\)

The gross clinical and pathological picture changes as lesions age. The endometrioma often buries in scar tissue. Such lesions encased in dense scar tissue are still perfused cyclically with hormones which stimulate the hemorrhagic response at menstruation. The vascular perfusion sometimes becomes inadequate because of scar tissue, leading to a vascular necrosis.

The patient in this report experienced progressive cyclical pain and bleeding from nodule at 15 days interval for three months with past history of vaginal hysterectomy one year back without perineal trauma at that time. The diagnosis of perineal endometriosis without perineal trauma is difficult and depends upon symptoms and gynecological examination.

Vincent et al\(^2\) reported the sonographic appearance of cutaneous endometrioma had an echogenic consistency with irregular outline. Diagnostic tools are trans-vaginal, trans-perineal and endorectal USG, magnetic resonance...
imaging and biopsy. Definitive diagnosis can be made on histological examination by the presence of at least two of the following-Endometrial glands, stroma, or hemosiderin pigment. In our case, trans-perineal ultrasound demonstrated a heterogeneous echogenic mass of 23 × 20 × 17 mm in size on the left side of the perineum, 1 cm lateral to episiotomy scar, suspicion of perineal endometriosis, confirmed with histopathology report after surgical excision of nodule. The definitive treatment is surgical excision, taking care not to rupture the mass to avoid re-implantation or not to leave any remnants. Surgical excision of perineal endometriosis should be the first choice, while hormonal suppression should be secondary treatment. If the lesion has been excised entirely, hormonal suppression is not necessary. Usually the lesion is small, limited in location and can be completely excised. Recurrence of perineal and scar endometriosis is a rare event, with few cases reported so far. Malignant degeneration of scar endometriosis is also described. Medical management with such drug as Danazol has been found to be ineffective. When anal sphincter is involved, primary sphincteroplasty is necessary. Incomplete excision leads to high recurrence rate. Anal endosonography is extremely useful to diagnose sphincter involvement. In this case, the patient showed no signs of recurrence even six months after surgical treatment.

REFERENCES

Femoral Neuropathy Following Vaginal Hysterectomy

Dr. Saini Mehta, Dr. Swathi N., Dr. Daxa Oza, Dr. Munalini Patel, Dr. Jhanvi Patel, Dr. Reema Vansola.

KEY WORDS: Femoral neuropathy, vaginal hysterectomy, lithotomy

CASE REPORT

INTRODUCTION

Peripheral nerve injuries often result from patient positioning. Mechanisms of injury include stretching, compression and ischemia. Common peroneal nerve injury is most commonly seen with lithotomy position. Reports of femoral neuropathy have been rare.

A 35 year old average built female was diagnosed with III degree uterovaginal prolapse. She had no other co morbidities. All routine investigations were normal. She was posted for Elective Vaginal hysterectomy. She was given Spinal Anaesthesia in left lateral position with 3.6 cc 0.5% bupivacaine and 5 μg dexmeditomedine using a 23 G spinal needle. She was given lithotomy position in swing stirrups on straight rods when level of anaesthesia reached T6 level and surgery lasted for 2 hours. Intraoperative and immediate post operative course was uneventful. Sensory and motor effect of spinal anaesthesia remained for 4-6 hours. On examination, there was complete sensory recovery. Motor power of right lower limb was 5/5 whereas in the left lower limb, motor power of hip and knee flexors was 3/5. The next day, she complained of tingling sensations over anterior part of the thigh. Paraesthesia was present over the anteromedial part of the thigh. She was reassured and physiotherapy was started from second day onwards. She was given Vitamin B12 intramuscular injections on alternate days. Neurophysician reference was sought for and oral pregabalin was initiated. Gradually over a period of 5 days, her neurological deficits completely resolved.

DISCUSSION

Femoral neuropathy was first described by Descartes in 1822 as “anterior crural neuritis.”. It is seen with various conditions and procedures, including hip replacement, femoral vessel catheterizations, obstetric and gynecologic procedures, general and urologic surgery explorations and hematologic or neoplastic conditions. Other possibilities are direct spinal cord trauma, cauda equina syndrome, complete extrusion of already protruded intervertebral disc, direct trauma to peripheral nerves, diabetes mellitus, leprosy, and various immunologic disorders. Duration of lithotomy for prolonged hours, a body mass index of 20 or less, history of smoking within 30 days of the procedure and radiation exposure also increase the risk for femoral neuropathy. In our patient, we could rule out all above problems except longer duration of surgical procedure in an unphysiological lithotomy position.

The femoral nerve is formed by the ventral rami of L2-L4, specifically the posterior divisions of the lumbar plexus. It travels posterior to the inguinal ligament within the muscular lacuna which contains ilioptsoas muscle. It provides motor innervation to the muscles of the anterior compartment of the thigh being quadriceps femoris, pectineus and Sartorius and sensory innervations to the skin of the anterior thigh and the anteromedial aspect of the leg through saphenous nerve. Injury to the femoral nerve typically produces: weakness of hip flexion, loss of knee extension (no patellar reflex), and sensory loss over the territories described above.

The intense analgesia and profound muscle relaxation obtained by any anaesthesia makes it possible to produce extremes of positioning due to reduction in muscle tone. The single straight rod with swing stirrups helps to avoid sciatic and peroneal nerve palsies, but allows exaggerated abduction of the thighs with marked external rotation at the hip. This causes the femoral nerve to enter the thigh acutely angulated and twisted beneath the tough and inelastic inguinal ligament leading to compression of its vasa nervosa, thus producing local ischaemia of the nerve trunk. Risk increases when this position is maintained for longer...
duration. One more factor which helps to increase the abduction of thigh and its external rotation, is that surgical assistants often lean against the inner aspect of the thighs.\(^{(1,3)}\)

The classic presentation of femoral neuropathy is the patient falling from bed when ambulation is attempted postoperatively. The clinical symptoms of femoral neuropathy are weakness of ipsilateral hip flexion, knee extension, and numbness over the anteromedial aspect of the thigh as well as hyperaesthesia and pain.\(^{(2)}\)

Diagnosis is by physical and neurological examination and should be confirmed is by electrodiagnostic studies. These tests are performed 3 weeks after injury and helps in diagnosing, locating the injury, and assessing the severity of the lesion. Nerve Conduction Studies includes sensory studies of the saphenous nerve and motor studies of the femoral nerve. Results on the symptomatic side should be compared with those on the asymptomatic side. On EMG, the quadriceps should show neuropathic changes. Recently, high-resolution sonography has shown high accuracy for localization, extent and the cause of peripheral nerve lesions by direct visualization of the nerve.\(^{(3)}\)

Treatment needs aggressive physiotherapy only if there is no substantial nerve injury immediately after diagnosis to prevent muscle atrophy and decrease the risk of thromboembolic complications associated with prolonged bed rest. Among the medications used to address neuropathic pain are the anticonvulsants pregabalin and gabapentin, as well as the antidepressants amitriptyline and duloxetine. Prognosis is generally regarded as good. Almost all patients have neurological full recovery; permanent deficits are very rare.\(^{(5)}\)

In order to prevent neuropathy two assistants required for giving position to the patient synchronously. The “candy cane” stirrup should be abandoned and the Lloyd-Davies leg support should be used in its place. Hip flexion and abduction angles should not exceed 45 degrees (height of the lithotomy pole should also be optimum for this) and a check is to be kept on the operating time and if prolonged, intermittently ease out the stretched externally rotated leg.\(^{(1,4)}\)

The patient should be followed clinically to evaluate for signs of recovery. Electrodiagnostic evaluation should be performed beginning at 6 weeks and repeated at 3 and 6 months after the event to evaluate recovery.

REFERENCES

1. Dr Ruchi Gupta, Dr Veena Valecha, Dr Walia S.S : Femoral neuropathy after lithotomy position- its treatment modalities, Indian J. Anaesth. 2006; 50(2): 143-144.
CASE REPORT

Rosai-Dorfman Disease

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KEY WORDS: Rosai-Dorfman Disease, Meningioma, Histioproliferative disease

Abstract:

Rosai-Dorfman Disease (RDD) is a rare idiopathic non-neoplastic histioproliferative disease characterized clinically by massive painless cervical lymphadenopathy, fever and weight loss. Extranodal involvement has also been recognized. Central nervous system (CNS) manifestations are extremely rare and patients with intracranial involvement usually present with clinical and radiological findings suggestive of a meningioma.

INTRODUCTION

The first report of sinus histiocytosis with massive lymphadenopathy (SHML) was described in 1959, by Destombes as a lipid storage disorder developing after inflammation. Rosai and Dorfman described the clinical syndrome caused by this rare, benign, lymphoproliferative disorder characterized by lymphophagocytosis for which they coined the term SHML. The patients tend to be young at the onset of symptoms and usually present with bilateral painless cervical lymphadenopathy, fever, weight loss, leucocytosis, elevated ESR (Erythrocyte Sedimentation Rate) and hypergammaglobulinemia. In 30% of cases, extranodal involvement is present and may include the skin, orbit, salivary glands, thyroid, upper respiratory tract, or testes. In very rare circumstances, the central nervous system can be affected. The disease tends to involve the older age group (mean 39.4 years). Isolated intracranial RDD has been documented in previous case reports. They are mostly dural based lesions presenting clinically and radiologically like meningiomas. Intraparenchymal lesions mimicking lymphomas, and intraventricular lesions have also been reported.

CASE REPORT

A 65 year old male presented with complaint of blurring of vision in both eyes since last 1 year, occasional episodes of low grade fever and occipital headache since last 8 months. Patient has history of diabetes mellitus for last 20 years and hypertension since 2 years for which he is taking regular medications. On examination his higher intellectual function and cranial nerves were normal but fundus examination showed pale disc. He had no spinomotor or sensory deficit and no cerebellar signs were present. His other systems were ordinary and there was no lymphadenopathy. His immune status was normal too.

Non contrast CT scan of brain revealed a well-defined hyperintense lobulated extra axial mass lesion in suprasellar location extending along planum sphenoidale anteriorly & posteriorly to retrocaval region & lt. basal cistern. (fig. 1 & 2). Contrast MRI too revealed a well defiend lobulated extraaxial mass lesion in suprasellar location along planun sphenoidale. Lesion appear hypointense on T1W1 & on T2W2 also. In postcontraststudy it shows moderately homogenous enhancing extraxial suprasellar lesionextending along planum sphenoidale anteriorly & posteriorly to retrocaval region & lt. basal cistern. Finding suggesting of planum sphenoidale en plaque meningioma(fig, 3, 4, 5, 6)CT scan of chest and abdomen did not reveal any lymph node enlargement, ultrasound examination of the neck was unremarkable. He underwent rt. Subfrontal craniotomy and excision of lesion. The lesion was tough, fibrous in consistency, avascular. The postoperative course was uneventful. Microscopic examination of lesion is composed of lymphocytes, plasma cells, large cell histiocytes, few with emperipolesis of lymphocytes and plasma cells. Immunohistochemistry for S-100 protein and CD68, PGM-1 confirmed the presence of histiocytes(fig. 7). Hence the lesion was diagnosed as intracranial rosai dorfman disease. Postoperative CT scan (p+c) showed evidence of small residual lesion in optical canal region(fig. 8 & 9). Patient was discharged on low dose steroid for a month.

DISCUSSION

The term SHML was first introduced by Ronald F. Dorfman and Juan Rosaibased on four cases, published in 1969, in the Archives of Pathology journal, with the title 'Sinus histiocytosis with massive lymphadenopathy: A newly recognized benign clinicopathologic entity'. The synonym of this condition is Destombes-Rosai-Dorfman
syndrome, named after Pierre-Paul Louis Lucien Destombes, Juan Rosai, and Ronald F. Dorfman. The disease is characterized by massive, painless, bilateral cervical lymphadenopathy, often associated with fever, leukocytosis, mild anemia, elevated erythrocyte sedimentation rate, and polyclonal hypergammaglobulinemia. Although extra-nodal involvement has been reported in diverse sites, CNS involvement, particularly in the absence of nodal disease is rare. The most common presentations of CNS involvement, in the largest series, include headaches, seizures, numbness, and paraplegia. Frequent lesion locations include cerebral convexities, parasagittal, supra-sellar, cavernous sinus, and petroclival regions. Purely intraparenchymal lesions have also been reported. There are isolated case reports involving the orbit, pituitary, cerebellar, and cervical extradural involvement. The other extra-nodal sites include skin, soft tissues, respiratory system, genitourinary system, bones, orbit, thyroid, and breast. Male to female ratio is about 1.4 : 1. The etiology, pathogenesis, and natural history of Rosai-Dorfman disease are still unknown. Although an infection has been suggested as an underlying cause, a definitive agent has never been isolated. Molecular studies using polymorphic regions of the human androgen receptor locus have demonstrated that RDD is a polyclonal disorder in contrast to Langerhans cell histiocytosis, which is a monoclonal disorder.

Histologically, Rosai-Dorfman disease is characterized by large histiocytes, which often show apparently viable and intact hematopoietic cells (mostly lymphocytes) within the cytoplasm without undergoing degenerative changes, a phenomenon known as Emperipolesis (lymphophagocytosis), derived from the Greek word 'em + peripolesis' = going about. On immunohistochemical examination, these are positive for S-100 protein and negative for CD1a, a marker of Langerhans histiocytosis.

There are no definitive treatment guidelines for Rosai-Dorfman disease. A majority of these undergo spontaneous regression. The mortality rate is approximately low, 7%. Major complications include airway obstruction, immunological disorder, and infection. Usually, concomitant immune dysfunction is present. The prognosis of CNS Rosai-Dorfman disease is not bad. Petzold et al. found tumor regrowth or recurrence of symptoms in 14% of the 29 patients, with a mean follow-up of 10.1 years. Only 52% of these patients had undergone brain imaging at follow-up. They concluded that a five-year follow-up with brain imaging was essential and advocated low-dose radiation to treat patients with sub-total resection and recurrence. Although a variety of treatment modalities had been used, including steroid therapy and radiation, surgical resection appeared to be the most appropriate approach. There have been some reports of success in treating Rosai-Dorfman disease with a combination of cytotoxic agents such as alkylating agents, vinca alkaloids, and prednisone. Decision to follow-up the patient with serial imaging is an accepted modality. Our patient was maintained on low steroids postoperatively, for a month. A repeat CT Scan did not reveal any residual involving the operative bed.
Fig 3 and fig.4: T1W1 and T2W2 axial view - hypointense lesion

Fig 5 coronal view

Fig 6 sagittal view

Fig 5 and fig 6: T1weighted MRI study with contrast material -moderately homogenous enhancing extraxial suprasellar lesion extending along planum sphenoidal anteriorely & posteriorly to retrocaval region & lt. basal cistern.

Fig.7a. histiocyte with lymphocytes in it

Fig.7b. large histiocytes & emperipolesis

Fig.7c. PGM-1 positive histiocyte

Fig 7d. S-100 positive
Rosai-Dorfman disease is a well recognized clinicopathological entity. The disease may be nodal or extranodal. It may present with only extranodal involvement of the skin, orbit, upper respiratory tract, testes, or rarely CNS. Rosai-Dorfman disease should be considered in the differential diagnoses of both dural-based and intraparenchymal lesions of the CNS, where dural based lesions mimic the radiological appearance of a meningioma, and intraparenchymal lesions may mimic granulomatous lesions. Thus, a definite diagnosis relies on the histological pattern and immunohistochemical characterization of the lesions. Surgical excision of the lesion is the treatment of choice. In cases with subtotal tumour resection or recurrence of the lesion, adjuvant therapy with local low dose radiotherapy and steroids can be considered. Prognosis is benign especially in the absence of nodal disease.

REFERENCES

CASE REPORT

Splenic Inclusion Cysts with Ectopic Pregnancy: A Case Report

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ABSTRACT

Splenic inclusion cysts are a rare entity with incidence of 0.07%. Most of them are asymptomatic and remain incidental findings during abdominal Ultrasonography or CT Scan. We report a case of large symptomatic splenic inclusion cyst which was present along with ectopic pregnancy. Laparoscopic deroofing of the splenic cyst and evacuation of right ectopic pregnancy was done and histopathologically confirmed.

A 30 year old female came with complaints of fullness in left-upper abdomen for last 2 months associated with generalised weakness, malaise, and generalised body ache with intermittent low-grade fever. Patient had history of first full-term normal vaginal delivery 6 months ago and delivered a healthy female child.

On examination, she was pale, normotensive, with all vital parameters within normal limits. Abdominal examination showed fullness below left costal region. Per vaginal examination showed fullness in the Pouch of Douglas, with a cystic lesion in right adnexa pushing the uterus upwards and cervix to the left.

Ultrasound showed a 13 cm x 13 cm cystic lesion with internal echoes and calcification in upper pole of spleen with another 9 cm x 8 cm septated collection in right adnexa. The Contrast Enhanced CT scan showed post-contrast enhancement of wall suggesting a possibility of splenic cyst and right tubo-ovarian mass respectively.

Patient's urine pregnancy test was negative. Tumour markers CA-125, β-hCG and CA 19-9 were initially mildly elevated but ultrasonography guided biopsy of the tubo-ovarian mass showed no evidence of any malignancy.

Laparoscopic deroofing of the splenic cyst and adnexal cyst was performed and cyst wall biopsy was taken. On puncture, cyst fluid was turbid and serous. Laparoscopic ports were closed after adequate peritoneal wash. Patient had an uneventful post-operative recovery. Histopathological examination results proved the cysts to be a simple infected splenic inclusion cyst and ectopic pregnancy with evidence of chorionic villi in the tubo-ovarian mass.

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Cystic lesion of spleen are not a very common finding; incidence of true splenic inclusion cyst being 0.07% in autopsy series.1

The classification of these cystic lesions is based on etiology and histological study of the cellular lining.2,3,4

Primary or True cysts are those with an epithelial lining. Depending on the type of lining on HPE, these have been further classified into epidermoid (stratified, non keratinised squamous), Dermoid (squamous lining with skin appendages like hair follicles and sebaceous cyst) and Mesothelial (low cuboidal/low columnar epithelium). They can be differentiated based on immunohistochemistry.

Their etiology has been explained by various theories which include;3,4

1. Invagination of capsular peritoneal mesothelium / collection of peritoneal mesothelial cells trapped in splenic sulci with subsequent squamous metaplasia due to chronic irritation
2. Embryonal inclusion cyst from epithelial cells of adjacent structure during splenic development (gonads, dorsal mesogastrium) followed by metaplasia.
3. Developmental displacement of epithelial tissue.
4. Cyst arising from normal lymph spaces in spleen.5

Splenic cysts are found predominantly in young females and children. Small cysts (<5 cm) may be asymptomatic and are usually incidental radiological findings. Large cysts may present as diffuse abdominal pain or heavy feeling or lump in left hypochondrium or cause pressure effect on other organs such leading to reflux oesophagitis (stomach), arterial hypertension (kidney and left renal artery), cough and pain in left shoulder (diaphragm) or rarely arrhythmias (heart). Its complications include intra cystic haemorrhage, cyst rupture (spontaneous or traumatic) and infection (leading to splenic abscess or sepsis). On ultrasonography, an epithelial splenic cyst is identified as an unilocular, anechoic or hypoechoic lesion with smooth well defined margins.3

The exact information about the site, size, location, position of cyst in relation to surrounding structure and composition of cyst fluid is obtained by CT/MRI.

Table: Classification of splenic cyst

<table>
<thead>
<tr>
<th>CLASSIFICATION OF SPLENIC CYSTS</th>
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<tbody>
<tr>
<td>1. PARASITIC</td>
</tr>
<tr>
<td>a) Echinococcus granulosus</td>
</tr>
<tr>
<td>b) Taenia echinococcus</td>
</tr>
<tr>
<td>2. NON PARASITIC</td>
</tr>
<tr>
<td>A) TRUE</td>
</tr>
<tr>
<td>a) Epidermoid</td>
</tr>
<tr>
<td>b) Dermoid</td>
</tr>
<tr>
<td>c) Mesothelial</td>
</tr>
<tr>
<td>B) FALSE</td>
</tr>
<tr>
<td>a) Pyogenic Abscess</td>
</tr>
<tr>
<td>b) Fungal Abscess</td>
</tr>
<tr>
<td>(Candida Albicans, Aspergillus fumigates, Cryptococcus neoformas)</td>
</tr>
<tr>
<td>c) Infarction</td>
</tr>
<tr>
<td>d) Peliosis</td>
</tr>
<tr>
<td>e) Post Traumatic</td>
</tr>
<tr>
<td>(Hematoma, Pseudocyst)</td>
</tr>
<tr>
<td>3. TUMORS</td>
</tr>
<tr>
<td>A) BENIGN</td>
</tr>
<tr>
<td>a) Hemangioma</td>
</tr>
<tr>
<td>b) Lymphangioma</td>
</tr>
<tr>
<td>B) MALIGNANT</td>
</tr>
<tr>
<td>a) Lymphoma</td>
</tr>
<tr>
<td>b) Metastasis</td>
</tr>
</tbody>
</table>

A differential diagnosis should include the various cystic lesions of spleen mentioned in the table above. If splenic cysts are associated with other cystic lesions in peritoneum, pelvis or thorax, a possibility of malignancy, parasitic echinococcal cysts, fungal granulomas or benign peritoneal cysts with splenic cysts should be ruled out.6

However, histopathology confirms the diagnosis.

Gross examination usually shows a large cyst with glistening smooth walls and occasional trabeculations or septations. Microscopic examination shows squamous epithelial lining with intracellular bridge and a thick collagenous wall with an interior epithelial lining.5,6 The cyst fluid contains cholesterol crystals, protein particles and breakdown products of haemorrhage, i.e. haemosiderin.

Small cysts are managed conservatively. Percutaneous aspiration and injection is associated with high
recurrence. Surgery is gold standard in cysts greater than 5 cm in diameter.

Though open complete splenectomy was the initial classic approach, with advancement in technique, partial splenectomy, total cystectomy, marsupialisation of cyst and cyst deroofing/decapsulation by open or laparoscopic method are the different surgical options which can be chosen as per patients age, localization and nature of cyst.7

Deroofing of cyst is a simple and more rapidly performed procedure with less blood loss with small risk of recurrence.(8) With use of minimal invasive laparoscopic approach it has become even simpler with concurrent insight into other intra abdominal pathology and a significant decrease in wound related complications.

Conflicts of interest: a video of laparoscopic technique of deroofing of splenic cyst was presented at AMASICON 2013. (International congress of Association of Minimal Access Surgeons of India 2013).

REFERENCES:

2. Horibe Y, et al. Epithelial Inclusion Cyst (epidermoid cyst) formation with epithelioid cell granuloma in an intrapancreatic accessory spleen. Pathol Int.2001 Jan;51(1);50-4
Vaginal Leiomyoma

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KEY WORDS: Vaginal Fibroid, Leiomyoma of Vagina

INTRODUCTION

The majority of leiomyomas arise from body of the uterus and sometimes from cervix. The extraterine sites of this tumour are round ligament, uterosacral ligament, ovary, inguinal canal and very rarely vagina and vulva. Primary vaginal tumors are rare. They are usually secondary to either cervical or vulval lesions. The benign solid tumors arising from the vaginal tissue include papilloma, hemangioma, mucous polyp and rarely Leiomyoma. In the vagina, leiomyoma usually presents as a solid single nodule mostly from anterior vaginal wall in women between the ages of 35-50 years. Since the first report by Denys de Leyden in 1733, approximately 300 cases of vaginal leiomyoma have been reported worldwide. Bennett and Erlich found only nine cases in 50,000 surgical specimens and only one case in 15,000 autopsies reviewed at Johns Hopkins Hospital. A case of primary leiomyoma of vagina is presented here.

CASE REPORT

A 50 year old postmenopausal female was admitted to gynecology department at our institute on 21st February 2012 with chief complaints of something coming out per vagina since last 15 years. Mass was painless, slowly growing, protruding through the introitus during squatting, coughing or sneezing. On local examination, there was solid mass of 7cm×6cm in size, arising from lower 2/3rd of anterior vaginal wall and extending up to external urethral meatus, with increased vascularity of vaginal mucosa overlying the mass. (Fig 1) On per speculum examination, cervix was high. On per vaginal examination, uterus was anteverted and normal in size. USG showed hypoechoic mass, 7cm×6cm in size (Fig 2), separate from anterior vaginal wall and posterior urethral wall and urinary bladder, with increased peripheral vascularity on color doppler. Uterus, cervix and both ovaries were normal. Probable diagnosis of vaginal leiomyoma was made. As her general condition, other radiological and laboratory investigations were within normal limit, and medical and surgical history were insignificant, enucleation of vaginal mass was planned. During surgery, anterior lip of cervix was caught by allies forceps, bladder sound was passed through the external urethral meatus to demarcate lower limit of urinary bladder. A Foley’s catheter was introduced in the urethra for protecting the latter. Transverse incision was kept just beneath the mass over cervico-vaginal junction and then a vertical incision was kept from midpoint of transverse incision after creating a cleavage beneath anterior vaginal mucosa from the mass. That gave a shape of an inverted ‘T’ incision as in anterior colporrhaphy. Sharp dissection was done and mass was enucleated from the vaginal mucosa. (Fig 3) As base of mass was adherent to bladder and posterior urethral wall, sharp dissection was done carefully and mass removed. Haemostasis was achieved. Excess of vaginal mucosa was excised and cut edges of vaginal mucosa were sutured as we do in anterior colporrhaphy with polyglactin 2-0.

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Gross examination revealed a 7 × 6 × 5 cm solid mass, weighing 120 gm. (Fig 4) Microscopic examination revealed a well-circumscribed leiomyoma with underlying squamous epithelium, consistent with the diagnosis of vaginal leiomyoma. Post operative period was uneventful.

DISCUSSION

The majority of leiomyomas arise from the body of the uterus and sometimes from cervix. The extraterine sites of this tumor are round ligament, uterosacral ligament, ovary, inguinal canal and very rarely vagina and vulva. They have varied clinical presentation, the most common being vaginal mass. Vaginal myomas can be asymptomatic. When symptoms present, they commonly are related to the urinary tract and include voiding difficulties, dysuria and urinary frequency. The most common gynaecological complaint is dyspareunia. However, many patients only describe a bulging mass. They are slowly growing and generally asymptomatic. It causes obstruction to birth passage if along with pregnancy or simply with feeling of mass in vagina.

These lesions tend to be single and less than 5 cm in diameter which are usually localised and vary from solid to cystic in consistency. They are usually firm and can undergo degenerative changes and feel soft. The majority are found in the anterior wall of the vagina and only 10 to 20 % are found in the lateral wall. They may arise from posterior wall, may present even after hysterectomy.

They may be confused with a variety of benign vaginal tumours. The solid tumors arising from the vaginal tissue include papilloma, hemangioma, mucus polyp and rarely leiomyoma. It is difficult to diagnose pre-operatively. On ultrasonography, it may appear as mixed or hypoechoic lesion but it is difficult to rule out any connection with uterus or cervix. Julie Goss' first described use of translabial and transurethral sonography using a 10-MHz linear transducer to determine extension of a tumor from the vaginal wall into the lumen of the urethra. Preoperatively, diagnosis by ultrasonography may be difficult, but magnetic resonance imaging usually clinches the diagnosis. In magnetic resonance imaging, they appear as well-demarcated solid masses of low signal intensity in T1- and T2-weighted images, with homogenous contrast enhancement, while leiomyosarcomas and other vaginal malignancies show characteristic high T2 signal intensity with irregular and heterogeneous areas of necrosis or hemorrhage. However, histopathological confirmation is the gold standard of diagnosis and also beneficial to rule out any possible focus of malignancy.

Surgery by vaginal route is the main modality of treatment. Excision and enucleation is the treatment of choice as was done in our patient and generally it is easy because of availability of good cleavage plain. Vaginal approach may cause severe haemorrhage if the base of tumour is not approachable or it is present in upper part of vaginal fornices. It is advisable to choose abdominal route for such cases. At times an abdominoperineal approach is needed to perform complete surgery.

If diagnosis could be made pre-operatively, GnRh analog can be tried to reduce their size or pre-operative embolization can be performed before excision to reduce intraoperative blood loss. The tumour is oestrogen-dependent and regresses after menopause. A rare case of huge vaginal leiomyoma recurrence was reported by Dhaliwal et al who suggested that if recurrence occurs with intact ovarian function ovariectomy should also be done.

Nel and Tiltman found no recurrence in a follow-up period that varied from 8 months to 20 years. There is a very
old case report of recurrence of this tumour during pregnancy with a suggestion of hormone dependency. Pathologically they are firm, well circumscribed homogenous and resemble their uterine counterpart. Though the lesion is usually regarded as benign, sarcomatous changes have been reported. There is a single study that has reported chances of recurrence and sarcomatous change. They are common in posterior wall of vagina.

REFERENCES

Anger is a physical and psychologic expression of a negative, aggressive feeling which is beyond tolerance in a given individual in a particular situation.

Anger usually lasts a few seconds or a few minutes. It may be repetitive when it is called bursts (or outbursts) of anger. Its residual feeling of disgust - contempt - turmoil may last minutes or even hours. During this period, the person is more prone to such outbursts because during this period, his sensitivity is high and tolerance is low.

Severe anger is called rage, wrath, fury.

Anger is almost universal, inherent, innate and is a constituent of one's temperament and personality.

Because of its universal presence, anger (at least to some extent) forces us to consider it as normal and physiological but it is to be considered abnormal, if in a given person, its quality, intensity, frequency or duration is found to be disproportionately increased without sufficient valid reason-s.

Universality of anger can be judged by the fact that even birds and animals are known to be angry, time and again.

Rishis (e.g. Durvasa) and even God (e.g. Bhagwan Shankar) are not free from anger!

There are several causes of anger. It occurs when a person's ego or self-respect is hurt, or when he feels insulted, cheated, humiliated, disregarded, misguided, ill-treated, betrayed or by-passed in some situation. It means that personal, professional and societal factors are responsible for genesis of anger.

Anger is harmful for the person who becomes angry (i.e. loses his temper) as also to the recipient or sufferer of anger, but the harmful, disturbing effects are much more on the perpetrator. Such adverse effects occur instantly and can also be dangerous in the long-run. Anger is like a stone pelted into a quiet, serene lake.

Persons who become angry on small, slight, flimsy reasons are called short-tempered.

If You Conquer Anger, You Conquer The World

Dr. G. G. Oza
Emeritus Professor of Medicine

Anger can be called live, visible conversion of ego while repentance can be termed its purified form.

Total liberation from anger (rarest of the rare case) can be called salvation, the ultimate freedom.

However, occasionally, a mock show of pre-planned, controlled anger may be required to induce discipline in children or students.

The immediate effects of anger are like leaping waves of fire while the long-term or residual effects are like hidden, lurking hot fire under the cold ashes.

**Suppressed anger** : When the sudden burst of anger cannot be expressed, cannot be diverted or is involuntarily or forcibly suppressed, it is called suppressed anger. It causes seething restlessness, discomfort and even feeling of suffocation. Some students of anger suggest that it is better to express the anger gently and carefully, guardedly rather than suppressing it forcibly. Whether this is true, nobody knows!

**Salient, external features of anger:**

- Feeling of anger becomes evident on the face.
- Flushing of the face (unusual redness)
- Frowning look
- Staring eyes
- Red tinge in the eyes
- Wrath written over the entire face
- Change in tone of the voice; it may become shrill or if the person is very angry, he may not be able to find appropriate words or he may go on shouting aimlessly and endlessly.
- He may thump the table with his fist or may thump his feet on to the ground.

**Signs of anger:**

- The face has a furious look full of rage.
- Eyes may appear bright red and menacing.
- Pulse runs faster.
• Blood pressure rises.
• Breathing is fast.
• Goose Skin.
• Sweating may be noted.
• Speech is explosive and saliva may exude from the mouth.
• The person may become abusive and unmanageable. He may attack the recipient or may break the nearby furniture. He may inflict head injury or may break recipient’s bones or teeth. He himself may sustain injury.
• The angry person may suffer heart attack or brain hemorrhage and this episode of anger may be his last burst of anger (farewell anger and farewell fury!)

• All these features may occur together or may occur sequentially, chronologically in a crescendo fashion. The whole episode may last few minutes. Also, all the features may not occur in every incident. But the relatives and friends or co-workers are conversant with the characteristic pattern in a given individual. But sudden alteration can also occur.

• **Effects on the psyche:**
  • Uneasiness, restlessness, discomfort etc. lead to a feeling of loss of peace of mind.
  • Sometimes, the person may divert his feeling of anger and frustration on others, especially family members, office staff or friends.
  • In a fit of anger, the person may take wrong decisions which he may have to regret later.

• **Why anger is more common in males?**
  The hormone, testosterone in males leads to aggressiveness, possessiveness, sense of ownership with a touch of autocracy and dominance. In contrast, females, usually, have a temperament of tolerance, mild and meek behaviour, ’let go’ attitude, forgiveness, modesty etc. These qualities are attributed to oestrogen, the female hormone. Similar difference in behaviour is also noted in birds and other animals. Personality and attitude of the mother and the education given by the parents to daughters also greatly influences build-up of their personality. However, exceptions are seen on either side, time and again.

• **How to conquer (decimate) anger?**
  This is a very complex and difficult problem which is universal and has troubled the mankind from its very beginning. To analyze this problem, this article can, at the most, be considered, tip of the iceberg. When rishis (who have attained highest peak of spiritualism) have not been able to abolish anger, what an ordinary man do about it ? Nonetheless, certain windows, if not doors, are open to venture efforts to alleviate, and, if possible, to eradicate anger, as mentioned below:

A firm, hard decision should be taken to get liberated from this menace, called anger. This means, the process of eliminating anger should start with and within the mind, individual’s thought processes and overall attitude. But just a decision parse, is not going to solve the problem, because anger is ingrained in the psyche right from childhood. Anger is inherent, inborn, habitual and, by now, it has become an integral part of his psyche and personality. In addition, the external and environmental triggers at home, office, workplace have become immutable and, therefore, difficult to change. However, an earnest and sustained effort is a ‘must’ if success, even if partial, is to be gained.

An anticipated, pre-designed decision like “Come what may, I am not going to be angry” must be taken up and pursued persistently. This may work to some extent but because anger has, by now, become a conditioned reflex, not much can be expected from this approach. However, if you can get permanent liberation from anger by this method, you are one of the few lucky persons.

Other approach is to avoid individuals, situations, and set-ups which have been the cause of anger in the past repeatedly. but this approach is also not always practicable because near and close relatives, office-staff may be the cause of anger and it is, therefore, neither feasible, nor possible and even not desirable to avoid or wish away these persons. In fact, they are an integral component of our life.

One more weapon is to learn and execute let-go policy and thereby ignore smaller issues and pinpricks because the most important issue in
your life is you (yourself) and therefore, your well-being should be, at the centre. Let-go policy should be implemented willingly, not grudgingly. Do not make every issue a prestige issue. Your health and happiness is more important. Let rest of the issues rest.

Perhaps, maximum hope can be expected from meditation. It appears that it can prove to be most effective remedy to eradicate the enemy, named anger. One should first understand that soul is always pure, self-luminescent and immutable. It is the mind which is prone to worldly impurities like greed, dissatisfaction, anger, vengeance etc. These might cast a web of such worldly impurities on the soul and mask it. Usually mind dictates the attitude of an individual. Regular meditation (in its real sense) can change one’s attitude (internal cleansing). Meditation can replace hostility by humanity, envy by equanimity, cunningness by kindness and fury by forgiveness. Thereby, it can change the entire “inner being” and the outer behaviour, attitude and outlook of that particular person. Such a individual can, now, start his journey from local to universal.

“We can not change the world
but we can change ourselves
to whatever extent possible, and feasible.”

Readers'Forum

GMJ is starting a new column under the above head where our reader can write his views and observations and upon that we invite comments, suggestions wand remarks from our esteem readers. Such first article is by a senior physician and professor emeritus Dr. G.G. Oza. You can send your comments and suggestions to us on our E-mail: gujaratmedicaljournal@gmail.com
5. No Objection Certificate from the institute / hospital is mandatory, along with the article sent for the publication.

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