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The Dean

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From the Chairman's Desk

"As we explore new advancements in healthcare and patient-care, clinical research and dissemination of clinical outcomes will play a critical role in the understanding and management of diseases. A good hospital and medical education must therefore support and facilitate the dissemination of high-quality research which can improve clinical practice and also bring in an understanding on the new frontiers that are evolving in medical care. The new 'GCSMC Journal of Medical Sciences' will go a long way in fulfilling these objectives. The journal is conceptualised as a knowledge sharing tool and an information source for the medical fraternity at large. The objective is to connect with members from different branches of medicine and enable sharing and understanding of ongoing clinical research. Besides this, the journal will also provide peer reviews, original findings, case reports and insights. The topics would range from insights and perspectives on new advancements in diagnosis and treatment, a breakthrough approach in disease management, understanding newer pathogenesis of diseases and other such topics of relevance. This biannual publication will also be available as an e-version to enable faster access and retrieval of information. We do hope that you will find the 'GCSMC Journal of Medical Sciences' interesting, informative and above all, a valuable knowledge source."

Pankaj R. Patel
Executive Chairman,
Gujarat Cancer Society
Ahmedabad

Message from the Dean

Gujarat Cancer Society- 50 years old trust, along with Government of Gujarat has established and is managing Gujarat Cancer & Research Institute since the year 1972. GCRI with a multidisciplinary close relationship between cancer care, research & education intends to provide the greatest hope to patients. GCRI with its state of art therapeutic efforts and with intensive educational efforts has grown to be the largest regional cancer hospital. In the year 2009 we have establish GCS Medical College, Hospital and Research Centre, Ahmedabad.

It is really a matter of pleasure moment to be proud, that GCS Medical College, Hospital & Research Centre, Ahmedabad is publishing its own journal in the very first year of the college, after its inception. We have just begun taking its first steps; it has to run many miles still.

I am confident that the new Institute GCS Medical College will soon become a recognized name in the vibrant and dynamic educational structure that is emerging in this globalized era.

I am very grateful to have all support for our progress by positive contribution from management, students, patients, Gujarat University, Govt. of Gujarat and Central Government. I am also thankful for implementation of vision in to fruitful action at all levels and hard work, humbleness, sincerity and commitment by faculty & supportive staff members of institute.

There is a difference between excellence and perfection. Excellence is about doing the best we can in a given time frame and space. Perfection is not time bound. You can take your time, but this is not suitable & applicable when working in an organization, so aim for excellence.

In pursue of excellence we have to create an obsession with excellence, we must dream of it only because it delivers better results, believe in it and find it instinctively satisfying to us. We must think of excellence not only with our mind but also with our heart & soul.

We must realize that one cannot be the best in everything. We must create a culture of team work. Everybody has to be included and involved to get the collective feeling of success. In this manner team work becomes a culture and a way of life and we progress as a cohesive unit.

Dr. Kirti M. Patel
Dean
GCS Medical College,
Hospital & Research Centre, Ahmedabad

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From the Desk of the Editors

Research is an integral part of any education system. Medical education system provides ample opportunities for research as it has multiple facets included under one roof only. Newer life saving drugs/molecules, vaccines and various interventional technologies has emerged this way only. For the advancement in various treatment methodologies in medical science as well as for continuous scrutiny and evaluation of existing methodologies, research is obligatory. With research, we can improve not only our competence and efficacy but also can diminish the suffering on the part of patients. All pre-clinical, para clinical and clinical branches under medical education system can explore various fundamental clandestine of human body which can help ultimately in advancement of various treatment modalities for the patients.

It is our great pleasure to launch the first issue of GCSMC Journal of Medical Sciences. This is an effort to provide a platform where all proficient from medical field can publish their research work. The readers of the journal will also be benefited as they will able to gain the knowledge of various aspects of medical science at one place.

We are looking forward to get the immense response from all the faculties of medical field. Hope the content of the journal will assist the researchers as well as the readers in acquiring most recent updates in their respective field.

Looking forward for your kind cooperation…..

Dr. Urvesh Shah
Editor in-chief
GCSMC Journal of Medical Sciences

Dr. Viral Dave
Joint Editor
GCSMC Journal of Medical Sciences

A Prying Influence of Antibiotic Usage : "Emerging Antibiotic Resistance"

Urvesh Shah*

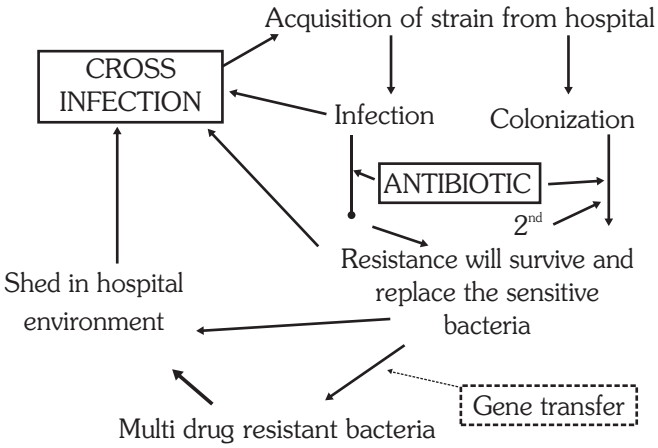
Antibiotic resistance existed before the discovery of antibiotics, but was rare or characteristic of the bacterial species. After each new agent become widely used, new strain of bacteria resistant to it ultimately emerged somewhere. If this resistant strain colonize or infect to a human or animal host being treated with the same antibiotic, it could multiply rapidly to replace the susceptible strain that the agent was killing. This selective increase in number of resistant strain helped it get to other hosts and then increase again on any of those hosts those were also being treated with the agent. [(1)]

The progeny of the resistant strain could thus spread selectively and carry its resistance gene widely through bacterial populations on hosts being treated with the agents. Along the way rare genetic events (transformation, transduction or conjugation) may transmit the resistant gene from one bacterial population to other. Another such event could also link that gene to another gene expressing resistance to a different agent so that copies of both genes would increase thereafter on hosts treated with either of the agents. [(1)]

In such manner, thousands of resistance genes have emerged, replicated and disseminated selectively through continuous bacterial populations on hosts being treated with antimicrobial agents and distributed all over the world. Most of such strains only colonize the host but some infect them and may result in treatment failure. Thus, the resistant gene that is in a strain infecting a patient and causing treatment failure usually did not emerge in the bacteria of the patient but years earlier somewhere else. It then spread through a network of bacterial population on hosts being treated with selected antimicrobials. [(1)]

The worldwide emergence of resistance has received a great deal of attention and is causing considerable concern among both clinicians and lay persons. Hospital-based physicians have long been aware of increasing resistance in microbial pathogens causing nosocomial infections. For example, half of the gram negative bacterial isolates from bacteraemic patients in the intensive care unit are Extended Spectrum Beta Lactamases (ESBLs) & other broad spectrum beta lactamase producers and require carbapenem for therapy. The increased use of carbapenem has, in turn led to the emergence of Carbapenem resistant bacteria, e.g., Acinetobacter, metallo-beta lactamase producing Pseudomonas and Enterobacteriacae. The focus of emerging resistance thus seems to be the hospital rather than the community.

Figure: 1 Hypothesis of dissemination of multidrug resistant bacteria in hospital environment



Community-based physicians have been less concerned with the problem of emerging resistance simply because they have not seen the clinical evidence for such resistance, which is the failure of empirical antimicrobial therapy in community-acquired infections. Whenever cost is considered in the context of antimicrobial resistance, it is generally the cost of patient care due to increased morbidity/mortality and excessive use of expensive newer antimicrobial agents for empirical therapy that is meant. However, there is another cost involved that is just beginning to be appreciated. This cost is the biological cost of antimicrobial resistance to the microbe. The ability of a microbial pathogen to cause infection in a human host is

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dependent on the fitness and virulence of the pathogen. Both of these microbial characteristics are continually evolving. Fitness generally means the ability of a bacterial clone to reproduce itself in the environment as well as in the infected host, the ability of the clone to be transmitted between hosts and the ability of the clone to avoid being cleared from the infected host. Antimicrobial agents are example of the selective pressures that microorganisms face in their attempt to survive. The ability of a microbial pathogen to adapt to antimicrobial agents - that is, to develop resistance - can be considered an important characteristic that may affect fitness. Both plasmid/transposon- and chromosomally conferred resistances result in loss of fitness and/or virulence. It is equally important to understand that natural selection over time can compensate for loss of fitness and reduced virulence. Compensatory mutations may restore fitness or virulence without concomitant loss of resistance. The conclusion that can be drawn from this discussion is that the current lack of treatment failures in the community despite the emergence of resistance may only be temporary as bacterial pathogens further mutate to compensate for acquisition of the mutations responsible for resistance. As these mutations occur, one can expect the clonal spread of the fittest microbial pathogens having good survival against antibiotic therapy and a considerable virulence which may worsen the condition in community acquired infections as well. Extended drug resistant M. tuberculosis is a classical example of this phenomenon.[2]

It is usually observed that, the Community acquired infections develop in otherwise healthy persons, is caused by more virulent bacteria but have relatively less problem with antimicrobial resistance; And Hospital acquired infections is caused by relatively less virulent bacteria, but as the patient's general or local immunity is poor they infect the patients, these bacteria are found to be multi drug resistant. Now the problem is developing in such a manner that, the potentially virulent bacteria causing Community acquired infections are also becoming Multi drug resistant and Hospital acquired infections caused by Multi drug resistant strains are gaining more virulence.

The nature of antimicrobial resistance thus suggests two general ways to manage it. One is to minimize survival and overgrowing of resistant bacteria over the susceptible ones by minimizing use of antimicrobials. The other is to minimize the transmission of such bacteria from one host to another.

Role of the microbiologist is to keep the watch on prevalence of antimicrobial resistance and disseminate the surveillance report on regular basis. The clinicians are having key role in management and monitoring this problem. They always need to consider first in selecting antibiotic is whether it is even indicated. The reflect action to associate fever with treatable infections and prescribe antimicrobial therapy without further evaluation is irrational and potentially dangerous.[3] The diagnosis may be masked if therapy is started before appropriate cultures are obtained. Whenever clinician is faced with initiating antimicrobial therapy on a presumptive bacteriological diagnosis, culture of presumed site of infection and / or blood culture should be taken prior to institution of therapy.[3]

Trends in antimicrobial resistance in community acquired bacterial infections:

1. Fluro - quinolone resistance in Enterobacteriacae

- E.coli, the commonest cause of Urinary Tract Infection, where quinolones are the choice of treatment, emergence of resistance to even newer quinolones had lead a large number of treatment failure. Quinolone resistance now being increasing reported in shigella sp. (responsible for bacillary dysentery). Few of salmonella typhi are also found resistant to quinolones.

2. MRSA, MRS

- These strains are considered as nosocomial ones; Becoming now more prevalent in community acquired infections (CA-MRSA) like cellulitis, prostatitis, UTI, foliculitis, necrotizing pneumonitis etc. Condition is further worsening with increasing prevalence of inducible methylase producing staphylococci.

3. ESBL producing enterobactaeriacae

- Which is one of the most common problem faced, restricting use of orally available and well tolerated cephalosporins. The problem originated in hospital, now being rapidly spread in community.

4. Inducible beta lactamase in Klebsiella pneumoniae

- Recently, emerged problem, prevalent in our area as well, though less reported from community acquired infections

5. Pseudomonas aeruginosa

- A known multidrug resistant bacteria, can cause various community acquired infections like otitis media, wound infection etc.; How ever, still community strains of pseudomonas are sensitive to quinolones and amino glycosides.

6. Multi Drug Resistant (MDR) Tuberculosis (Resistant to isoniazide and rifampicin)

- is now highly prevalent in our area; But today a few no. cases also been reported as Extended Drug Resistant (ExDR) and Total Drug Resistant (TDR) tuberculosis, where there is no treatment option remains.

7. Beta lactam and macrolide resistant Streptococcal pneumoniae

- Streptococcus pneumoniae (Pneumococci) is one of the most common cause of community acquired pneumonia and meningitis. Till today penicillin remains the best choice. But, few of the infections are now been reported to be resistant to entire beta lactam group and macrolides, where the choice of the treatment would remain Vancomycin, Oxazolidone or quinolones.

8. Beta lactams and fluro-quinolone resistant Haemophilus influenzae

- H. influenzae is again a common cause of community acquired respiratory tract infections and meningitis. Few strains are now resistant to betalactams by various mechanisms like beta lactamase and modified Penicillin Binding Proteins. Associated resistance to quinolones is now a warranting situation, where the treatment options are limited (i.e. Clarithromycin)

  However the prevalence of above mentioned two strains are increasing in western countries, very few cases are reported from India.

9. High level macrolide resistance in various streptococcal sp.

- Various streptococcus spp. are common cause of upper respiratory tract infections. Where macrolides are still the first choice, resistance is being reported in large number.

10. Metronidazole resistant anaerobic streptococcal infection.

- Anaerobic streptococcus (Peptostreptococci), a common cause of primary and secondary empyema, Pelvic Inflammatory Diseases and puerperal sepsis are now shown to be resistant to metronidazole in vitro; However, penicillins and lincosamides have shown a good sensitivity.

Trends in antimicrobial resistance in Hospital acquired bacterial infections:

1. Methicillin Resistant Staphylococcus (MRSA, MRS)
2. Vancomycin Resistant Enterococci (Being reported less in our area)
3. Vancomycin Intermediate Staphylococcus
4. Enterobacteriacae producing beta lactamase of multiple varieties (ESBL, amp C Beta lactamase, OXA, metallobeta lactamase etc.)
5. Metallozyme positive Pseudomonas and related species - though they are very less virulent and more so colonizing the patient with long hospitalization, it is a most difficult strain to be treated or irradiated were warranting the therapy for it.
6. Carbapenem resistant Acinetobacter spp., they also seems to be increasing in virulence, leading to fatal ventilator associated pneumonia and septicaemia.

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Biosimilars: What are the challenges ?

Usha H Shah[*], *Geetha S Iyer*[**]

Abstract :

Biopharmaceutical drugs are fast becoming the mainstay in many chronic diseases like diabetes mellitus, rheumatoid arthritis and carcinomas. However, the development of their generic versions "biosimilars" presents many challenges, especially with their efficacy, safety and framing of their regulatory guidelines. This review discusses the importance and challenges of the biosimilar drugs.

Introduction

The growth of pharmaceutical industries all over the world is a testament to the innovative research and modern technology which has led to the development of innumerable new drugs. The focus in the 20th century was treating diseases with traditional pharmaceuticals and the emphasis in the 21st century is on the biopharmaceutical products. These products have been defined as "Any medicinal product developed by means of biotechnology practices: recombinant DNA, controlled gene expression or antibody methods".[1] The first biopharmaceutical drug to be manufactured was human insulin. Other examples include growth hormone, erythropoietin, monoclonal antibodies like trastuzumab, and interferons etc. These biopharmaceuticals have revolutionized the treatment of long standing conditions like diabetes mellitus, rheumatoid arthritis, Hepatitis C, chronic renal failure, malignancies etc. Development of biologically similar and clinically comparable agents to the innovator biopharmaceutical drugs is underway, which are known as "biosimilars". Biosimilars attempt to copy the process which leads to the production of the original innovative biotechnological medicine. It is important to state that biosimilars are not (bio)generics. Biosimilars are attempted copies of existing biological medicinal products or protein drugs. However, they are made with a different cell line and a different manufacturing and purification process, and the final product is "similar", not identical. In the US and Canada, biosimilars are called 'Follow on Biologics' and 'Subsequent Entry Biologics', respectively.[2] There are certain basic distinctions between traditional and biological drugs, especially in the context of their molecular size and structure, the manufacturing process and cost.[1,3] Some of these differences are mentioned in Table 1.

Table 1. Differences between traditional and biological drugs

Parameter	Traditional drugs	Biopharmaceuticals
Molecular size	10 – 1000 Daltons	10,000 to over 1,50,000 Da
Molecular structure	Simple spatial structure, easily identified by analytical methods	Complex three dimensional structure with folds, difficult to determine
Manufacturing process	Chemical synthesis, can easily be replicated	Specific and intricate process, vary among difference companies
Manufacturing costs	Low	High
Stability	Stable	Highly sensitive to environment, can denature if not stored or handled properly

Regulatory approval

The European Medicines Agency (EMA) was among the first to put down guidelines for approval of biosimilar drugs. These guidelines are meant as a rough draft which can be adapted according to the biopharmaceutical product.[4,5] The basic requirements are

- Clinical data which demonstrates "comparable" efficacy and safety to the reference product
- Immunogenicity testing is required as serious adverse events (SAEs) have been noted
- Pharmacovigilance program needs to be established in order to monitor the safety and efficacy even after obtaining marketing approval.

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The US also has come up with a set of regulations for approval of these biosimilar products. The Patient Protection and Affordable Care Act has created a pathway for biological products that are demonstrated to be "biosimilar" to or "interchangeable" with an FDA-licensed biological product via the Biologics Price Competition and Innovation Act (BPCI Act). Under this act, a biological product may be demonstrated to be "biosimilar" if data show that, among other things, the product is "highly similar" to an already-approved biological product.[6] The guidelines require structural analysis of the biosimilar followed by its functional analysis to justify animal testing. This is followed by animal toxicity and immunogenicity studies. Lastly human clinical data, immunogenicity studies and post marketing safety considerations are mentioned.[7] Both the EMA and US FDA can extrapolate the clinical data available for the biosimilars to include new indications. India is among the leading producers of biosimilar drugs and the regulatory authorities have already proposed a National Biotechnology Regulatory Act 2008, which will regulate the research, manufacture, importation and use of products of modern biotechnology (including recombinant blood and plasma derived products).[8]

Challenges associated with the development of biosimilars

In spite of the regulations imposed by the regulatory authorities, the development of biosimilars are fraught with difficulties. Some of them are discussed below:

Molecular structure

Biologicals, being predominantly protein in nature, are larger, ranging from 5000 – 20,000 Da^1 and also undergo conformational changes to attain its three dimensional structure. Unlike generic pharmaceuticals, where similarity of the chemical structure of the active drug is primary to ensure bioequivalence, biologicals need similarity in both the protein structure and its folds. This structure is difficult to duplicate.

Manufacturing process

The problem is further complicated by the manufacturing process of these drugs where the relevant gene is cloned and transferred into a host cell (E.coli, yeast), which is then cultivated in an appropriate cell line. A complex process of purification and validation is usually conducted as the last step.[9] Since companies who want to manufacture biosimilars do not actually have access to original manufacturing process from the proprietary company, developing an exact, identical product with the same spatial structure is very tricky. The pharmaceutical companies are not required to share their process even after expiry of the patent.[1] Between 1988 and 2004, a total of 506 reports of erythropoietin induced pure red cell aplasia (PRCA) were identified by the US FDA.[10] After extensive study, it was concluded that the most likely cause in majority of the cases was a change in the formulation. This demonstrates that even a small change in the manufacturing process can lead to severe and life threatening adverse reactions.[11]

Efficacy

- The difference between the innovator and the biosimilar drugs can be highlighted by a study which compared the bioactivity of 11 erythropoietin brands from 4 countries.[12] The in vivo bioactivity of the products ranged from 71% to 226% of the innovator drug. Similarly, a study comparing quality parameters of 16 biosimilar brands taken from the Indian market and with those of the innovator drug products (recombinant human pegylated G-CSF, recombinant human G-CSF and recombinant human erythropoietin) showed a lack of comparability between the two.[13] For these reasons, substitution is not advisable for such products.

- Furthermore, substituting one brand for another can confound the safety data in case of any adverse event. The event would not be able to be linked to a specific product during the assessment, or it could be ascribed to the wrong brand. Hence interchangability of the brands is not preferred with biopharmaceutical products.

Safety considerations

- Immunogenicity is an important safety concern for biopharmaceuticals. They are biologically active molecules and are liable to cause an immune response.[14] The risk of immunogenicity can be increased by the presence of impurities in biological products, structural modifications as a result of the manufacturing process and/or suboptimal storage conditions.[15]

- The route of administration of the biopharmaceutical can also affect immunogenicity. Generally, intravenous administration is less immunogenic than intramuscular or subcutaneous administration, as was the case with erythropoietin.[10] Most of the tests conducted during its development cannot predict immunogenicity. Hence, the best way to establish the safety of a biosimilar is via clinical trials.
- Post-marketing surveillance is another tool by which the safety can be continuously monitored as the differences between biosimilars may not become apparent in the pre-approval period, where a limited numbers of patients receive the product over a short time period.[4] Both European Union and United States have well established pharmacovigilance systems and require stringent post-marketing surveillance data to be submitted by the pharmaceutical companies.[16, 17] The Government of India has introduced the Pharmacovigilance Programme of India (PvPI) which is working towards encouraging the practice of adverse reaction reporting among prescribers.

Extrapolation of clinical data

Extrapolation refers to the approval of a drug for indications for which it has not been evaluated in clinical trials. It is only applicable in a handful of cases such as new formulations, indication in closely related diseases etc.[18] Both the EMA and the US FDA have endorsed the extrapolation of indications for biosimilars. The rationale is that if the biosimilar shows adequate comparability to the innovator product for one indication, it may be reasonable to extend the approval of the biosimilar to all the indications of the innovator product. Recently, two biosimilar growth hormones have been approved which included extrapolation of clinical data for some indications. The reasons for the same were cited as the long history of safe use of growth hormone, high therapeutic index, the rarity of reports of neutralizing antibodies and assays available to characterize the biological activity of growth hormone.[19]

Less than 15 biological drugs were approved by the US FDA in the early 1990s but by the end of 2009, biologicals in phase III clinical development made up 38% of all pipeline products for the pharmaceutical industry[20] which make up sales worth $US130 billion.[1] India is not far behind with over 50 biopharmaceutical brands getting marketing approval. The biotechnology industry is also gaining impetus, with revenues of over U.S. $2 billion in 2006, biopharmaceuticals being responsible for almost 70%. These are projected to reach up to $580 million by 2012.[1] Biosimilars have attracted the interest of health care providers chiefly due to the potentially significant cost-savings they offer. It has been suggested that an initial wave of biosimilars could generate savings equivalent to over $2 billion in Europe.[20] This could lead to greater affordability among patients especially in developing countries.

The time for biological therapies has arrived and it is extremely important that the issues in the development of biosimilars be sorted out. The clinicians should be aware that biosimilars are not interchangeable products and that safety of these drugs has yet to be established. The ultimate success of biosimilars depends upon the implementation of adequate pharmacovigilance systems and regulatory guidelines. The development of biosimilars brings us one step closer to providing economical and proper care to the patients especially in India.

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An Outbreak Investigation of Viral Hepatitis E in Urban Slum Area of Ahmedabad City of Gujarat, India.

Viral Dave[*], *Venu Shah*[*], *Jignesh Garsondiya*[**], *Asha Solanki*[***], *K N Sonaliya*[****]

Abstract :

Background : Hepatitis E is water born viral disease. Water or food supplies contaminated with faeces in which the virus is excreted have been implicated in major outbreaks reported in all part of the world as well as in Gujarat. Similar outbreak of hepatitis E had occurred in catchment area of GCS General Hospital, Ahmedabad. **Aims and objectives:** 1) To study the socio demographic profile of patients affected with hepatitis E. 2) To study time, place and person distribution of current outbreak in community. 3) To assess water quality and educate the people regarding various cost effective water purification techniques. **Materials and Method:** Investigation of HEV outbreak was carried out in an observational cross-sectional manner in Nikol ward of Ahmedabad Municipal Corporation. House to house visit was carried out. 760 households among affected area were surveyed. **Result:** 257 jaundiced cases presenting with signs and symptoms of acute hepatitis were reported. Commonly affected age group was 10-39 years. Attack rate was more in Males (6.5%) as compared to females. Only 2.3% of affected households had the satisfactory level of residual chlorine in drinking water. Sixty percents were using appropriate water purification method. **Conclusion:** Majority of the families were using bore water which are deriving water from the upper layers of earth. The same was found contaminated due to unsatisfactory sewage treatment. There is need to educated the people regarding use of proper water purification methods as well as good hygienic practices.

Key words : Water borne hepatitis, Chlorination, Outbreak, Secondary attack Rate

Introduction

Repeated occurrence of outbreaks of particular disease in any community is certainly result of negligence, not only on the part of community but also on the part of public health experts, who are supposed to play a key role to unlock the common causes of its occurrence. There is a need to plan protective measures in such a way that never allow reoccurrence of outbreaks.

Water borne diseases are one of such notorious problems annoying almost all developing countries. Feco-orally transmitted viral hepatitis E is one such example. In India, it has enrooted so deep that virtually all outbreaks of viral hepatitis are considered to be due to feco-orally transmitted hepatitis non-A non-B virus (hepatitis E). [1] [2] [3]

The first major epidemic was reported in New Delhi in 1995-96, where 30,000 cases were recorded of hepatitis E[4]. The Delhi, India, epidemic that occurred from December 1, 1955 to January 20, 1956 was the first reported outbreak of disease attributable to "novel" ET-NANB viral hepatitis [5] [6]. From a population of 1.6 million, approximately 29,300 jaundice cases occurred, with an estimated 67,700 nonicteric infections. Numerous outbreaks of HEV have been reported from both urban and rural areas across the Indian Subcontinent. Extrapolating from reports of outbreaks and sporadic disease, approximately 2.2 million adult cases of hepatitis E are believed to occur in India annually [7].

There was a sudden increase in number of cases of hepatitis in month of November 2011 in one of the teaching hospitals of Ahmedabad city. All the cases were serologically proven for Hepatitis E. On analyzing the history, it was found that most of the cases belonged to common inhabited area. Rapid survey was carried out in the same area and it was found to be an outbreak! So, the detailed outbreak investigation was done in order to find out the possible etiological factors as well as to take preventive measures.

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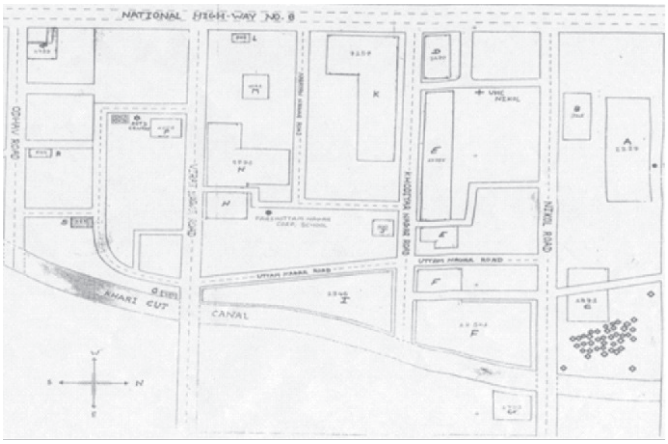
Material and Methods

Present study of the HEV outbreak in the Ahmedabad city was carried out in an observational cross-sectional setting at the referral teaching hospital in Ahmedabad, India. The study area, where the outbreak was reported belonged to Nikol ward of Ahmedabad Municipal Corporation. (figure 1). Total 760 households among the affected area were surveyed. 257 consecutive jaundiced cases (among 239 affected families) presenting with signs and symptoms of acute hepatitis were evaluated.

Figure 1 Clustering of cases in affected area of Nikol ward of Ahmedabad Municipal Corporation, India, October 2011- February 2012.



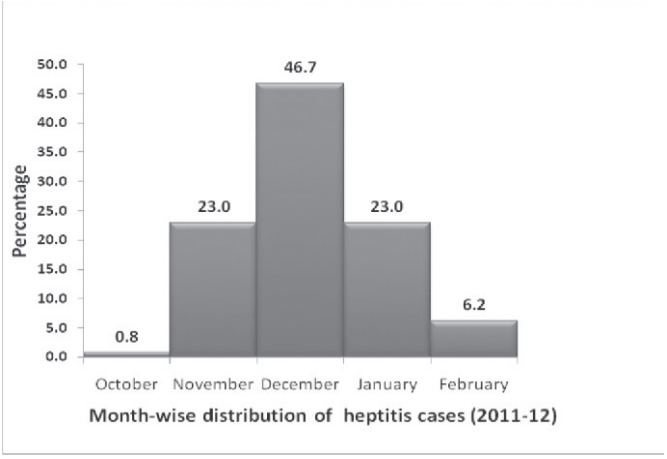
Rapid surveillance was carried out in affected area to find out suspected cases in the community. Faculties from Community Medicine Department interviewed the patients and their family members. Hepatitis was defined as a yellow discoloration of the conjunctivae or of a typical prodrome followed by deep-colored urine. Individuals who were still affected at the time of the visit were examined clinically to exclude other causes of jaundice and to confirm the clinical diagnosis of hepatitis. Confirmation of the diagnosis for those who had already recovered was based on the past records of clinical examination and laboratory profile, if available. Detailed history regarding name, age, sex, occupation, date of onset of illness, date of hospitalization, signs and symptoms and former injections/vaccinations was taken. Clinical signs and symptoms were icterus, anorexia, nausea, vomiting, malaise, dark colour urine and right-sided pain in the abdomen.

The study was carried out during December 2011 to February 2012 and cases occurred during month of October and November 2011 were also included as to cover the maximum incubation period of the disease, i.e., around 60 days. Data entry and analysis was done by using SPSS 15.0 version.

Results :

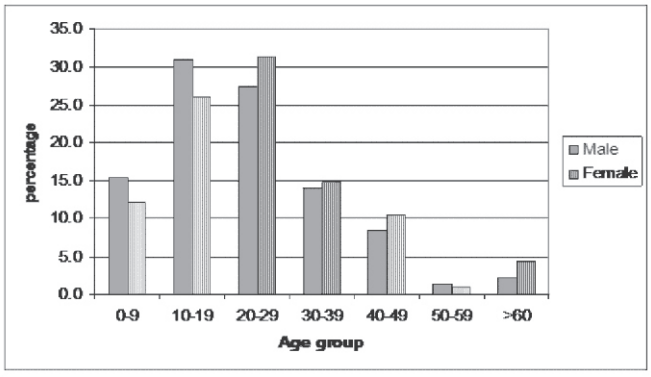
Total 760 houses were surveyed in the affected area. Total 257 cases of water born hepatitis were reported. Cases were increasing from the month of November; peak was seen in the month of December. Thereafter, there was fall in number of cases. (Figure 2)

Figure 2 Month – wise distribution of cases of hepatitis



Mean age of the patients was 23 years with standard deviation of 13 years. Maximum numbers (58%) of cases were between 10 and 29 years. (Figure 3)

Figure 3 Age and Gender-wise distribution of cases



Out of 257 cases, 27(10.5%) were graduates and above, while 21(8.2%) were illiterate.42 % of cases belonged to socio economic class 2 according to modified Prasad classification. Influence of socioeconomic status on

occurrence of disease was found to be statistically significant. (ANOVA; F= 3.3 P<0.05)

Table 1 Age and gender wise attack rate

Age group	Male	Female	Total
0-9	4.7(22)	3.6(14)	4.5
10-19	9.3(44)	7.9(30)	8.7
20-29	10.0(39)	10.6(36)	10.3
30-39	6.5(20)	6.4(17)	6.5
40-49	5.3(12)	6.5(12)	5.8
50-59	1.2(2)	0.8(1)	1.0
>60	2.0(3)	3.6(5)	2.8
Total	6.5(142)	6.2(115)	6.4
Total population affected	142	115	257

Chi-square value: 0.02; P value:0.887

Attack rate was more in Males (6.5%) as compared to females (6.2%) Chi-square = 0.020, DF = 1, P = 0.887. (Table 1)

Intrafamilial spread of the disease was studied. Secondary or "later" cases were defined [4] as those persons who developed illness a minimum of 2 weeks after the index case in a household. Out of 239 families affected, 226 were sole case of Hepatitis among their family while 13 families have multiple cases (secondary cases) per family.(Table 2)

Table 2 : Distribution of 257 Hepatitis cases in families with single or multiple cases affected

No. of cases per family	No. of families	No. of cases	
		Index	Fresh
1	226	226	0
2	9	9	9
3	3	3	6
4	1	1	3
Total	239	239	18

Data on source of water supply showed that the area was having water supply from corporation as well as bore. Out

Out of 257 cases, 130(50.6%) had taken any type of outside food within 3 months of illness. On asking about hygienic practices followed to avoid illnesses, it was found that 150(58.3 %) of the cases, wash their hands with soap and water after defecation while only 39(15%) mentioned that they wash their hands with soap and water every time before meal.

Discussion:

Large-scale waterborne epidemics of HEV have occurred in many tropical and subtropical countries in which thousands of individuals developed acute hepatitis following ingestion of contaminated water. From 1985 to 2004, ten major epidemics of HEV have been recorded involving 327,280 reported human cases in the Indian subcontinent and Southeast and Central Asia [8].

The epidemiological features of the present epidemic resemble those reported for previous HEV epidemics[7] [9] [10] [11], i.e., a high attack rate among young people but relatively few cases among children. Only12 % of the cases were below 9 years of age. 72% were aged 10-39years.

In present study, attack rate among male and female was almost equal. Again in similar studies done by Gurav Y K et al [12] at rural Maharashtra and Das D et al [13] at slums of Kolkata revealed the same finding, i.e. the difference in the attack rate of infective hepatitis of both the sexes was not statistically significant while in the study carried out by Chauhan et al [10] statistically significant gender wise difference was found for attack rate. However, some studies of outbreaks in Nepal, Pakistan, and India have suggested that adult men may have upto twofold higher risk than women of the same age of developing clinical illness [14,15]. A higher proportion of cases in males may be caused by behavioral factors that result in differential exposures as well as gender differences in health-seeking behaviors may exist in these communities.

In present study 42% of cases belonged to socioeconomic class-II while in the 1955 Delhi epidemic and a 1973 outbreak in the Kathmandu Valley of Nepal, attack rates were 4-8 times higher among persons of high socioeconomic status [7] . In both of these examples, lower socioeconomic status individuals tended to live under poor hygienic conditions, indicating that some protective immunity may exist as a result of frequent environmental exposure to HEV.

In the study carried out by Naik et al [16], 62.7% cases were single case per family while in current study 87.9% of cases were the only case in their family. In the same study 22.5% cases were secondary cases among their family while in the present study only 7% cases were secondary cases among their family. This shows that in the present study the secondary attack rate was lower, which may be due to early interventional activities taken by public health authorities as well high awareness on the part of affected families.

Although around 98% of the affected households reported inadequate residual chlorine in their drinking water in present study, when an HEV epidemic is already enduring, all drinking water should be boiled or imported, since chlorination alone may be unsuccessful in controlling epidemics [17] [18] .

The addition of high levels of chlorine to the contaminated water did not have an appreciable impact on the progression of the hepatitis epidemic [7] , in such condition distribution of chlorine tablets at household level by health volunteers will not work efficiently.

Conclusion :

The study area was a peculiar slum area of a city developing at high pace. The same ward was recently included in municipal corporation area where the various civic developmental activities like sewage pipeline, water pipeline, road pavement are going on. Due to such multiple constructional works, the underground pipelines are repeatedly damaged.

As a part of water conservation, the municipal corporation is supplying water to its territory in certain fixed morning hours only. When water is intermittently pumped through broken or cracked piping, as has been observed, negative pressure can pull in fecally Contaminated water from the surface above the pipes, thereby increasing the risk of HEV contamination.

So many areas were using either soakage pit for their sewage removal or indiscriminate disposal of sewage water in open field nearby residential area – which is contaminating the upper soil layers of the ground. Again as the public is running scarcity of water, they are managing

the same by making shallow bore for personal or small scale use at society level. These bores are deriving water from the upper layers of the earth which are obviously lacking the natural decontamination of water done by various deep earthen layers. On the contrary this water is contaminated due to above mentioned reasons which are aggravating the incidence of waterborne diseases' outbreaks.

At the household level, the appropriate water purification measures were not undertaken. Lack of awareness in general was found as far as use of chlorine tablets or boiled water usages were concerned. Good hygienic practice were also lacking in most of the families.

Recommendation

In outbreak settings, the handling and disposal of human waste must follow strict sanitary guidelines. The patient's excreta must be disposed of properly to prevent secondary household cases. Better community sanitation and sewage Management would also reduce rate of HEV transmission. Improvements in drinking water storage, treatment and distribution should be encouraged as a means of reducing HEV transmission.

Health education about personal and environmental hygiene in high risk communities might reduce the likelihood of HEV outbreaks.

Acknowledgement

The help done by medical social workers of the community medicine department, GCS Medical College, Ms.Rizwana Mansuri and Ms.Shweta Waghela is acknowledged herewith in data collection as well as in teaching health hygienic practice to raise the awareness in the affected community.

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Assessment and Treatment of Chronic Pain in Children

Heena Parikh*

Abstract :

Background and Aims : This article focuses on the methods of pain measurement, assessment and treatment in children. The concepts of reliability, validity and the available types of oral, parental, regional therapy along with self report and behavioral measures are addressed. Finally, some practical suggestions for pediatric pain assessment and treatment are provided. **Material and Methods:** In a randomized controlled group study, we recruited 60 children of age 1- 12 years of either sex, American Society of Anaesthesiologists (ASA) I/II. All patients were allocated to three groups of 20 each to receive oral therapy in Group I, Parental therapy in Group II and regional therapy in Group III. All these groups supplemented by behavioral therapy (cognitive placebo and hypnosis). After treatment patients pulse rate, blood pressure, respiratory rate, pain score and complications were recorded up to 12 hours and final assessment made up to 48 hours. **Results :** With non-invasive methods 60% of pain was relieved. Transcutaneous Electrical Nerve Stimulation reduced the pain approximately 30 % along with oral medications. However in aggressive pain conditions, parental and regional techniques were used. In group I, statistically, significant difference was observed. In group II patients were not co-operative. Moreover in group III the possibility of potential complications is likely to be encountered in attempting to locate a nerve trunk or caudal or epidural space. Behavioral therapy supplemented in both non-invasive and invasive methods **Conclusion:** Oral therapy including opioid and non-opioid analgesics for cancer and non-cancer type of chronic pain in children is better to reduce the pain and to improve the patient's quality of life.

Key Words : Chronic Pain, Children, Analgesics, Behavioural therapy.

Introduction

Chronic pain is a significant problem in the pediatric population, conservatively estimated to affect 15% to 20% of children. Chronic pain in children is one of the most ignored and undertreated symptoms of disease. Over the last decade there have been numerous studies in the literature that have addressed pain in children, its measurement and management.[1] Children and their families experience significant emotional and social consequences as a result of pain and disability. The financial costs of childhood pain also may be significant in terms of health care utilization as well as other indirect costs such as lost of daily wages. In addition, the physical and psychological squeal associated with chronic pain may have impact on overall health and a may predispose for the development of adult chronic pain. The international association for the study of pain (IASP) characterized chronic pain as less than 1 month , 1 to 6 months and greater than 6 months. (Tax force on taxonomy, 1994) Formerly chronic pain was defined as having pain for longer than 6 months. Chronic pain may begin as acute pain but it continues beyond the normal time expected for resolution of the problem or persists or recurs for other reasons. Chronic pain in contrast to acute pain, rarely is accompanied by signs of symphatetic nervous system arousal.

Chronic pain in children is the result of a dynamic integration of biological processes, psychological factors and socio cultural context considered within a developmental trajectory. This category of pain includes persistent (ongoing) and recurrent (episodic) pain with possible fluctuations in severity, quality, regularity and predictability. Chronic pain can occurs in single or multiple body regions and can involve single or multiple organ systems. Ongoing nociceptive stimuli can result in a sensitization of the peripheral and central nervous system to produce neuroanatomical, neuro chemical and neuro physiological changes.

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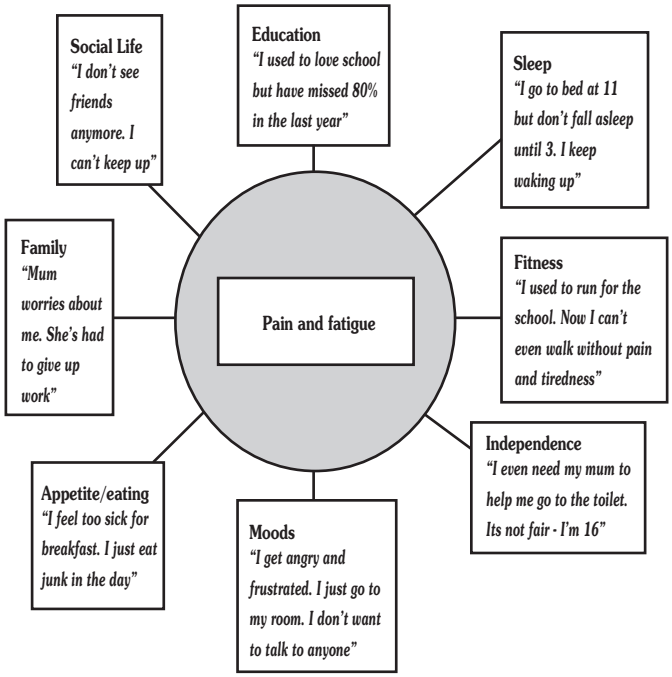
It is important that assessment and treatment strategies be based on this definition and related dimensions.



Material and Methods :

Study Design : This was a randomized controlled group study.

Randomization : Simple randomized sampling was done by computer system

Sample Size : Sixty patients were studied

Inclusion Criteria: ASA I/II patients between age group of 1 – 12 years of either sex were included. Patients having cancer pain, headache, trauma, visceral pain, pain during terminal illness and neuropathic pain were included.

Exclusion Criteria: Patients with known allergy to study drugs, suspected coagulopathy, infection or deformity of vertebral column, history of developmental delay and neurologic diseases were excluded.

Allocation: After obtaining institutional ethical committee approval and written informed consent from the parents, the children were randomly allocated into three groups.

Group 1 (n=20) was taken as oral therapy.

Group 2 (n=20) was taken as parental therapy

Group 3 (n =20) was taken as regional therapy.

We started evaluation with a history of the current problem including a careful description of the pain detailing the sensory characteristics, intensity, quality, location, duration, variability, predictability, exacerbating and alleviating factors and impact of pain on daily life (eg. Sleeping, eating, school, social and physical activities, family and peer interactions).

We elicited history of past pain problems in the child and in other family members. Current treatments for the pain about home remedies, alternative and complementary therapies through family have been reviewed.

In addition to pain history, other history regarding medical surgical illness, birth and early childhood history, developmental milestones, family and social history was reviewed.

Complete physical examination was carried out which include child's general appearance, posture, guilt and emotional and cognitive state. We have assessed muscle spasms trigger points and areas of somatic sensitivity to light touch.

A complete neurological examination was conducted (somatic pain sometimes elicited when the child tenses his/her muscles due to fear of examination.

Height and weight were measured vital signs were monitored like baseline blood pressure, heart rate and temperature. Post therapy also same vital signs were monitored at interval of every 15 minutes up to 1 hour, every 30 minutes up to 4 hours, every hourly up to 6 hours, every 2 hourly up to 12 hours and final assessment up to 48 hours.

We used several pain scales for the assessment of chronic pain during pre and post therapy. (Table 1)

Table 1: Self Report Measures of Pain

Sr. No.	Measure	Description	Age - Range	Advantages	Disadvantages
1	FPS – R (Faces Pain Scale – Revised)	Faces indicating intensity of pain	6 – 8 years	Adequate test/ retest reliability. Adv. Over FPS is absence of smile and tear in this faces scale.	No validity tests completed
2	Visual Analog	Vertical line with numerical anchors	5 yrs and over	Reliable valid and versatile can relate in dimensions	Must understand proportionality
3	Oucher Scale	6 photos of children indicating pain	3 – 12 years	Presentations of pictorial and numerical range: Broader age proportionality	Must understand concept

Oral Therapy group 1 were including

1) Tab. Ibuprofen 5-10 mg/kg P.O. every 6-8 hourly
2) Tab. Diclofenac 1 mg/kg P.O. every 8-12 hourly
3) Tab. Morphine 0.15 – 0.3 mg/kg P.O. every 4-6 hourly
4) Tab. Codeine / Syrup Codeine 1 mg/kg P.O. every 4 hourly

Adjuvant Analgesics drugs were used according to the condition of the child.

1) Tab. Amitryptyline 0.2 – 05 mg/kg P.O.
2) Tab. Gabapentin 5 mg/kg/day P.O.
3) Tab. Carbamazepine 10 mg/kg/day P.O.
4) Tab. Diazepam 0.025-0.2 mg/kg P.O. every 6 hourly
5) Tab. Cetrizine 0.2 mg/kg/day P.O.
6) Corticosteroids – Dexamethazone 0.2 mg/kg/ I/V
7) Fentanyl 25 ?g patch transdermal (72 hour duration of action)

Parental Therapy → group 2

10 patients received I/V diazepam and 10 patients received I/M Diclofenac at the time of aggressive pain conditions.

Regional Therapy → group 3

Patients who were going for regional techniques, they were advised pre-operation fasting six hours prior to the procedure. Inside the operation theatre, venous access was obtained with a 22 G or 24 G I/V cannula and intravenous ringer lactate drip was started.

All resuscitative equipments, along with Boyle's anaesthesia machine were kept stand by to prevent any possible adverse reaction.

Standard tech. of epidural and caudal was used with Bupivaccine 0.1% 1 ml/kg.

All three groups were supplemented by non-drug therapies like

(1) Cognitive

→ Information
→ Choices and control

- → Distraction and attention
- → Guided Imagery
- → Psychotherapy

(2) Behavioural

- → Exercise
- → Relaxation therapy
- → Behavioural modification

(3) Physical

- → Massage
- → Physiotherapy
- → Thermal stimulation
- → TENS

Observation and Results

Table 2 shows sex distribution of all patients. Figure 1 shows age (years) and Figure 2 shows weight (kg) distribution of all patients, there was no significant difference observed in these parameters. (P value > 0.05)

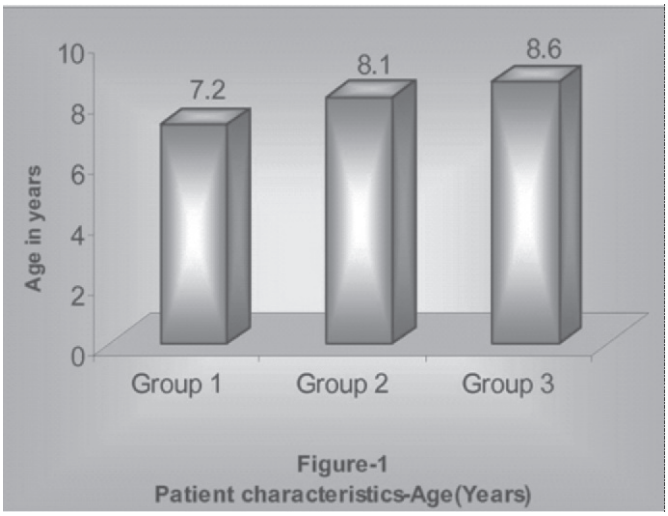


Figure-1
Patient characteristics-Age(Years)

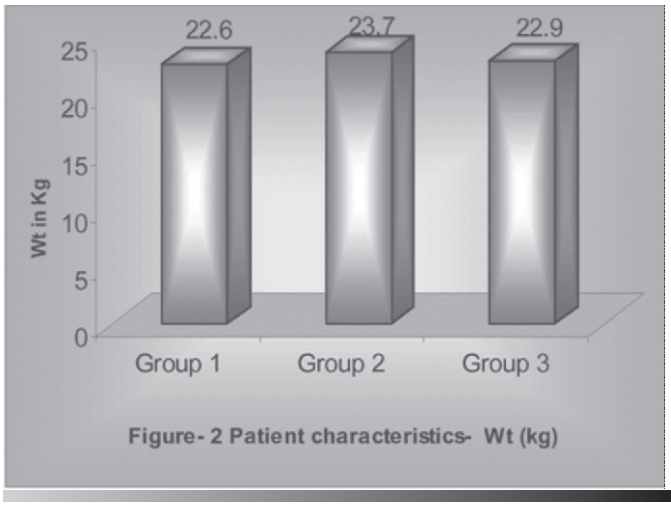


Figure- 2 Patient characteristics- Wt (kg)

Table 2: Patients Characteristics

Parameters	group 1	group 2	group 3
Sex Distribution Female : Male	8 : 12	11 : 9	7 : 13

Values are in mean in all three groups. This graph shows post therapy hrs against pulse rate. There was no significant difference among the three groups. (P value > 0.05) (Figure 3)

This graph shows combined therapy against % of pain relief. There was significant difference. (Figure 4)

Table 3 shows incidence of side effects in all three groups.

group 1 : 4 pts had vomiting, 2 required antiemetic drug.

group 2 : 2 pts had bradycardia, not required treatment, 1 pt had hypotension, treated by administration of fluid therapy

group 3 : 1 pt had respiratory depression, treated by O2 mask

Table 3 : Incidence of side effects

Side effects	No. of patients (%)		
	group 1 (n=20)	group 2 (n=20)	group 3 (n=20)
Vomiting	4 (20%)	0	0
Bradycardia	0	2 (10%)	0
Hypotension	0	1 (05%)	0
Respi. Depression	0	0	1 (05%)

Figure-3: Post therapy hours vs pulse rate

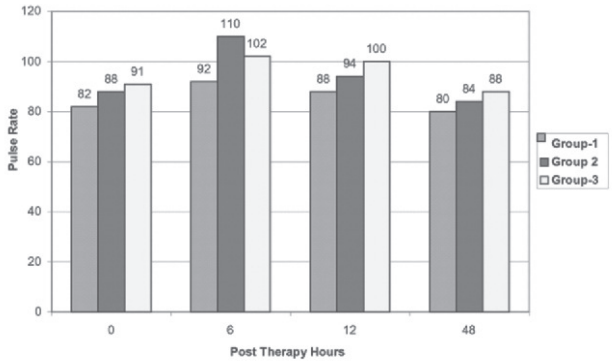
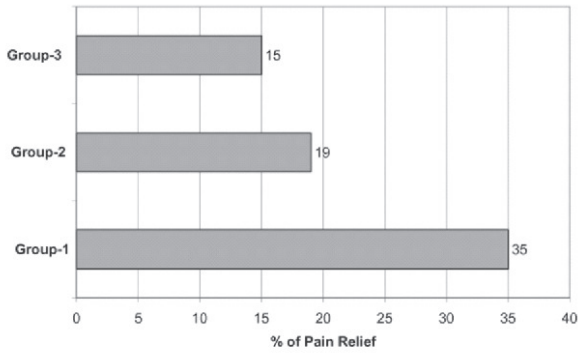


Figure- 4: Percentage of pain relief among three groups



Discussion :

Chronic pain may include varying amounts of disability from none to severe and may be independent of the amount of tissue damage and perceived severity. Biological, psychological, social, cultural and developmental factors can impact pain related functioning. A multi model approach often is more effective than a single sequential treatment approach for chronic pain in children and treatment strategies should be based on the findings of the assessment and should address the inciting and contributing factors.

We studied several self report measures like faces pain scale revised, visual analogy and Oucher scale. According to Bieri D et al.,[2] the faces pain scale incorporates conventions used by children has achieved strong agreement in the rank ordering of pain has indications that the intervals are close to equal and is treated by children as a scale. The test retest data suggest that it may prove to be a reliable index over time of self-reported pain. Several other authors studied FLACC pain score and CHEOPS children's hospital of Eastern Ontario Scale along with oucher and analogue chromatic continuous scale as a behavioral measure in post-operative patients.[3,4] Stinson JN et al.,[5] invented electronic diaries a real time data capture as a new standard for pain measurement.

In group II and group III patients were not co-operative, therefore we used sedative and analgesic drugs to relieve anxiety and pain associated with procedure. [6] Treatment strategies based on all multi disciplinary pain treatment included physicians, nurses and psychologists and used as rehabilitation model that were incorporated a wide variety of pharmacological, psychological and physical therapies. [7]

Limited accessibility leads to variable and prolonged wait times for pediatric patients suffering from chronic pain.

Treatment techniques of non-drug therapies include education about the pain experience and the pain problem, cognitive strategies (like information choices and control, distraction and attention, guided imagery, psychotherapy) behavioral strategies (like exercise, relaxation therapy, behavior modification) physical interventions like massage physiotherapy, thermal stimulation and Transcutaneous Electrical Nerve Stimulation. TENS is a valuable therapeutic modality for some patients with chronic pain.[8]

Evidence based treatment should be used whenever available. Controlled trials are needed to address safety and efficacy in this population. Cohen et al., [9] investigated eleven measures met criteria for "well established", Six "Approaching well established" and zero were classified as "promising" for evidence based assessment of pediatric pain.

Education of the public will increase community awareness and support of children with chronic pain and shape appropriate public policy. Mass media coverage of chronic pain in children should be promoted. More research is needed to provide evidence based treatments in chronic pediatric pain.

Conclusion:

For most painful conditions, there is no strong evidence that one form of therapy is more effective than another. A combined therapy of oral with non drug like behavioural, cognitive and physical is helpful in reducing the chronic pain in children.

Targeted government and private funding for research in pediatric chronic pain should be augmented. Outcome variables should be broad and include measures of pain and distress function, quality of life and health care utilization.

The mission is to advance pain related research, education treatment and professional practice.

Acknowledgement:

I wish to express my sincere gratitude to Prof. and Head of the Department, Dr. B.K. Jha (late), Anaesthesia Department. C.U.Shah Medical College, Surendranagar. Last but not least I wish to avail myself of this opportunity, express a sense of gratitude and love to my beloved parents for their manual support, strength, help and for everything.

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Angioedema: Fixed Dose Combination of Ibuprofen and Paracetamol : A Case Report

Geetha Iyer[*], *Nayan Patel*[**], *Anjana Shah*[***], *Usha Shah*[****]

Abstract :

Angioedema is a quick, abrupt swelling of the subcutaneous and submucosal tissues which can be hereditary or drug induced. Non steroidal anti-inflammatory drugs (NSAIDs) are among the most common group of drugs responsible. We present a case of angioedema in a 3 year old child after ingestion of a fixed dose combination of ibuprofen and paracetamol.

Key words : Angioedema, Ibuprofen, Paracetamol

Introduction :

Adverse drug reactions (ADRs) have been found to be the 4th to 6th common cause of mortality in the United States [1] with an incidence of 10.9% and 1% among children (hospitalized and outpatient[2] respectively). Non steroidal anti-inflammatory drugs (NSAIDs) are one of the most common drugs causing hypersensitivity reactions which include non steroidal anti-inflammatory drugs and antipyretics. A few predisposing factors for the same have been identified (history of atopy, female gender, young adulthood and a history of chronic urticaria). Possible mechanisms include shunting of the arachidonic acid metabolites towards lipoxygenase pathway, as cyclo-oxygenase pathway is blocked, increasing the synthesis of inflammatory cysteinyl leukotrienes.[3] Here we present a case of a 3 year old child presenting with angioedema, after ingestion of a syrup.

Case Report :

A 3 year old boy complained of fever for which his mother gave him left over syrup from a previous episode of fever which was a fixed dose combination of ibuprofen and paracetamol. Within hours of taking the drug, the patient developed swelling around his eyelids and lips. He was brought to the Pediatric outpatient department after which he was referred to the Dermatology department. Upon eliciting further history, it was found that a similar reaction (edema around eyes) had developed 2 months ago. The patient was prescribed syrup Ibuprofen plus paracetamol by a private practitioner and upon taking the drug, developed edema around his eyelids. The mother was reassured and it was not suspected to be an ADR in the past. The mother also reported that she had on several occasions given paracetamol alone to the patient without any such reaction occurring. He was not taking any other medicines and no laboratory tests were conducted in the past. No history of food allergy was reported. Preasantly the patient was diagnosed as a case of drug induced angioedema and the suspected drug was stopped. He was treated with injection dexamethasone and pheniramine maleate (single dose) with syrup cetrizine to be taken twice a day for 2 days. The reaction subsided within 6 hours and the patient was feeling better.

Causality assessment of the adverse drug event was carried out using WHO-UMC scale and Naranjo's algorithm. In this case, the patient improved after dechallenge (withdrawal of drug) and no confounding factors were observed. The patient also had a similar episode in the past. Hence the adverse event was probably caused by the fixed dose combination of ibuprofen and paracetamol (WHO-UMC scale – probable, Naranjo's algorithm – 7). The reaction was moderate in severity (Modified Hartwig and Siegel scale) and definitely preventable (modified Thornton and Schumock criteria).

Discussion :

Angioedema is a swelling of the deep layers of the subcutaneous and submucosal tissue or both. It occurs most commonly on the lips, tongue and around the eyes. It is a consequence of local increase in capillary permeability

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causing local plasma extravasation in response to mediators such as histamine or bradykinin.[4] Non steroidal anti-inflammatory drugs (NSAIDs) are known to cause angioedema in 0.1 to 0.3% of patients of which ibuprofen and aspirin are the most common offending agents. Paracetamol is found to well tolerated in patients with documented NSAID induced urticaria/angioedema.[5] In our case, a combination of ibuprofen and paracetamol was given to the patient for complaints of fever which was followed by development of edema around eyes and lips. The reaction abated after stopping the drug, hence dechallenge was positive. Also history of similar reaction in the past is present. These factors raise a suspicion regarding the relationship between the drug given and the adverse event. However, performing rechallenge in patients with hypersensitivity is not preferred, and if needed, should be done under strict supervision. Hence, on assessment of causality, the combination was probably the cause of the adverse event. The reaction was definitely preventable, as the drug was re-administered inspite of a similar reaction in the past and moderately severe in nature.

Ibuprofen, a propionic acid derivative non steroidal anti-inflammatory drug and paracetamol, a para-aminophenol derivative COX-3 inhibitor are both used extensively in children for treatment of fever. However, a fixed dose combination of the two drugs does not offer any advantage to any one single drug e.g. paracetamol alone is effective in cases of fever while ibuprofen alone can be used in inflammatory conditions.[6] Despite this, the combination is one of the most prescribed analgesic drugs in general population. In our case, the patient had been given paracetamol alone previously with no reaction. Hence, the prescription of ibuprofen and paracetamol combination is not only irrational but also resulted in hospitalization due to an adverse event.

Conclusion :

While hypersensitivity reactions are a known adverse effect of NSAIDs, it could have been prevented in this case with careful history taking and keeping in mind regarding ADRs as a differential diagnosis.

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Pregnancy with large ovarian tumor: A case-report.

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Abstract :

A huge ovarian cyst of 28x27 cm was diagnosed at 32-34 weeks pregnancy in primigravida. As benign nature was confirmed on sonography and colour doppler study conservative approach was adopted and pregnancy was carried till term. Cesarean section was done for nonprogress of labour. Cystectomy was completed without difficulty and cyst turned out to be dermoid cyst.

Key words : Pregnancy, Ovarian tumor, Dermoid

Introduction

The incidence of ovarian tumors in pregnant women is estimated on 1/1000 deliveries. Depending on the increasing size of uterus during pregnancy, the appropriate diagnosis of adnexal mass is based on the initial pelvic and ultrasound examination. [1] Most nonphysiological ovarian masses discovered during pregnancy are benign e.g. epithelial tumors, germ cell tumors .[4] In presence of pregnancy, increased incidence of ovarian tumor complications namely torsion , rupture , intracystic haemorrhage and infection may be encountered . Presence of ovarian tumor in advanced pregnancy can prevent engagement of presenting part. [2] They usually present the dilemma of weighing the risks of surgery and anesthesia during pregnancy versus the risks of untreated adnexal mass. [3]

Case Report

A 23 yr old primi patient presented in our antenatal clinic for routine checkup at 7 ½ month amenorrhoea. Physical examination showed over distended abdomen with palpation of separate cystic mass apart from uterus occupying the entire left side of abdomen. On ultrasound examination it was revealed that she was carrying a Single live fetus of 34 weeks with normal growth along with a left sided huge unilocular simple ovarian cyst measuring 28 x 27 cms with no solid component and low vascularity on Color Doppler study. As sonographic findings were of benign tumor, patient was managed expectantly with regular follow ups. On further follow up fetal growth was normal and cyst size was consistent with no symptoms.

At 39 weeks she presented with labor pains and as Bishops score was good, labor was augmented with oxytocin for trial of labor. After 6 hrs of active labor, partogram showed no progress. Due to pressure effect of large ovarian cyst, uterine axis was disturbed leading to non descent of head and arrest of cervical dilatation. Emergency caesarean section was decided. A live male child of 3.5 kg was delivered by lower segment caesarean section. After uterine closure, Cyst was examined. Cyst was huge occupying the entire upper abdominal cavity extending from liver up to left lumbar region. Opposite ovary was normal. Cystectomy was done and cyst was sent for histopathological examination.

Histopathology report showed cyst wall lined by stratified squamous epithelium with keratin, hair follicle and epidermal appendages with areas of fibrosis giving diagnosis of Mature Teratoma of Ovary (Dermoid cyst). Post operative period was uneventful.

Discussion

An increase in the incidence of adnexal masses revealed during pregnancy has occurred concurrently with the adoption of near universal use of prenatal ultrasound. The majority of these masses being physiological resolve by the second trimester. Persistent masses continue to be at risk for significant sequelae such as torsion, rupture, and obstruction of labor. Most nonphysiological ovarian masses discovered during pregnancy are dermoid cysts.[3] They usually present the dilemma of weighing the risks of surgery and anesthesia during pregnancy versus the risks of untreated adnexal mass. Most references state that it is more advisable to treat bilateral dermoid cysts of the ovaries discovered during pregnancy if they grow beyond 6 cm in diameter. This is usually performed through laparotomy or very carefully through laparoscopy and should preferably be done in the second trimester. [5]

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The risk of a possible malignancy can sway the decision for intervention versus expectant management. The etiologies of ovarian masses are reflective of the patient's age; and therefore, benign entities such as functional ovarian cysts, benign cystic teratomas, and serous cystadenoma predominate.

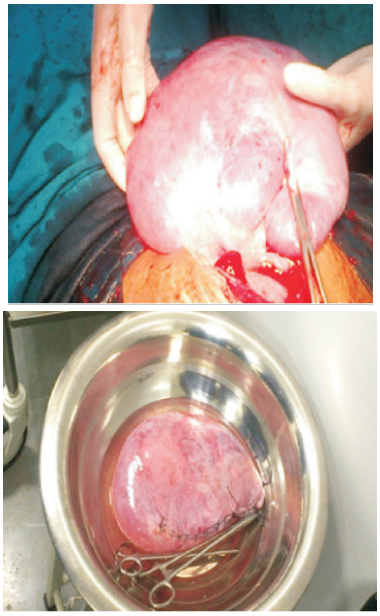

Figure 1 & 2: Large Dermoid Cyst removed along with Caesarean section

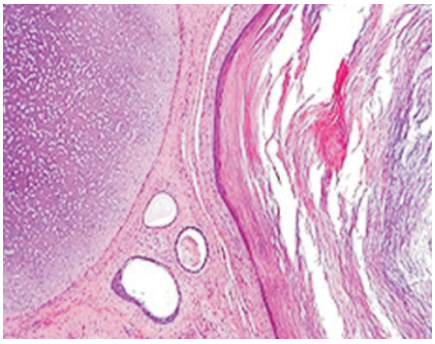

Figure 3: Microscopic photograph showing stratified squamous epithelium with keratin, hair follicle and epidermal appendages with areas of fibrosis giving diagnosis of Mature Teratoma of Ovary (Dermoid cyst).

Ultrasound with use of Color Doppler is the primary modality used to detect ovarian masses and to assess the risk of malignancy. Morphologic criteria more accurately identify benign cysts compared with malignant tumors. Grafenberg et al reported that ovarian cyst characteristics were reliably predicted by sonographic examination. Pappilary projections on the internal cyst wall are most predictive of malignancy.[7] Sassone et al reported an index that scored four different morphologic characteristics of ovarian cyst architecture, including wall structure, cyst wall thickness, septation, and echogenicity. The index is highly sensitive (100%) and moderately specific (83%) in the differentiation of benign masses from malignant masses. DePriest et al reported a morphologic index system, which scored only three structural characteristics (ovarian volume, cyst wall, and septae). [8]

Tumor markers are used primarily to monitor disease status after treatment rather than establish the ovarian tumor diagnosis as a result of lack of specificity, because several markers can be elevated inherent to the pregnancy itself (e.g., CA-125, beta-hCG). Expectant management is recommended for most pregnant patients with asymptomatic, nonsuspicious cystic ovarian masses. Surgical intervention during pregnancy is indicated for large and/or symptomatic tumors and those that appear highly suspicious for malignancy on imaging tests.[6] If the mass is thought to be benign and unlikely to cause complications, expectant management and follow-up scans are recommended.

As our patient presented in late third trimester and sonographic findings were suggestive of benign cyst and patient was asymptomatic, expectant management was done. Cystectomy during caesarean section if required is recommended. If patient delivers vaginally, surgery in immediate postpartum period is advisable.

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Bronchogenic Cyst Presenting as a Persistent Wheeze in Seven Month Old Infant: Case Report

Hetal Jeeyani,[*] Anjana Shah,[**] Pinakin Trivedi,[*] P.K. Dave[***]

Abstract :

Wheezing although a common symptom in infancy, if it is persistent, with poor response to bronchodilators, high index of suspicion should be kept for congenital anomalies involving trachea and bronchi. Bronchogenic cyst is a rare cause of persistent wheeze in infants and children. Sometimes it can even lead to life threatening apneas. Hence, its early diagnosis and surgical management are necessary. Computerized tomography has proved to be an important diagnostic modality which completely delineates the position of the bronchogenic cyst and surrounding vital structures and aids in surgical management.

Key words : bronchogenic cyst, persistent wheeze

Introduction

Wheezing is a relatively frequent and particularly troublesome manifestation of obstruction of lower respiratory tract in infants and young children. The site of obstruction can be anywhere from intrathoracic trachea to the small bronchi or large bronchioles. Isolated episodes of acute wheezing, such as may occur with bronchiolits and reactive airway disease are not uncommon but wheezing that recurs or persists for longer than four week suggests other diagnosis.[1] Here we present a case of seven month old infant who presented with persistent wheeze.

Case history

A seven – month – old male infant presented with complaints of cough, low grade fever and difficulty in breathing for four days. He had past history of hospitalization before one month when he was diagnosed as wheeze associated viral lower respiratory tract infection. However, since then mother had noticed persistent noisy breathing. The patient was a full term baby with birth weight of three and half kilogram born to non consanguineous parents without any perinatal complications. He was immunized for his age and his developmental milestones and anthropometric measurements were within normal limits.

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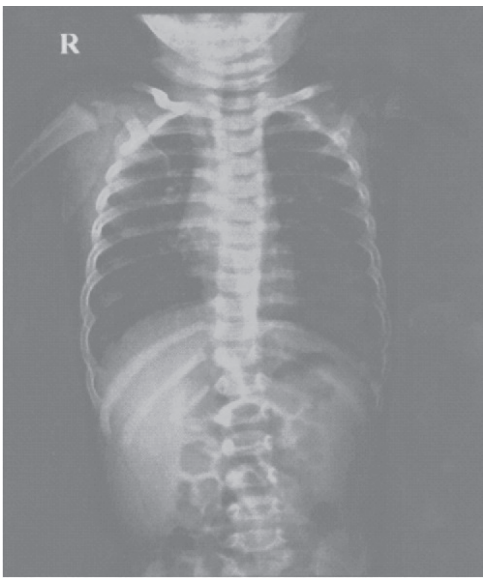

Figure 1. Chest radiograph of patient showing normal lung fields, mediastinal and cardiac shadow

On examination he was febrile – 99.4 degree F, pulse rate 140/min, respiratory rate 64/min, oxygen saturation – 92% with severe respiratory distress and audible wheeze. Routine hematological, biochemical investigations and chest radiograph were normal. He was treated with oxygen, intravenous fluids and bronchodilators, however only partial response to bronchodilators was observed. Hence considering low age of presentation, persistent wheeze and incomplete response to bronchodilators patient was submitted for contrast enhanced computerized tomographic (CECT) scan of thorax. CECT thorax showed presence of well defined cystic lesion of 27x22 mm size in subcarinal region compressing and displacing right main bronchus with possibility of bronchogenic cyst. He was

referred to pediatric surgeon for further surgical management. During surgery, 2x2 cm cyst was excised from subcarinal region and sent for histopathological examination which confirmed the diagnosis of bronchogenic cyst. Post operatively the patient was stable. On three month follow up he is completely symptom free.

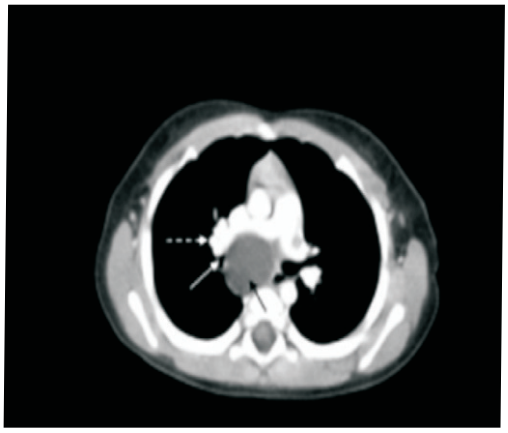

Figure 2. Computerised Tomography image of chest shows presence of well defined cystic density lesion in subcarinal region (black arrow) compressing right main pulmonary artery (dotted arrow) and right main bronchus(white arrow)

Discussion

Bronchogenic cyst is a rare clinical entity that occurs due to abnormal development of the foregut. It constitutes 20% of all cystic lung lesions. [2]

Bronchogenic cysts are most often spherical, unilocular cystic masses in contact with the tracheobronchial tree. Majority of bronchogenic cysts are thoracic in location however rarely they may be found in extrathoracic locations also. Maier divided their locations into five groups: paratracheal, carinal, hilar, paraesophageal and miscellaneous - anterior mediastinum, pericardial cavity, paravertebral sulcus and abdomen. [3]

The cysts contain a whitish-gray mucinous material. The common lining is a single layer of respiratory epithelium made up of ciliated columnar cells. A lamina propria may contain bronchial glands, connective and smooth muscle tissue and cartilage. In the presence of infection the epithelial layer may be absent or the cyst may contain frank pus. [4]

Most of the symptoms are caused by the compression of the cyst on the adjacent structures. The symptoms are frequent in the children and rare in the adults. The smaller thoracic volume and the malleable airways of the children predispose them to compressive symptoms earlier when the cyst enlarges. The majority of patients (two-thirds) manifest subacute symptoms and present early in childhood. In additon some bronchogenic cysts are detected with antenatal ultrasonography or as an incidental mediastinal mass noted on chest radiograph. Infection is the most common presentation of bronchogenic cysts. Cough, wheezing and fever are most common symptoms. The most urgent presentation involves airway obstruction due to extrinsic compression of major airway or an enlarging cyst within airway wall due to mucus production, hemorrhage or infection. [5]

In older children and adults, substernal pain is the most common symptom (27%) followed by cough (16%), dyspnoea (16%) and dysphagia (9%) caused by irritation and inflammation of surrounding pleura, bronchi or esophagus by the cyst. Expectoration of purulent sputum (5%) indicates either infection of the cyst with fistulization or pneumonia of the adjacent lung. Hemoptysis (3%) is unusual but reported. [6]

Bronchogenic cysts are seen on the chest roentgenogram as an opacified or lucent mass, cyst with an air-fluid level or they may simply be suggested by postobstructive emphysematous changes. Ultrasonography can be useful to demonstrate the cystic nature of the lesion and to define any compression on cardiac chambers and vessels. Patients with post obstructive emphysematous changes on chest radiograph may require bronchoscopy to rule out airway foreign body particularly in infancy and childhood. Esophagograpy should be done in patients who present with dysphagia. Once the compression is identified computerised tomography (CT) should be performed to identify the mass and define its anatomy. [5]

Surgical exploration is recommended for nearly all patients with an abnormal mediastinal mass found by radiographic examination as it is required not only to establish definitive histological diagnosis but also to alleviate symptoms and prevent complications like infection, hemorrhage in the cyst, fistualization and malignancy. [4]

Children who present with infection should first undergo treatment with antibiotics. However, when the postobstructive phenomenon does not permit complete resolution of infection, intervention should be done. Airway obstruction or deviation is an indication for urgent resection. Those patients with dysphagia, mass related symptoms, or incidental findings should have resection performed electively. Complete excision is the procedure of choice; however when total removal is difficult or not possible, areas where the cyst is invested in vital surrounding structures may require peeling or fulguration of the small amount of cystic epithelium left behind. Proximal endobronchial lesion that rapidly expands requires urgent rigid bronchoscopy. Small lesions in the proximal airway can be resected endoscopically and residual mucosa can be fulgurated by laser. [5]

The development of video-assisted thoracic surgery has brought new approach to the diagnosis and treatment of mediastinal cysts. The potential advantages are decreased pain, shorter hospital stay, a better cosmetic outcome and rapid return to normal activity. Drawbacks are limited exposure and less than complete excision resulting in recurrences. [4]

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Pulmonary Sporotrichosis caused by Sporothrix schenckii var. luriei in AIDS patient – A case report.

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Abstract :

Pulmonary Sporotrichosis caused by Sporothrix schenckii var. luriei is a rare clinical condition. We report such case for the first time from Gujarat. Patient was a carpenter. He was AIDS patient with low CD4 count (200 / cmm) and gain suboptimum response with antifungal. With secondary bacterial infection, further lowering of CD4 cells and poor compliance it ended with fatal out come.

Key words : *Sporothrix schenckii var. luriei, AIDS, pulmonary infection*

Sporothrix schenckii is found worldwide in both temperate and tropical zone. The fungus is found in soil, vegetable debris, moist wood and wood pulp.[1] In India, Sporothrix schenckii is endemic in North and East region.[2,3]. The disease, Sporotrichosis is a chronic mycotic infection mainly involving cutaneous, subcutaneous and lymphatic tissues.[4] Visceral Sporotrichosis occurs mostly in patients who are immuno compromised. In 1969, new variety of pathogen was designated in honor of Lurie as Sporothrix schenckii var. luriei.[5] In India, first case of pulmonary Sporotrichosis caused by Sporothrix schenckii var. luriei was described by Padhye AA and colleagues from Chandigarh in 1992.[6] Infection with Sporothrix schenckii has never been reported from Gujarat. Sporotrichosis in AIDS patient with disseminated cutaneous infection with high mortality has been reported [7]; but pulmonary Sporotrichosis in AIDS patient has never been reported as per our knowledge. Therefore, we report a unique case of pulmonary Sporotrichosis in AIDS patient from Gujarat.

Case Report

A 26 years old male carpenter and resident of Ahmedabad, which was a known case of HIV infection since 3 years presented with chronic cough, breathlessness, low grade fever and acute attack of haemoptysis. As per routine protocol, CD4 count and sputum for Acid Fast Bacilli were done. CD4 count was 200 / cmm. The X-ray finding suggested cavitory lesion in left upper lobe with mild pleural effusion. The 3 days morning sputum samples were negative for acid fast bacilli.

Another fresh sample of sputum was received for Pneumocystis carinii, pyogenic and fungus culture. On gross examination, sample was mucopurulent and tinged with blood. It was negative for Pneumocystis carinii. KOH examination revealed occasional budding yeast cells. Bacterial culture revealed growth of Pseudomonas aeruginosa. Sample was inoculated on Sabouraud's Dextrose Agar with and without Cycloheximide; two different sets were incubated at 37° C and at room temperature. Earliest growth was appeared after 3 days on Sabouraud's agar incubated at room temperature. There were yeast like colony, showing budding elongated yeast cells on Lacto phenol cotton blue mount, germ tube test negative; so, it was reported as Non albican Candida.

Initially patient was started Fluconazole as well as Ciprofloxacin for Pseudomonas and Cotrimoxazole along with Anti retroviral therapy. After further incubation, on Sabouraud's Dextrose Agar streaks appeared on the growth. The colour of colony was cream to white initially and gradually turns brown after 15 – 17 days with velvety appearance. Lacto phenol cotton blue mount prepared from this colony revealed hyalinic septate hyphae with conidial pattern mimicking Sporothrix schenckii [8]. It also revealed presence of

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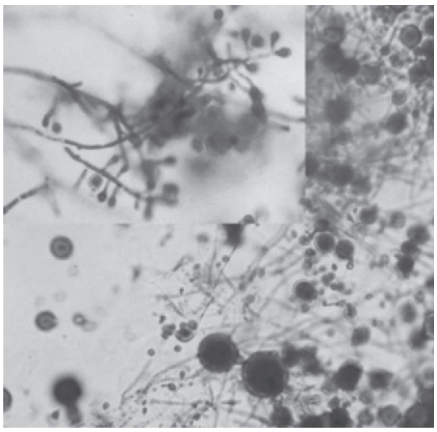
globose, sclerotic bodies resembling that of Sporothrix schenckii var. luriei. [8] Growth at 37° C was slow and scanty. The diagnosis was confirmed by 25th day of receiving of sample. Patient came after one month for follow up. There was improvement in breathlessness and X ray findings; but the cough was persistent. A follow up sample of sputum was also collected and processed which revealed no bacterial growth; but the similar growth of Sporothrix schenckii was observed. Patient was now continued Iatraconazole. After 6 month patient again examined, CD4 count was repeated which were 97 / cmm. By that time patient started continuous fever; cough was non productive. Patient's further compliance and treatment adherence was poor, after 2 months patient was admitted in emergency with critical ill condition and died of acute respiratory failure.



Discussion:

Though the sub Himalayan region is endemic for Sporotrichosis, sporadic cases have been reported from various part of India.[9] The present case of pulmonary Sporotrichosis is first ever case of Sporotrichosis been reported from Gujarat. Patient was a carpenter, likely have occupational exposure of this fungus as suggested by most of the authors[5]. Amongst the entire occupational hazardous group, carpenter has higher possibility of aerosol route of acquisition. In review of 51 case of pulmonary Sporotrichosis described by KJ Kwon-Chung and John E Bennett[8], cough and low grade fever were the predominant symptoms, 85 % presented with cavitation in upper lobe and 18 % presented with haemoptysis. The present case was presented with cavitation in upper lob, low grade fever, chronic cough and haemoptysis. In a case of pulmonary Sporotrichosis reported by Padhye AA et al, immune status of the patient was poor because of prolonged treatment with corticosteroids, this may helped the dissemination of infection and fatal outcome. In present case, the patient was HIV positive and immuno - compromised with CD4 count 200 cmm, this might be responsible for invasive infection and suboptimum response with antifungal. Over all, in a present case of Pulmonary Sporotrichosis with Immuno - compromised status due to AIDS and low CD4 count (97 / cmm) as well as secondary bacterial infection and poor patient compliance lead fatal outcome of the patient.

The present case is noteworthy because it is a first case of Sporotrichosis from Gujarat; there was pulmonary infection which is a rare clinical presentation of Sporotrichosis; Explain occupational correlation of pulmonary Sporotrichosis; Explain Correlation of invasive and fatal infection of Sporothrix Schenckii var. luriei with AIDS and Immuno compromised status of the patient.

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Guidelines for preparation of Manuscript

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1. Journals

   a. Shukla N, Husain N, Agarwal GG and Husain M. Utility of cysticercus fasciolaris antigen in Dot ELISA for the diagnosis of neurocysticercosis. Indian J Med Sci 2008;62:222-7.

2. Books and Other Monographs

   a) Personal author(s): Ringsven M and Bond D. Gerontology and leadership skills for nurses. 2nd ed. Albany (NY): Delmar Publishers; 1996.pp 616

   b) Editor(s), compiler(s) as author: Norman IJ, Redfern SJ, editors. Mental health care for elderly people. New York: Churchill Livingstone; 1996.pp 617.

   c) Chapter in a book: Phillips SJ and Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: pathophysiology, diagnosis, and management. 2nd ed. New York: Raven Press; 1995. pp. 465-78.

3. Electronic Sources as reference

   a. Journal article on the Internet

      Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [serial on the Internet]. 2002 Jun [cited 2002 Aug 1 2];1 02(6):[about 3 p.]. Available from:

      http://www.nursingworld.org/AJN/2002/june/Wawatch.htm

   b. Monograph on the Internet

      Foley KM and Gelband H, editors. Improving palliative care for cancer [monograph on the Internet]. Washington: National Academy Press; 2001 [cited 2002 Jul 9]. Available from: http://www.nap.edu/books/0309074029/html/

   c. Homepage/Web site

      Cancer-Pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources, Inc.; c2000- 01 [updated 2002 May 16; cited 2002 Jul 9]. Available from: http://www.cancer-pain.org/.

   d. Part of a homepage/Web site

      American Medical Association [homepage on the Internet]. Chicago: The Association; c1995-2002 [updated 2001 Aug 23; cited 2002 Aug 12]. AMA Office of Group Practice Liaison; [about 2 screens]. Available from: http://www.amaassn.org/ama/pub/category/1736.html

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- Department of Anaesthesia
- Department of Orthopedics
- Obstetrics & Gynecology
- Department of Dermatology & Skin
- Department of Dentistry
- Department of Ophthalmology
- Department of Psychiatry
- Department of TB & Respiratory Diseases

Department of Medicine

- Physical Checkups
- ECG
- Counseling Session

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- Checkups
- Dressing Facility
- Counseling Session
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- Laparoscopy
- Tubectomy Ligature (T.L.)

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- Root canal treatment
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- Crowns and Bridges
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- Treatment for all kind of Allergies and Pimples and other skin related problems

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- Minor procedures
- Cataract Operations

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- Counseling session

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परस्परं भावयन्तः श्रेयः परमवाप्स्थ ॥ ३ : ११ ॥

श्रीमद्भगवद्गीता

પરસ્પર ભાવપૂર્ણ કાર્યો કરતાં રહીને પરમ કલ્યાણ પ્રાપ્ત કરશો.

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Donation Given to Gujarat Cancer Society exempted up to 175% by I.T. Dept.