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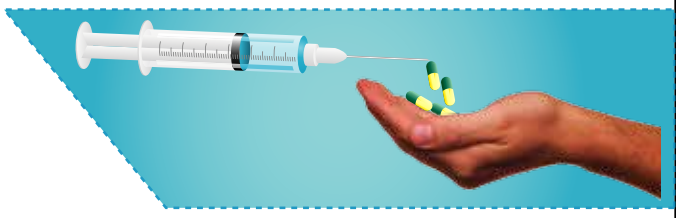
To reduce the chances of such complications, Cefixime is the ideal option for

Switch therapy



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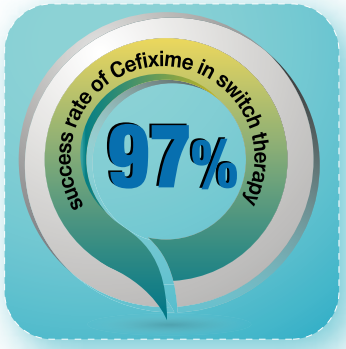

Diseases : Pneumonia
Trial Type : Controlled randomized study
Drugs Used : Parenteral Ceftriaxone 50 mg/kg/day for 2 days followed by 8 days of oral therapy with Cefixime 8 mg/kg/day.

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Fig.: Impurities level in Cefixime API*

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Ref.: 1. Dont-Clown-Around-Education-Package_Peninsula-Health
2. Jacob Amir,M.D.,1, 1996 Research Article
3. Data on file

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The ORION Medical Journal

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The Orion Medical Journal is rejoicing nineteen years of trust and service to the medical community. The Orion Medical Journal achieves the choice of thousand readers nationally and in the international arena. This medical journal contains information from reputable sources and although reasonable efforts have been made to publish accurate information. Any information or guidance contained in this book is intended for use solely by medical professionals strictly as a supplement to the medical professional's own judgement, knowledge of the patient's medical history, relevant manufacturer's instructions and the appropriate best guidelines.

Editorial article (P-02) of this issue "Pan Airways Disease". This study overview according those diseases that affect one part of the airways disease hypothesis, in fact, maintains that upper and lower airways disease are both manifestations of a single inflammatory process within the respiratory tract, and a unified diagnostic approach to upper and lower airways disease as well as will constitute a basis for a common therapeutic management.

The first original article (P-06) "Clinical presentation of patients with cirrhosis of liver in a tertiary care hospital " .This study to see the clinical profiles of patient with cirrhosis of liver attending a tertiary care hospital.

Second original article (P-11) "Maternal morbidity and mortality in placenta previa & abruptio placenta". The objective of this study to find out the relative frequency of placenta previa and abruptio placenta in hospital delivery. And to find out the morbidity and mortality related to placental cause of APH.

Review article (P-16) "Recurrence is a problem for the treatment of Rhinosporidiosis." This study concluded with the decision is that modern treatment options are not enough to prevent the recurrence of Rhinosporidiosis.

Observational Study (P-30) "Common Problem Faced By Orthopaedic and Trauma Surgeons An Observation At District Level Hospital, narsingdi For Last Eighteen Years."

Thanks all of readers, contributors & reviewers for their continued support.

"A kind word is a form of charity." Prophet Muhammad (peace be upon him).

Good health and good sense are two of life's greatest blessings. May the Almighty bless you with good health, give you a healthy life.

DR. SINTHIA ALAM
Chief Editor
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Pan Airways Disease

ABSTRACT

Any disease process that affects the upper airway is likely to affect the lower airway, and vice versa, by both direct and indirect means. Hence, rhinitis and asthma represent the manifestations of one syndrome in two parts of the respiratory tract. At the lower end of the severity spectrum, rhinitis may occur alone; in the middle range, rhinitis and Airway Hyper Responsiveness (AHR) may be present; at the top end of the spectrum, rhinitis and asthma may both be present, with the severity of each condition tracking in parallel. Disease manifestations in the upper and lower airways may be linked via a systemic inflammatory response. Several mechanisms have been proposed to explain the interaction between the upper and lower airways: The most likely is that localized airway inflammation leads to a systemic response, with bone marrow involvement resulting in the release of progenitor cells that are then recruited to tissue sites. Several observations support the concept of Pan Airways Disease(PAD) existing outside a purely allergic context. Infective inflammation occurring in both the upper and lower airways is often attributed to a direct viral effect at both sites, but the two may also be linked by indirect means. The pan airways disease hypothesis, in fact, maintains that upper and lower airways disease are both manifestations of a single inflammatory process within the respiratory tract, and a unified diagnostic approach to upper and lower airways disease as well as will constitute a basis for a common therapeutic management.

Keywords: Asthma, Rhinitis, Rhino sinusitis, Sinusitis, Chronic Obstructive Pulmonary Disease, Pan Airways Disease, Airway Hyper Responsivness, Interleukin-6, Intranasal Interleukin-8, C-reactive protein & Lower Airway Eosinophilia.

INTRODUCTION

Diseases that affect one part of the airway often impact other parts. Upper and lower airway diseases are both manifestations of a single inflammatory process within the respiratory tract, there is growing evidence of a systemic link between the upper and lower airways.[1]

Any disease process that affects the upper airway is likely to affect the lower airway and vice versa, by both direct and indirect means. Hence, rhinitis and asthma represent the manifestations of one syndrome in two parts of the respiratory tract. At the lower end of the severity spectrum, rhinitis may occur alone; in the middle range, rhinitis and Airway Hyper Responsiveness (AHR) may be present; at the top end of the spectrum, rhinitis and asthma may both be present, with the severity of each condition tracking in parallel.[2,3]

Disease manifestations in the upper and lower airways may be linked via a systemic inflammatory response. Several mechanisms have been proposed to explain the interaction between the upper and lower airways: The most likely is that localized airway inflammation leads to a systemic response, with bone marrow involvement resulting in the release of progenitor cells that are then recruited to tissue sites.4,5 Several observations support the concept of Pan Airways Disease(PAD) existing outside a purely allergic context. For example, infective inflammation occurring in both the upper and lower airways is often attributed to a direct viral effect at both sites, but the two may also be linked by indirect means.[1]

The presence of AHR without symptoms of asthma has been well documented in population studies, although the relationship between AHR and inflammation is complex, with many studies not supporting a clear link between the two.

As airway inflammation is central to the concept of PAD, it is possible that the upper airway may not be involved in isolated, non asthmatic AHR. Eosinophilic bronchitis, a newly identified condition of the lower airway associated with persistent cough, is an example of lower airway inflammation without AHR, but as yet upper airway disease has not been investigated in association with this condition.[6]

It is well documented that allergic rhinitis is associated with increased AHR, even if asthma is not present. People suffering from allergic rhinitis have AHR present both outside the pollen season (11% to 73%) and during the pollen season (50%).1 Clinical studies indicate that 80% to 100% of patients with asthma have rhinitis and 50% of patients with rhinitis have asthma and that both the presence and severity of rhinitis are associated with poor asthma outcomes.[1]

DISCUSSION

An association between asthma and sinusitis has long been recognized. In a recent study, 100% of subjects with severe asthma (requiring steroid treatment) had abnormal sinus at computed tomography scans versus 77% of subjects with mild to moderate asthma.8 However, perhaps the most direct

evidence of the relationship between rhinitis, sinusitis, and asthma comes from studies that show significant improvement in asthma symptoms when sinusitis is appropriately treated.[9]

Under the umbrella term of PAD, two coexistent relationships between the upper (nasal) airway and lower airway have been proposed: a horizontal relationship and a vertical one. The concept of a horizontal relationship is based on evidence of a wide spectrum of disease severity in PAD, with disease manifesting in different parts of the respiratory tract according to the severity, eg. at low severity only in the nasal area versus at high severity in both upper and lower airways with asthma & rhinitis combined.

The concept of a vertical relationship implies that events taking place in the upper airway may negatively affect what happens in the lower airway. For instance, the nose may act as an air conditioner to warm and humidify the air before it reaches the lower airway, but, if the nose is congested, that process is impeded. We also know that patients with asthma who get a sinus infection may often begin to wheeze. This delicate and complex interrelationship between the upper and lower airways, which most likely is at least partially mediated by the autonomic nervous system, is not yet well understood.

Supporting the notion of both a horizontal and vertical relationship between the upper and lower airways is the fact that the vast majority (>80%) of patients with asthma also have concomitant rhinitis or rhinosinusitis. Patients with asthma have more severe rhinitis or rhinosinusitis than patients without asthma. Often in a given patient, several measurable outcomes of rhinitis and asthma show a close correlation. Patients with rhinitis are at higher risk of developing asthma. Patients who have allergen introduced into the nasal airway may show both functional and inflammatory changes in the lower airway. Studies also demonstrated also that treatment of nasal symptoms results in beneficial effects for the lower airway.

Several factors may account for this interrelationship: for example, when the nose is congested, patients often breathe through the mouth. When this occurs, the warming, filtering & humidification of inspired air does not take place as it does when they breathe through the nose. With mouth breathing, the air may also have a higher concentration of inspired particulates & gaseous irritants. Second, patients with rhinitis who have increased responsiveness to irritants, presumably occurring via sensory nerves in the nasal membranes, may manifest broncho constriction via parasympathetic nerve pathways.10 Sensori neural stimulation of the nasal airway may also stimulate increased bronchial responsiveness via the central nervous system to receptors actually present in the lower airway. This phenomenon is called the bronchial reflex. This falls under the concept of central sensitization, first noted by researchers studying pain medicine.[10]

Upper airway inflammation may also propagate systemically & affect the lower airway. Experimentally, there is evidence for this concept. For example, intranasal allergen challenge has been found to result in increased expression of adhesion molecules in the pulmonary vasculature & Lower Airway Eosinophilia (LAE).

From a treatment point of view, two main aspects should be emphasized:

• the unity of the respiratory airways and the influence exerted by the nose on the bronchi;

• the fact that both symptoms and allergic inflammation should be targets for treatment.

Indeed, there is evidence suggesting that optimal control of rhinitis has a beneficial effect on asthma in terms of reduction of bronchial responsiveness during natural exposure to the offending allergens. Thus, one of the new clues to the treatment of PAD is the evidence of a synergistic effect of drugs used in both rhinitis and asthma. This aspect is relevant, since it would allow treatment to be harmonized, possibly reducing the dosage of each drug. Ultimately, this may result in better control of the disease(s) and fewer side effects.[11] The existence of persistent airway inflammation suggests the need for continuous rather than on-demand treatment. Studies have demonstrated a decrease in exacerbation rate in asthmatic patients treated to control airway hyperresponsiveness or eosinophilia compared with those treated to control clinical parameters only.12,13 There is also evidence that airway hyperresponsiveness continues to improve in response to long-term anti-inflammatory therapy, emphasizing the importance of continuing regular controller treatment even when clinical endpoints have been normalized.

Another lower airway inflammatory disease, chronic obstructive pulmonary disease (COPD), may also be an example of PAD. COPD is associated with elevated levels of intranasal interleukin (IL-8), which correlate with sputum levels, indicating concomitant upper and lower airway inflammation.14 In COPD exacerbation, there is, pan-airway response, evidence of a systemic response as determined by elevated serum levels of IL-6 and C-reactive protein. With a predominantly infective stimulus, however, it is more difficult to separate site-specific effects of the provoking agent from underlying systemic processes.[15]

Our traditional understanding of COPD has focused on the presence of chronic airflow obstruction and, accordingly, therapy has been mainly directed to relieve this. More recently, it has been demonstrated that airflow limitation is associated with an abnormal inflammatory response and that the latter appears to be responsible for specific effects on mucociliary function, structural changes in the airways and lung parenchyma, and extrapulmonary effects (the systemic effects of COPD,

including impairments of metabolism and inflammation, that lead to comorbid conditions).[16,17] Optimal therapeutic target of COPD depends on a clear understanding of the precise mechanisms of these complex processes and correct evaluation of disease severity.

At present, a combination of pharmacological and nonpharmacological approaches seems to be the most effective strategy for confronting this multicomponent disease. As regards pharmacotherapy, bronchodilators and inhaled corticosteroids have shown complementary mechanisms of action, targeting different arms of the vicious cycle of COPD: A combination of the two types of drugs has the potential to address several major components of the disease, including airflow limitation, mucociliary dysfunction, and airway inflammation.[22] This translates into improvement of several clinical outcomes, such as dyspnea, exacerbations, and quality of life. Furthermore, since COPD is a progressive disease, with lung function worsening over time, a major target of the therapy is to modify its clinical course, in other words, slow down the evolution of lung damage to respiratory failure and improve survival. Recent evidence suggests that appropriate pharmacological therapy can reduce the long-term decline of FEV1 in patients with moderate-to-severe COPD, thus slowing disease progression, and this has a favorable trend on survival.[19, 20]

CONCLUSION

Diseases that affect one part of the airway often impact other parts. The pan airways disease hypothesis,in fact, maintains that upper and lower airways disease are both manifestations of a single inflammatory process within the respiratory tract, and a unified diagnostic approach to upper and lower airways disease as well as will constitute a basis for a common therapeutic management.

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Clinical presentation of patients with cirrhosis of liver in a tertiary care hospital

Kabir MA [1], Biswas PS [2], Ahmed N [3], Dutta BR [4], Yasmin D [5]

ABSTRACT

Background: Liver cirrhosis is an important health problem worldwide and is a common disease in our country. The aim of the study to see the clinical profiles of patients with cirrhosis of liver attending a tertiary care hospital. **Methodology:** This observational, descriptive, cross-sectional, prospective hospital based study was carried out in the Department of Medicine, Gazi Medical College Hospital (GMC), Khulna. All cases attending the Department of Medical Gastroenterology as outdoor and/or admitted in ward with clinical features, laboratory and sonological findings suggestive of chronic liver dysfunction along with sonological and/ or endoscopic evidence of portal hypertension were included in the study. **Results:** Majority 109(83.8%) patients had abdominal distension, 107(82.3%) had jaundice, 106(81.5%) had ascites, 90(69.2%) had loss of body hair, 77(59.2%) had spider naevi, 47(36.2%) had melena, 45(34.6%) had palmar erythema, 43(33.1%) had fever. Sixty three (48.5%) patients had Child Pugh C, 50(38.4%) had Child Pugh B and 17(13.1%) had Child Pugh A. Eighty one (62.3%) patients had MED score 10-19, 35(26.9%) had MED score 20-29 and 14(10.8%) had MED score ≥30. The mean MED score was found 19.51±6.73. **Conclusion:** More common clinical presentation of liver cirrhosis were abdominal distension, jaundice, ascites, loss of body hair, spider naevi, melena, palmar erythema and fever. Child Pugh C and B were most common.

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INTRODUCTION

Liver cirrhosis is an important health problem worldwide and is a common disease in Asian country.1 Epidemiology of liver cirrhosis suggests that although Hepatitis B and C are still common in developing countries, alcohol related cirrhosis is increasing.2 Cirrhosis of liver refers to a progressive, diffuse, fibrosing, nodular condition that disrupts the entire normal architecture of the liver. The majority of cases are attributed to excessive alcohol consumption, viral hepatitis, or nonalcoholic fatty liver disease worldwide.3 A large proportion of cirrhosis patients only come into clinical attention until complica¬tions arise and previously undiagnosed cir¬rhosis is still frequently found at autopsy.It can be primarily divided into two; com¬pensated cirrhosis and decompensated cirrhosis. Initial clinical presentation of patients with decompensated cirrhosis is still common and is characterized by the presence of dramatic and life-threatening complications, such as haemorrhage, asci¬tes, spontaneous bacterial peritonitis, or hepatic encephalopathy.[4]

MATERIALS AND METHODS

This observational, descriptive, cross-sectional, prospective hospital based study was carried out in the Department of Medicine, Gazi Medical College Hospital (GMC), Khulna, Bangladesh from January 2015 to December 2017. Informed consent was taken from patients or/ and patient relatives. All cases attending the Department of Medical Gastroenterology as outdoor and/or admitted in ward with clinical features, laboratory and sonological findings suggestive of chronic liver dysfunction along with sonological and/ or endoscopic evidence of portal hypertension were included in the study. On the other hand, those with cirrhosis with hepatic encephalopathy III / IV, critically ill patients and those who fail to give consent were excluded from the study. Detailed history with data regarding demographic variables, clinical features, symptomatology, modes of presentation, complications, etc. were collected and alongside blood investigations like complete blood count, platelets count, blood grouping, liver function test , prothrombin time / international normalized ratio(PT / INR), coagulation profile and viral serologies were collected.

Abdominal ultrasound was done for liver and spleen size, parenchymal echogenicity, portal vein diameter, and ascites after an overnight fasting. Each patient underwent UGI endoscopy usually within 24 hours of presentation by standard flexible gastro-duodenal endoscope and diagnostic findings were documented. Patients with acute variceal hemorrhage were treated with injection terlipressin or vasopressin and variceal band ligation. Clinical outcomes during hospitalization including rebleeding and mortality were assessed. Data were collected on a structured proforma. All categorical data were expressed in percentage and absolute number. All numerical continuous data were expressed in mean ±SD. The data analysis was done using SPSS version 23. All tests were analyzed with a 95% confidence interval and a P value of <0.05 was considered significant.

RESULTS

Out of 130 patients majority 45(34.6%) patients belonged to age 41-50 years. The mean age was found 47.5±13.7 years. Males were predominant 116(89.2%). Male: female ratio was 8.3:1. Majority patients came from urban area (59.2%). Seventeen (13.1%) patients had family history of cirrhosis (Table I). Majority 109(83.8%) patients had abdominal distension, 107(82.3%) had jaundice, 106(81.5%) had ascites, 90(69.2%) had loss of body hair, 77(59.2%) had spider naevi, 47(36.2%) had melena, 45(34.6%) had palmar erythema, 43(33.1%) had fever. Other results are depicted in the table (Table II). Table III shows 63(48.5%) patients had Child Pugh C, 50(38.4%) had Child Pugh B and 17(13.1%) had Child Pugh A. Eighty one (62.3%) patients had MED score 10-19, 35(26.9%) had MED score 20-29 and 14(10.8%) had MED score ≥30. The mean MED score was found 19.51±6.73 (Table IV). The biochemistry findings were depicted in the table V.

Table I: Sociodemographic characteristics of the patients (n=130)

Sociodemographic characteristics	Frequency	Percentage
Age (years)		
≤20	7	5.4
21-30	17	13.1
31-40	22	16.9
41-50	45	34.6
>50	39	30.0
Mean±SD	47.5±13.7	
Sex		
Male	116	89.2
Female	14	10.8
Residence		
Urban	77	59.2
Rural	53	40.8
Family history of cirrhosis	17	13.1

Table II: Clinical features in the cirrhosis patients (n=130)

Clinical features	Frequency	Percentage
Abdominal distension	109	83.8
Jaundice	107	82.3
Fever	43	33.1
Hematemessis	38	29.2
Melena	47	36.2
Ascites	106	81.5
Loss of body hair	90	69.2
Spider naevi	77	59.2
Palmar erythema	45	34.6
Clubbing	21	16.2
Parotid swelling	31	23.8

Table III: Frequency of Category of Cirrhosis as Per Child Pugh Class (n=130)

Child Pugh Class	Frequency	Percentage
Child A	17	13.1
Child B	50	38.4
Child C	63	48.5

Table IV: Frequency of Category of Cirrhosis as MED score (n=130)

MED score	Frequency	Percentage
10-19	81	62.3
20-29	35	26.9
≥30	14	10.8
Mean±SD	19.51±6.73	

Table V: Biochemistry findings in Cirrhosis patients (n=130)

Biochemistry findings	Mean	±SD
Hb (mg/dl)	9.21	±2.71
TLC (mm3)	14548.57	±8521.12
Neutrophils (mm3)	75.08	±11.31
Lymphocytes (mm3)	24.3	±12.22
Lymphocytes (mm3)	24.3	±12.22
Platelet count	170461.51	±144261.43
Creatnine(mg/dL)	1.152	±0.821
Sodium (mmol/l)	130.4	±7.53
Potassium (mmol/l)	3.972	±0.897
RBS (mg/dl)	105.6	±43.3
PT (sec)	18.92	±9.61
T.Bilirubin (mg/dl)	7.05	±6.58
C.bilirubin (mg/dl)	4.52	±3.53
T.protein (mg/dl)	5.99	±1.37
Albumin (U/L)	2.37	±0.51
AST (U/L)	125.7	±99.3
ALT(U/L)	63.45	±97.59
GGT (U/L)	154.72	±253
Alkaline phosphtase	335.1	±211.5
Ascitic Fluid analysis		
TLC (mm3)	9178.19	±2610.53
Neutrophils (mm3)	7001.62	±2321.12
Lymphocytes (mm3)	219.51	±411.9
Protein (mg/dl)	1.501	±2.68
Sugar (mg/dl)	125.23	±66.3

DISCUSSION

In present study showed that majority 45(34.6%) patients belonged to age 41-50 years. The mean age was found 47.5±13.7 years. Males were predominant 116(89.2%). Male: female ratio was 8.3:1. Majority patients came from urban area (59.2%). Seventeen (13.1%) patients had family history of cirrhosis. In the Vijayan et al.5 study, the majority of the patients (34%) belonged to the age group of 51–60 years, followed by the age group of 41–50 years (26%). Only 2.67% of the patients were in the age groups of 21-30 years and 2% for 71–80 years. None of the patients were above 80 years and below 20 years. The young¬est patient was 23 years old and oldest 74 years and the male to female ratio were 20:1. It also showed that (57.33%) of the patients were from urban area and the remaining (42.67%) from rural area. Only 14.67% of the patients had a family history of cirrhosis and in majority of patients there was no history of cir¬rhosis in the family. In a retrospective study, the risk for bacterial endocarditis in cirrhotic patients: a population based 3 year follow up study by Tsung-Hsing et al.6 showed 71.1% males and 28.9 females. It also showed that most patients are in the age group between 60–74years (34.7%). In the retrospective study conducted by Rongey et al.7 30% patients live in rural or highly rural areas. The change in lifestyle and stress factor is the most reliable reason for the result. Positive family history was noted in few patients. In study of Bhattacharyya et al.2 also found similar observation they reported out of one thousand cirrhosis patients, 883 (88.3%) were males and 117 (11.7%) females with M: F ratio of 7.54:1. Majority (63.6%) belonged to 35-54 years age group. Mean age at presentation was 45.8+ 10.45 years (M: 46.63years and F: 47 years). 13.4% were < 35 years of age. Majority (70.1%) were from rural background versus 29.9% urban. Maskey et al.8 observed that one hundred and five (72 males; 33 females) consecutive patients who met the inclusion criteria were studied. The mean age of the patients was 49.06 ±11.27 years (range 23-73 years). Ninety patients were adult cirrhotics (age ≥35 yrs) and the remaining 15 patients were young (age ≤35 yrs). Ninety out of 105 patients were having alcohol related cirrhosis. In this study majority 109(83.8%) patients had abdominal distension, 107(82.3%) had jaundice, 106(81.5%) had ascites, 90(69.2%) had loss of body hair, 77(59.2%) had spider naevi, 47(36.2%) had melena, 45(34.6%) had palmar erythema, 43(33.1%) had fever.

In this study majority 109(83.8%) patients had abdominal distension, 107(82.3%) had jaundice, 106(81.5%) had ascites, 90(69.2%) had loss of body hair, 77(59.2%) had spider naevi, 47(36.2%) had melena, 45(34.6%) had palmar erythema, 43(33.1%) had fever. Similar observation was found in different studies. In study of Bhattacharyya et al.2 observed that common symptoms at presentation were leg swelling (80.5%), abdominal swelling (74.3%), Gastro intestinal bleed (43.4%), jaundice (36.3%), low urine output (31%) and altered sensorium (23%). Other non specific manifestations were fatigability (49.1%), anorexia (40%), fever (14%), vomiting (13.4%) and pain abdomen in 22.7% patients. Maskey et al.8 the commonest presenting symptoms were abdomen distension (100% in

young cirrhotics vs. 84.4% in adult cirrhotics) and jaundice (93.3% in young cirrhotics vs. 84.4% in adult cirrhotics. Vijayan et al.5 study reported that majority (29.67%) of the only 6.67% of the patients had abdominal pain alone as symptom. Abdominal pain was the most seen symptom in cirrhosis.

In this study 63(48.5%) patients had Child Pugh C, 50(38.4%) had Child Pugh B and 17(13.1%) had Child Pugh A. Vijayan et al.5 study revealed 50% of population were in category C followed by 35% in B and 11% in A. In the pro¬spective study, Factors Associated With Poor Health- Related Quality of Life of Patients With Cirrhosis by Marchesini et al.9 showed 38% patients each in both Pugh class A and Pugh class B; 24% in Pugh class C; whereas our study showed most of the patients belonged to the Child Pugh Class C category. Bhattacharyya et al.2 showed similar findings they showed approximately 50% had Child C disease, 40.4% Child B cirrhosis and Child A was seen in only 9.8% patients. In a study by Aziz et al.10 Child A was seen in 39.5%, Child B in 35.3% patients, and Child C in 25.1% patients. Khan et al.11 too showed that majority were Child A category (83.3%).

In present study 81(62.3%) patients had MED score 10-19, 35(26.9%) had MED score 20-29 and 14(10.8%) had MED score ≥30. The mean MED score was found 19.51±6.73. Bhattacharyya et al.2 study observed that the mean MELD score was 17.80+ 7.51. 60% patients had MELD scores between 10-19, 23.1% had MELD between 20-29 and MELD of >30 was seen in 8.8% indicating advanced disease.

CONCLUSION

Majority of subjects were male, middle aged. More common clinical presentation of liver cirrhosis were abdominal distension, jaundice, ascites, loss of body hair, spider naevi, melena, palmar erythema and fever. Child Pugh C and B were most common. Early detection of alcoholic liver diseases and viral hepatitis has survival benefits and their management may reduce the burden of cirrhosis.

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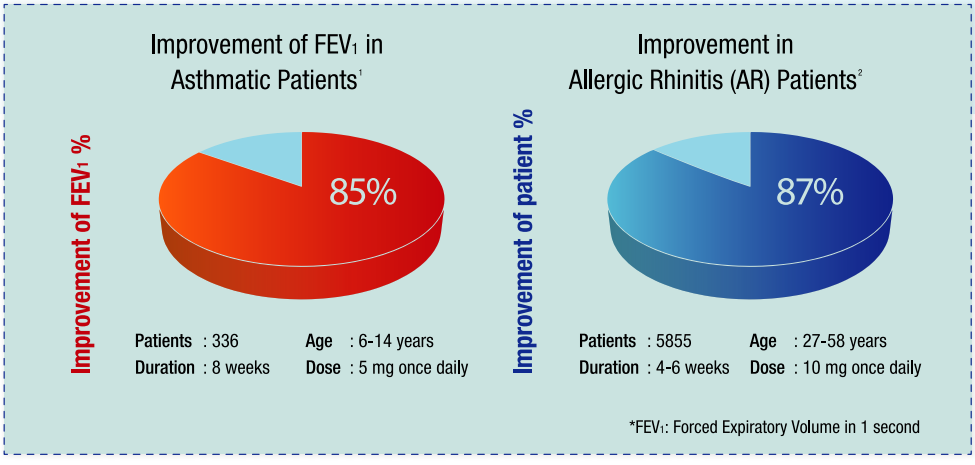

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Maternal morbidity and mortality in placenta previa & abruptio placenta

Nasrin R [1] , Runa S [2], Afroz D [3] , Khan S [4]

ABSTRACT

Background: Antepartum haemorrhage (APH), mostly placenta previa and abruption placenta comprises about 70% of it. APH is the most important cause of maternal morbidity and mortality. **Objectives:** a)To find out the relative frequency of placenta previa and abruptio placenta in hospital delivery. b)To find out the morbidity and mortality related to placental cause of APH. **Materials and Methods:** It was a descriptive cross sectional study carried out in the department of Obstetrics & Gynecology, Jahurul Islam Medical College and Hospital, Kishoregonj from November 2013 to May 2014. Total 72 patients of placental cause of APH (placenta previa & abruption placenta) were included in this study. Data were collected in a pre-designed data collection sheet. **Results:** The commonest age group of placenta previa and abruption placenta was 26-30 years. Most of the placental causes of APH occurred in multi gravid women. Both in abruptio placenta & placenta previa, more than fifty percent patient received irregular antenatal checkup. Only 9.7% patient received regular antenatal checkup. Moderate anemia was present in more than sixty three percent patient. Severe anemia was more prominent in patient's with abruptio placenta than placenta previa. More than fifty eight percent patient came with labour pain & majority (48.61%) of them was with active hemorrhage without shock on admission. Maternal mortality was found in 2(7.8%) cases in abruption placenta. Almost ninety percent patient needed blood transfusion due to anemia. 2nd most frequent post-partum complication was PPH (12.5%). **Conclusion:** In our country couples get more children due to lack of proper education and low socio economic condition, which increases the chance of developing both placenta previa and abruption placenta. Hemorrhage in pregnancy is still the leading cause of maternal mortality.

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INTRODUCTION

Antepartum hemorrhage (APH) is defined as bleeding from or into the genital tract after the period of viability until delivery of fetus. Etiology includes placenta previa, abruptio placentae, local causes, systemic causes and idiopathic origin.1 Antepartum hemorrhage (APH) is an important cause of perinatal mortality and maternal morbidity in pregnant women with placenta previa in the world. However, the epidemiological characteristics are not completely understood.2 On an average (2 – 5)% of all pregnancies are complicated by antepartum haemorrhage.3,4 The main causes of APH are placenta previa, abruption placentae, unexplained cause and local causes of genital tract. In developed countries, maternal mortality due to antepartum haemorrhage has been reduced significantly due to better obstetrical facility and care. But in developing countries like India maternal and perinatal mortality is still very high due to associated problems like anemia, difficulties in transport in cases of emergency and restricted medical facilities.5 The complications in pregnancy with APH are malpresentation, premature labour, postpartum haemorrhage, shock, retained placenta, higher rates of caesarean sections, peripartum hysterectomy, coagulation failure and maternal death. Perinatal complications include premature delivery, low birth weight, intrauterine death, congenital malformations and birth asphyxia.6,7 The present study is to understand the etiology of APH and to formulate the preventive guidelines, to improve the obstetric outcome.

METHODOLOGY

The cross sectional study was carried out Department of Obstetrics and Gynecology of Jahurul Islam Medical College Hospital. Women attending in the Department of Obstetrics and Gynecology, JIMCH, having history of Antepartum hemorrhage both due to placenta previa and abruption placenta were included. Antepartum hemorrhage due to extra placental cause, with H/O any medical or surgical disorder that may affect the maternal and perinatal outcome were excluded in this study. All patients who had fulfilled the inclusion criteria were selected as cases for this study. All data were collected using predesigned data collection sheet. A detailed patient history was taken, who has been identified as having APH due to

placenta previa and abruptio placenta. After a thorough examination, appropriate investigations were conducted. The required conservative management or surgical procedure to rectify any complications were carried out in the department of Obstetrics and Gynecology, Jahurul Islam Medical College Hospital was also noted. Details of the complications and treatment outcome were recorded. After collection of data they were analyzed by computer based program Statistical Package for Social Science (SPSS) version 23 after meticulous checking and rechecking. Data were presented in the form of tables and graphs.

RESULTS

Maternal age ranged from <20 to >35 years in this study.The commonest age group of placenta previa and abruption placenta was 26-30 years (Table I). In this study more than two third patient were multipara. Twenty two percent patient were primi gravid. Most of the placental causes of APH occurred in multi gravid women (Table II). Both in abruptio placenta & placenta previa, more than fifty percent patient received irregular antenatal checkup. Only 9.7% patient received regular antenatal checkup (Table III). Moderate anemia was present in more than sixty three percent patient. Severe anemia was more prominent in patient's with abruptio placenta than placenta previa (Table IV). More than fifty eight percent patient came with labour pain & majority (48.61%) of them were with active hemorrhage without shock on admission (Table V). More than twenty three percent patient delivered per vaginally, who had minor degree of placenta previa and abruptio placenta with IUD (Table VI). Maternal mortality was found in 2(7.8%) cases in abruption placenta (Table VII). Almost ninety percent patient needed blood transfusion due to anemia. 2nd most frequent post-partum complication was PPH (12.5%). (Table VIII).

Table I: Distribution of the study patients by age (n=72)

Age in years	Placenta previa		Abruptio placenta		Total
	n	%	N	%	
<20	1	1.4	0	0.0	**1(1.4%)**
21-25	10	13.89	2	2.78	**12 (16.6%)**
26-30	21	29.16	4	5.56	**25(34.0%)**
31-35	9	12.50	3	4.17	**12(16.70%)**
>35	19	26.39	3	4.17	**22(30.60%)**
Total	**60**	**83.34**	**12**	**16.67**	**72 (100%)**

Table II: Distribution of the study patients by gravidity (n=72)

Gravidity	Placenta previa		Abruptio placenta		Total
	n	%	n	%	
Primi Gravida	12	16.67	04	5.6	16 (22.3%)
Multi Gravida	48	66.67	08	11.11	56 (77.7%)
Total	**60**	**83.34**	**12**	**16.67**	**72 (100)**

Table III: Distribution of the study patients by antenatal care (n=72)

Antenatal care	Placenta previa		Abruptio placenta		Total (%)
	n	%	n	%	
Regular	5	6.94	2	2.78	7 (9.70%)
Irregular	30	41.67	7	9.72	37 (51.4%)
None	23	34.72	3	4.17	28 (38.9%)
Total	**60**	**83.3**	**12**	**16.67**	72 (100%)

Table IV: Distribution of the study patients by severity of anemia (n=72)

Severity of anemia	Placenta previa		Abruptio placenta		Total (%)
	n	%	n	%	
Mild	2	2.78	1	1.39	**3 (4.2%)**
Moderate	40	55.56	6	8.33	**46(63.9%)**
Severe	18	25.0	5	6.94	**23(31.9%)**
Total	**60**	**83.3**	**12**	**16.67**	**72 (100%)**

Table V: Distribution of the study patients by clinical presentation (n=72)

Clinical presentation	Placenta previa		Abruptio placenta		Total (%)
	N	%	n	%	
Without labour (n=30)					
Hemorrhage with shock	5	6.94	2	2.78	**7(9.72%)**
Hemorrhage without shock	20	27.8	3	4.17	**23(31.9%)**
In Labour (n=42)					
Hemorrhage with shock	2	2.78	1	1.39	**3(4.17%)**
Hemorrhage without shock	30	41.7	5	6.94	**35(48.6%)**
No Active Hemorrhage	3	4.17	1	1.39	**4(5.56%)**
Total	**60**	**83.3**	**12**	**16.66**	**72(100%)**

Table VI: Distribution of the study patients by mode of delivery (n=72)

Mode of delivery	Placenta previa		Abruptio placenta		Total (%)
	N	%	n	%	
Vaginal delivery	9	12.51	8	11.11	**17(23.61%)**
LSCS	51	70.83	4	5.56	**55(76.39%)**
Total	**60**	**83.34**	**12**	**16.67**	**72 (100%)**

Table VII: Relationship between APH & maternal mortality (n=72)

Mortality	Placenta previa		Abruptio placenta		Total (%)
	N	%	n	%	
Maternal mortality	0	0.0	2	2.78	**2(2.78%)**
Total	**0**	**0.0**	**2**	**2.78**	**2(2.78%)**

Table VIII: Distribution of the study patients by major post partum complications (n=72)

Major post partum complications	Placenta previa		Abruptio placenta		Total (%)
	N	%	n	%	
Prolong hospital stay	4	5.56	1	1.39	**5(6.95%)**
Acute renal injury	0	0.0	2	2.78	**2(2.78%)**
ICU Admission	2	2.78	2	2.78	**4(5.56%)**
Peripartum hysterectomy	2	2.78	1	1.39	**3(4.17%)**
Need for blood transfusion	55	76.39	9	12.5	**64(88.39%)**
Anemia	55	76.39	9	12.5	**64(88.39%)**
DIC	0	0.0	2	2.78	**2(2.78%)**
PPH	7	9.72	2	2.78	**9(12.50%)**
Puerperal sepsis	2	2.78	1	1.39	**3(4.17%)**

DISCUSSION

Maternal age ranged from <20 to >35 years in this study. The commonest age group of placenta previa and abruption placenta was 26-30 years. In the Kedar et al.8 study mean age of patients of APH were (25- 29) years. Incidence of Abruptio Placenta was found to increase from 19.11% (age group 20-24 years) to 32.35% (age group 30-34 years). Pedowitz et al.9 and Das et al.10 have also reported maximum number of cases in the same age group. Ananth et al.11 found increased incidence of placenta previa with advancing age. William et al15 also reported increased risk of AP with advancing age. Majumder et al. 13 APH is more common (60%) in 21-30 years combined age group which is the most common reproductive age group.

In this study more than two third patient were multipara. Twenty two percent patient were primi gravid. Most of the placental causes of APH occurred in multi gravid women. In the Kedar et al.8 study it was observed that the incidence of APH was more common in multipara than in nullipara and the mean parity was 1.6±1.3. The incidence of Placenta previa was 5 times higher in multipara than primi para. Chakraborty et al.14 reported that prevalence of APH was higher among multigravidas. Results of present study is consistent with study of Cotton et al.15 who found that 83.2% of their patients with Placenta previa were multiparous and 16.78% were nulliparous. Crenshaw et al.16 reported that 10% patients with Placenta previa were primi gravida. Ananth et al.11 showed that risk of placental abruption increased with high parity.

In this study showed the both in abruptio placenta & placenta previa more than fifty percent patient received irregular antenatal checkup. Only 9.7% patient received regular antenatal checkup. In study of Kedar et al.8 85 patients of APH were unbooked as compared to 46 who were booked. Maximum numbers of Abruptio placenta were unbooked (69.11%). This was found to be significant (p value 0.559, Chi square test). The importance of antenatal visits in prevention of AP has also been stated by Baskette et al.17 who reported that in their series 3/4th (75%) of cases were unbooked.

In this study we observed that moderate anemia was present in more than sixty three percent patients. Severe anemia was more prominent in patient's with abruptio placenta than placenta praevia. In Kedar et al.8 study anemia was the most common complication in APH patients followed by postpartum hemorrhage (PPH).

42.64% patients of Abruptio placenta had anemia as compared to 55% patients of Placenta previa. In case of Abruptio placenta 25 patients had PPH as compared to 16 patients with placenta previa. One patient died because of renal failure in abruptio placentae. Although the same has been reported by other studies, we cannot conclude that anaemia is the direct adverse outcome of placental causes of APH that is placenta previa or abruptio placenta, as most of the patients were nonbooked with no antenatal record.. Also APH causes acute hemorrhage hence results of hemoglobin level does not reflect the severity of anemia. This high frequency of maternal anemia might have also been contributed by underlying chronic maternal nutritional deficit common in Lake Victoria zone18.

In current study, more than twenty three percent patient delivered per vaginally, who had minor degree of placenta previa and abruptio placenta with IUD. Kedar et al.8 study reported Maximum patients of APH delivered by caesarean section (65.64%) as compared to vaginal delivery (34.35%). 56 (93.33%) patients of Placenta previa underwent caesarean section. Whereas 30(44.11%) patients from Abruptio placenta underwent caesarean section. This was found to be significant (p value 0.0001, chi square test).

In current study showed almost ninety percent patient needed blood transfusion due to anemia. 2nd most frequent post-partum complication was PPH (12.5%). DIC was found in 2(2.8%) mothers who had abruptio placenta. This finding was lower compared to other study. Due to limited laboratory investigation for DIC in our setting, we might have missed some cases of coagulopathy ending up with lower incidence of DIC. Other studies have shown mortality due to DIC ranges between 2 to 5%19; This study showed 5(6.9%) women required massive transfusion of more than 4 units. Various of studies have shown blood transfusion required in (50-62)%; while Nigerian study 91.4% required transfusion with an average of 3 units per patient and was associated with maternal survival22. This study did not find an association between a need for blood transfusion and maternal death possibly because the direct cause of maternal death was DIC and not anemia. Hysterectomy was performed in 3(4.2%) cases due to primary postpartum hemorrhage. These results are almost similar to a study done by Iran et al. 2006 who reported anincidence of 1.9%21.Maternal Shock was found in 17(17.9%) and these findingswere almost comparable with a study done by Pitaphorm et al. 2006 where shock was the leading complication seen in 19.4%22.

CONCLUSION

In cases of placenta previa especially suspected cases of morbidly adherent ones, senior obstetrician and anesthetist must be available during delivery. In these cases, a preoperative planning with multidisciplinary involvement should be followed. In our country couples get more children due to lack of proper education and low socio economic condition which increases the chance of developing both placenta previa and abruption placenta. Now it is mandatory to spread family planning knowledge throughout the country, proper antenatal checkup, detection of vulnerable groups, and early diagnosis of placenta previa & abruption placenta and manage accordingly.

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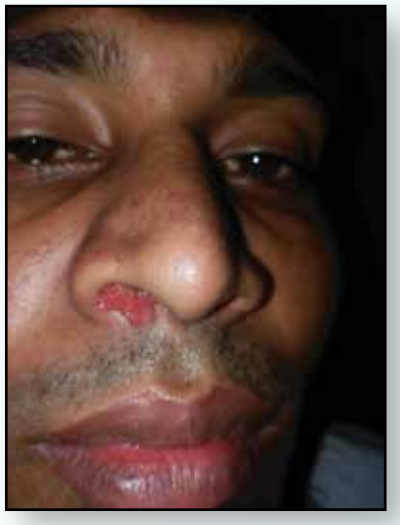
Recurrence is a problem for the treatment of Rhinosporidiosis.

Abdur Rahman[1]

INTRODUCTION

Rhinosporidiosis is an infectious disease caused by an aquatic protozoan previously considered to be a fungus. The aetiologic agent of Rhinosporidiosis, Rhinosporidium seeberi, is closely related to several protoctistiae fish pathogens. The nasal mucous membranes and ocular conjunctivae of humans and animals are affected mainly producing slowly growing masses that degenerate into polyps1.

ENT surgeons are always concerned for the adequate treatment of Rhinosporidiosis and its recurrence, because recurrence is common. If recurs, it recurs in a more bizarre form. When recurrence occur, patient losses faith over respective surgeon. Repeated recurrences frustrates patient. So they switched over the surgeon, even to unconventional treatment method, e.g. homeopathy, ayurvedi, kobiraji, quacks or even to religious clerics. This is the cause for drop out in follow up. After wandering from doctors to doctors, hospitals to hospitals, they become more frustrated and sometimes psychologically upset. Surgeons found Rhinosporidiosis usually attaches with a single stalk in a fresh case and with multi stalks with extensive and difficult areas in recurrent case. So the Surgeons belief if patient would come with regular follow up in proper time, recurrence could be assessed and extension of the disease could have been arrested. Rhinosporidiosis is a notoriously recurrent disease. Cause of recurrence of Rhinosporidiosis yet to be established, but believed to be multiple.



A case of Recurrence Rhinosporidiosis

What is the causative agent of Rhinosporidiosis?

Microscopic organisms are collectively referred to as microorganisms, microbes. Major groups of microorganisms are bacteria, archaea, protozoa, fungi, helminths, and viruses. There is another very important group of organisms called algae. Single-celled organisms arose on this planet about 3.5 billion years ago, among them three types of cells named as bacteria, archaea, and a specific cell type called a eukaryote. Eu-kary- means "true nucleus," and these were the only cells containing a nucleus. Bacteria and archaea have no true nucleus. For that reason, they have traditionally been called prokaryotes, meaning "prenucleus."2

The first case of Rhinosporidiosis was reported by Malbran in 1892 and was published in 1900 by Seeber, who described an apparent sporozoan parasite in nasal polyps from patients living in Argentina3. Seeber's teacher, Wernicke, named the organism Coccidium seeberia after the protozoal subdivision Coccidia and his pupil, Guillermo Seeber4. In 1923, Ashworth described the life cycle of the organism, argued that it is a fungus, and proposed the name R. seeberi5.

Debate of Rhinosporidium seeberi in taxonomy:

As scientist could not culture R. seeberi in vitro till now, debate always arises about its place in taxonomy. Now it is established that the R. seeberi as a member of the DRIPs (Dermocystidium, the rosette agent, Ichthyophonus, and Psorospermum) clade of microbes which allows hypotheses to be generated about how it causes human disease by analogy, drawing on the knowledge and experience of the veterinary sciences. The separate but linked observations that rhinosporidiosis in humans is associated with exposure to water and that R. seeberi belongs to a clade of aquatic parasites, i.e., the natural hosts of R. seeberi are fish or other aquatic animals, and humans acquire infection when they come into contact with water containing these fish and their parasites. Conversely, knowing that R. seeberi is a member of the DRIPs clade may help us understand this important, distinct group of microbes that appear to form the deepest branch in the animal lineage6.

Raquel Vilela and Leonel Mendoza reviewed the key microscopic, ultrastructural and the molecular studies of the past 110 years and concluded that R. seeberi: i) does not share the microscopic or ultrastructural features with that found in the genera Microcystis or Synchytrium spp., ii) has entirely different life cycle traits than those reported for the genus Microcys-

tis the chytridiomycetes or the ascomycetous fungi, iii) possesses a nucleus with a prominent nucleolus and distinctive features distinguishable from those associated with the nuclei of its infected hosts, iv) is a mesomycetozoa microbe based on DNA and phylogenetic analysis, v) has microscopic and ultrastructural characteristics that are in agreement with the characteristic of the Mesomycetozoa, but not with that of the members of lower fungi or ascomycetes vi) develops mitotic figures in prophase, metaphase, and anaphase without cytokinesis in its immature sporangia and, thus it is a typical eukaryote microbe taxonomically and phylogenetically different from the fungi, vii) may have acquired plastid from a cyanobacterium ancestor, and viii) does not develop uniflagellate cells in any of its developmental stages7.

In tissue, this organism forms characteristic abundant, large, thick-walled sporangium-like structures containing large numbers of endospores. It has long been unclear whether this organism is a fungus, but sequencing of the 18S small subunit ribosomal DNA sequence from R. seeberi has led to its recent

reclassification as a member of the protoctistan Mesomycetozoa. Attempts to isolate R. seeberi in culture have failed and thus far it has not been recovered from an environmental source8.

Early investigators found the presence in R. seeberi of a typical nucleus and mitotic figures in tissue sections. The finding of synchronized nuclear division with the formation of endoconidia only in the latest mature stages, supports the placement of this unique pathogen in the mesomycetozoa and away from the fungi5,9,10.

Transmission to host

Soil and stagnant water harbor the spores of these pathogens and hence water and soil act as reservoir for this pathogen11,12. While drinking water, abraded nasal mucosa may get the infection (70% cases) and through dust fomites conjunctiva may gave rise to ocular form (15%) of disease. It is neither contagious nor transmitted through sexual contact. Incubation period is very long. Cases are more frequently observed in communities residing near swamp areas as contaminated water serves as source of infection, hence earlier it was considered as aquatic fungus. It indicates possibility of probable synergism among aquatic micro-organisms and Rhinosporidium seeberi for the spread of infection through stagnant water. Transmission may occur by direct contact with spores through aerosols, inhalation of dust particles, infected clothing and through swimming in torpid contaminated water13,14.

Mode of Dissemination of disease within host

Autoinoculation into breached skin or traumatized epithelium through transepithelial infection, lymphatic and haematogenous routes may also significantly contribute as predisposing factor in the entry and dissemination of spores in the body. Auto-inoculation into adjacent epithelium may takes place if endospores may come out from polyps after any trauma or surgical intervention. For anatomically distant sites in the body of host haematogenous dissemination from a subclinical form of upper respiratory focus of infection (nasal or nasopharynx) can be one probable route of spread5,15. A study showed that there is involvement of regional lymph nodes at the site of lesion13. The lymph node had fibrous capsule along with presence of sporangia16.

Prevalence & Endemicity of Rhinosporidiosis

The natural habitat of the organism is unknown, but it is believed, based on the epidemiologic data, that stagnant pools of fresh water are an important source. The disease is most prevalent in rural districts, among persons bathing in public ponds or working in stagnant water, such as rice fields. Rhinosporidiosis is most common in persons in the age range of 15–40; males are more commonly affected than females8.

Rhinosporidiosis is endemic in Sri Lanka, parts of India, and Bangladesh17 and approximately 90% of all reported cases were from here18,19.

Francílio Araújo Almeida et al found 32 patients of Rhinosporidiosis in Maranhão, Northeast Brazil in their 5 year retrospective study20.

In Singapore, three cases had been reported to date, with the first two cases in 1966 and 1986, respectively. In 2001, S S Chao and K S Loh described another case with unique clinical features. Over a recent 5-year period, four cases of Rhinosporidiosis have been diagnosed and managed there21.

Balasubramanian et al in their surgical audit of sinonasal diseases in 267 nasal surgical cases found Deviated Nasal Septum was the commonest, in 165 cases (62%). In the rest, Ethmoidal polyp in 23 (9%), Antrochoanal polyp in 21 (8%) and others contribute 58 cases (21%). Among the others 58 cases, 8 cases are Nasolabial cyst, 7 cases of Rhinosporidiosis, 3 cases of Juvenile Nasopharyngeal Angiofibroma, 4 cases are Nasopharyngeal Carcinoma, 5 cases of Benign tumors of the nasal cavity, 5 cases of Carcinoma of the maxillary sinus, 3 cases of Bleeding polypus of septum, 5 cases of Fungal sinusitis, one case of Cerebrospinal fluid Rhinorrhea, 3 cases of Nasal myiasis, 4 cases of Rhinolith and 10 cases of Fracture of nasal bone. 7 cases of Rhinosporidiosis were treated by excision and cauterization of the base using bipolar diathermy, but there was recurrence in 2 cases22.

Narayanaswamy G. N et al in their 4 year study found out of 70 cases, 35 cases (50%) were non-neoplastic with 28 cases (80%) were Rhinosporidosis. Benign lesions contributed to 30% (n=21) of patients. Commonest lesion was 8 cases (38%) of inverted papilloma. There were 14 cases (20%) of malignancy.

Carcinoma maxilla was the main malignancy 35 % (n=5).23

Suneer and Sivasankari in their study found male preponderance (76%) between 11-20 years age group. They also found 35 and 6 of their total 50 cases in nasal cavity and nasopharynx respectively. In nasal cavity, common site of attachment is nasal septum 12(35%), floor 10(28%) and lateral nasal wall 13(37%).24 Guru et al and Ahmed et al also found male preponderance in their studies 168 out of 242 (70%) and 39 out of 54 (72%) respectively25,26. For common age group involvement of Rhinosporidiosis, Ahmed et al and Guru et al reported cases between 21-30 years of age group. Kalyani et al reported cases between 11-20 yrs age group27.

How Rhinosporidiosis presents?

The nose is the commonest site of Rhinosporidiosis which causes the production of large sessile or pedunculated lesions that affect one or both nostrils and being affected in more than 70 percent of cases. Rhinoscopic examination will reveal papular or nodular lesions that become pedunculated. The lesions

are pink, red or purple in colour. Spontaneous remission is unusual and, left untreated, the polyps will continue to enlarge. The diagnosis is established by histopathologic examination of tissue sections. These contain large, round or oval sporangia up to 350 mm in diameter, with a thick wall and an operculum. The largest sporangia are filled with spores8.

Clinically, Rhinosporidiosis can be presented in four forms: nasal, ocular, cutaneous and disseminated form. It occur mainly in nasal, ocular regions; cutaneous and disseminated forms are relatively rare.

Nasal form is the most commonly occurring form. Characterized by epistaxis and development of sessile, pink to purple, pedunculated polypoidal mass. It may be unilateral or bilateral mostly in the upper respiratory tract remarkably on the anterior nares, nasal septum, inferior turbinate and at floor of the nasal cavity filled with opaque grey or white granular material. It may also be situated on soft palate, larynx and nasopharynx.

Ocular form begins as a sessile growth, which worsen to friable pedunculated polypoidal mass in the eye. Polyps formed in the eyes are mostly flat, comparatively soft, bluish or pinkish to reddish in colour, lobular and express pin head sized spots due to presence of underlying mature sporangia. Usually 15% of rhinosporidial infections subsist on bulbar and palpebral conjunctiva, lacrimal sac and naso-lacrimal duct comprising ocular form of Rhinosporidiosis. There is evidenced that the primary predilection site of Rhinosporidiosis is lacrimal sac from which infection spreads downward through the naso-lacrimal duct to the nasal passage for polyp formation.

Cutaneous form usually occur as tiny papule which becomes wart-like lesion with a friable crenulated surface, which easily develop into ulcer.

Disseminated form is rarely reported and whenever present is characterized by presence of spherules of *R. seeberi* in the bone, liver, lung, viscera, spleen, trunk, limbs and brain upon autopsy16.

It generally affects the mucous membrane of nose and nasopharynx but occasionally involves conjunctiva, lacrimal sac, lips, palate, uvula, maxillary antrum, epiglottis, larynx, trachea, bronchus, ear, scalp, skin, penis, vulva and vagina. Osteolytic lesions in the bones of hands and feet are also reported. It is usually limited to surface epithelium but may present as widespread visceral involvement28,29. The cutaneous lesions were either small, non-tender nodules or warty dark coloured excrescences with small pedicles. Ulcerated skin lesions had fungating irregular surface, which bleed on touch. The growths were firm, mildly tender and had everted margins. These lesions were difficult to distinguish from soft tissue malignancy. The subcutaneous and intramuscular lesions were of two types, firm and cystic. The firm lesions were lobulated, pale yellow with homogenous cut surface, which looked

similar to brain tissue. The single cystic ovoid intramuscular lesion had smooth surface with a thick fibrous capsule and contained about 20 ml of thick creamy fluid, which, on microscopy, showed presence of numerous sporangia of different stages of maturation. The fibrous capsule, on the other hand, did not show any presence of granulation or spore. The involvement of penis presented either as discrete pink polypoidal mass with granular surface, protruding from the urethral meatus or as a smooth globular sessile mass arising from the glans penis. Involvement of the bone in Rhinosporidiosis presented as almost painless swelling over the wrist joint with restriction of movement. The skin covering the swelling got ulcerated and grew to form a huge fungating ulceroproliferative mass. The laryngeal lesion was a solitary pink polyp attached to the left aryepiglottic fold with a short stalk. None of the cases in this series showed any enlargement of the regional lymph nodes30. Osteolytic lesions of Rhinosporidiosis involving tibia31,32, fibula31, femur33, scapula34, hand and foot32,35, talus31 and calcaneum31,36 have been reported.

The most common presenting symptom of Rhinosporidiosis are nasal mass, nasal obstruction, epistaxis and nasal discharge37,38.

Bandyopadhyay et al found most of the nasal lesions had pink fleshy mass with white dots on the surface, which is typical of Rhinosporidiosis. Out of the 114 nasal and nasopharyngeal lesions, 67 (60%) had pedunculated lesion and the rest 47 (40%) had sessile or mixed crops of some sessile and some pedunculated lesions. Larger masses hanging into the oropharynx, on the contrary, had the look of fleshy polyps with smooth lobulated surfaces without the history of recurrent episodes of bleeding. 83 of the nasal/nasopharyngeal lesions (73%) were single and multiple fleshy masses were seen in the rest 31

(27%). Floor of the nasal cavity and the nasal septum were found to be the sites most commonly involved. The conjunctival lesions were pink globular mass with finely irregular surface, attached to the lower palpebral conjunctiva with a short narrow stalk. There was white discharge from the affected eye. The cutaneous lesions were either small, non-tender nodules or warty dark coloured excrescences with small pedicles. Ulcerated skin lesions had fungating irregular surface, which bled on touch. The growths were firm, mildly tender and had everted margins. These lesions were difficult to distinguish from soft tissue malignancy30.

In a study by Amritanand R et al found 70% of the reported cases were involved the nasal mucosa and about 15% were in the eye31.

Ocular and genitourinary involvement came next with involvement in 2.5% each. Ocular Rhinosporidiosis is usually airborne37,39. Ascending infection from the nose is implicated for involvement of the lacrimal sac. Occasional involvement of lips, palate, epiglottis, pharynx, larynx, trachea, bronchus, ears, conjunctiva, lacrimal sac, skin, vulva, vagina, penis, scalp and bone has also been reported18,32.

Treatment Modalities

SURGERY

The treatment of choice is surgical excision of lesions, with or without cauterization. No drug treatment has proved effective8. Surgical excision with cautery of the base of lesion is known to reduce the risk of recurrence. It is thought that the cauterization of the lesion's base may abate recurrence resulting from spillage of endospores on the adjacent mucosa.

The principle of surgical treatment to excise and wide base normal healthy tissue cauterization or destruction with the intention not to recur from surrounding neighbor healthy tissue as spore of Rhinosporidiosis remains there. Surgery may be done by simply cold metal technique, Unipolar or bipolar diathermy, LASER or even by cobblation. Assistance of magnification may be taken by endoscope or by microscope for well visualization of site of attachment, extension and delineation of margin of the disease.

Marfatia and Kirtane states that surgical excision with nasal endoscope is a newer concept as it helps in better visualization and easier to reach the pedicle of Rhinosporidiosis. Thus removing the whole mass right from the root of the pedicle without creating a raw surface. They also stated that it is usually peduculated in nasal variety and attached with a stalk. Inadequate excision results in recurrence from the same site or from the adjacent areas of raw surface. The spread of infection also occurs by permeation along the subepithelial connective tissue resulting in involvement of contiguous mucous membrane distal to the original site40.

Sonkhya et al found no visible mass on anterior rhinoscopy, but nasal endoscopy revealed Rhinosporidiosis arising from posterior 1/3 of the septum involving choana. They excised out of this unusual case of Rhinosporidiosis by bipolar cauterization under endoscopic guidance. Endoscopic guidance helped in enbloc removal of mass without any significant bleeding41.

Mohan Kameswaran et al in their study tried to find out the efficacy of the KTP- 532 laser over conventional diathermy excision of Rhinosporidiosis. As, Rhinosporidiosis is a difficult granulomatous disease of the nose, notorious for its high rate of recurrence and vascularity, the study looked at three main criteria, 1. clearance of the disease. 2. effect on post Laser recurrence of Rhinosporidial mass at same site or different sites and 3. effect on blood loss. Their prospective study of 22 patients treated for Rhinosporidiosis, half of the 22 cases (group A) were treated by Laserization of the Rhinosporidial mass using KTP/532 Laser, the remaining (group B) were treated by conventional surgery with cautery to the base. The rate of recurrence of the Rhinosporidium was also calculated and it was found out that in group B recurrence was about 63% while that in group A was 27%. In three patients of group A recurrence occurred, of which interestingly in two patients (18%) it was seen that the new Rhinosporidial mass did not arise from the exact same site of initial presentation but rather from a different site. One patient had recurrence in the same site. In the study, it was seen that the KTP-532 laser helped in reducing the chances of recurrence. This could also be attributed to the fact that treatment with laser can be achieved without direct contact of the infected granulomata thus avoiding tissue contamination42.

Addition of systemic Dapsone for a period of 1 year following wide local excision with cauterization of the base is known to prevent reoccurrence as it arrests the maturation of sporangia and promotes fibrosis15,41,43.

In a case report of recurrent Rhinosporidiosis by Nichlani, in which they excised the lesion using *diode laser*, they followed up the case for 1 year, in which no recurrence was reported44. In 2014 a recurrent case has been reported by J. Chery,C. Bacskai, and E. Mendoza which they excised by harmonic scalpel, citing the superior hemostasis of the instrument while preserving the local integrity of local tissue45. In a prospective study by surgical excision with electrocautery, can cause localized tissue trauma and in addition expose the unaffected sites to the blood during surgery, which in turn can cause inoculation and possibly explains the recurrence. As the temperature does not exceed 60^0C in Coblation mode, there is less thermal damage to surrounding tissues as seen with cautery and laser. Also, there is constant cooling due to simultaneous irrigation. With the use of Coblation system, they could achieve complete resection of the lesion, with minimum bleeding and less blood

contamination, also preserving the integrity of local tissue. They did follow up the patient for 1 year and found no evidence of occurrence46.

Leni et al stated that ketoconazole has been used only once in nasal Rhinosporidiosis along with cryotherapy and surgery with complete response. They also stated that cryosurgical excision of lesion was also tried to check the recurrence and spread of infection47.

A Das et al in their case Rhinosporidiosis presented as nasopharyngeal mass could have been missed in the previous surgeries. The use of endoscope in such case helps in removing the entire mass which could not be seen by anterior rhinoscopy/conventional surgery. Complete excision of the nasal mass along with its nasopharyngeal extension was done and the base was cauterized with Nd YAG Laser (20 watt pulse). They started on Dapsone therapy after surgery for three months. On one year follow up after surgery they did not have any recurrence. As physical contact of the tissue with laser is less and hence the chances of seeding are reduced. They concluded

Laser and endoscopic excision promises to be mainstream treatment of nasal/nasopharyngeal Rhinosporidiosis in the future48.

The advent of Sinus Endoscope has facilitated the clearance of smaller granuloma but bleeding from larger granuloma can impair vision and pose difficulties. The introduction of surgical LASER for fulguration and vaporization of this granuloma would be logical step, as one would expect this to reduce the bleeding and also improve vision with the endoscope. An additional advantage of using laser is minimum physical contact with the fungal granuloma, thus surrounding tissue seedling is minimal49.

In a large Rhinosporidiosis mass where the stalk could not be seen or difficult to see, some tried with application of adrenalin soaked gauze for few minutes resulting the mass squeezed to a smaller one and helps in viewing the stalk and catch. Sometimes it acts as an important tips for surgery. It also controls bleeding.

Advantage of Endoscope

It reduces the risk of recurrence. Removal of entire mass can be done with endoscope which cannot be seen on routine anterior rhinoscopy. It gives better illumination for removing the entire pathology precisely with minimal manipulation and least resection of surrounding normal mucosa. Post-operative complications like hemorrhage and synechiae are less. For lesions located posterior aspect of nasal cavity and nasopharynx, endoscopic visualization is must and en bloc removal can be done only after endoscopic guided cauterization of the base. Bleeding is minimal provided the stalk of the lesion is identified endoscopically50

Recurrence

Some recent studies on Rhinosporiodosis reporting recurrences:

Author, Year	Country	Total Cases	Period of Study	Site	Common Age Group	Male/ Female	Bathing Habit	Recurrence Rate
Saha SN et al (16, 2001) [51]	India	98	10 years	78/98 in nose & nasopharynx	34/98 in 21-30 yrs	75/23	Ponds	17.34%
Arsecularatne et al (5), 2010 [52]	Sri Lanka	143	14 years	Nose & nasopharynx (78%) Ocular (18%)	26% in 21-30 yrs. 60% in 11-40 yrs age group	2.3:1 in nose & nasopharynx	Lacustrine water (83%), River (12%)	37%
Bandyopadhyay et al (13), 2015[30]	India	119	2 years	114 out 119 in nose & nasopharynx	(17%) in 11-20 years of age group	83/36	-	5%
Debdulal Chakraborty etal 2015 [53]	India	112	3 years	52.68% in nasal septum	Common in 10-19 yrs age group	60/52	Ponds	3 cases 2.68%
Sharfuddin Mahmud et al. 2015[54]	Bangladesh	49	01 yrs	Nose, Nasopharynx 39 out of total 49	Nose, Nasopharynx 39 out of total 49	37/12	-	4.08%
FrancílioAraújo Almeida et al 2016[18]	Brazil	25	5 yrs	All in nose & nasopharynx. 16 (64%) in left nasal fossa	7-24 years	21/4	daily activities in ponds, rivers and lakes	2 cases (8%)
Abdul Qayum Chowdhury 2016[55]	Bangladesh	34	2 yrs	Different parts of nasal cavities	21/34 in 6-20 yrs age group (61.76%)	24/10	31 (91.18%)	-
Sirshak Dutta et al 2017[56]	India	39	1 yr study	Nasal cavity was the predominant site involved	10-20 yrs age group mostly involved	23/16	82% from rural habituated in pond bathing	13%
Suneer R et al. 2018[24]	India	50	2 yr study	70% in nasal cavity	24% in 11-20 yrs & 20% in 31-50 yrs age	38/12	Ponds	-

Reasons for Recurrence after Surgery

Debdulal Chakraborty et al in their study found recurrence in 3 cases (2.68%), all the recurrences were the lesions in the nasopharynx. They found that the clearance of Rhinosporidiosis from nasopharynx was the most difficult job because of multiple attachments and difficulty in exposure and instrumentations53.

Literature reviews suggests a residual or recurrence rate between 10 and 70%. Most of the reports show an incidence on average of 10%, related to incomplete excision of the mass57.

Recurrences are common, probably due to incomplete excision or intraoperative contamination of adjacent tissues or cells with residing endospores making condition further grave, hence electro cauterization at the site of excision is recommended as a future preventive measure. Surgery by hot or cold snare technique is the treatment of choice and endoscopic removal of naso-oropharyngeal polyps is also practiced58.

Most of the recurrences are thought to be due to incomplete removal of mass due to excessive bleeding or auto-inoculation by surgical trauma38.

Morelli et al stated that recurrence of the lesion mean a true relapse in their study, excluding the possibility of a reinfection, more probable in the endemic areas59. As the habitat of R. seeberi is identified as ground water, people who use these sources either for swimming or drinking purposes should be free from injuries as the pathogen gains entry through wounds11.

Role of Medical Treatment

At present, the treatment for rhinosporidiosis is the surgical excision. Some authors proposed a medical therapy with Dapsone59. Medical treatment is trialed or reserved for prevention of recurrence.

Rhinosporidiosis is generally considered to be insensitive to the antimycotic or antibiotic treatment60,61. Local injection of depot corticosteroids into the polypoidal masses29, systemic course of Amphotericin-B and Dapsone are used to treat Rhinosporidiosis29,62. The use of Amphotericin is usually recommended when either surgical excision is incomplete or there is recurrence63. Nair found no recurrence in 71.4% of patients after using Dapsone with three years follow up64. Venkatachalam et al tried postsurgically Itraconazole (100 mg twice daily) in two cases along with alkaline nasal douche in one case and Amphotericine B nasal douching in other. They regularly followed up with endoscope and found no recurrence37.

Jeshina Janardhanan et al found a 42 year old male with recurrent cutaneous lesions all over the body for 3 years. He had undergone surgery seven times for similar recurring lesions and had been treated with Dapsone for several years. Owing to the multiple recurrences while on Dapsone and surgery, they tried with amphotericin B at a dose of 1.5 mg/kg/day for 6 weeks. Although some reduction in the size of the lesions initially but recurred within a year and the patient died. They suggested for multi-drug regimens that include Dapsone65. Radiotherapy was also tried against Rhinosporidiosis but found not effective66.

S. N. Arseculeratne et al. stated that since the early decades of the twentieth century, several drugs and proprietary preparations have been used with variable clinical outcomes. The absence of methods for in vitro culture of Rhinosporidium seeberi has restricted the development of in vitro drug susceptibility assays. A new method of 3-[4,5-dimethyl-2-thiazolyl] -2,5-diphenyl-2H tetrazolium bromide (MTT) reduction was recently introduced to assess the viability of rhinosporidial endospores, the putative infective stage of R. seeberi. Using this modification for the microscopy of target endospores, eight antimicrobial agents have been found to be effective anti-rhinosporidial activity (in order of decreasing potency): imidocarbdi proprionate e.g. Imizol, diminazine aceturate e.g. Berenil, cycloserine, dapsone, trimethoprim-suphadiazine, ketoconazole, sodium stibogluconate, and amphotericin B. Berenil is used in human trypanosomiasis and babesiosis, Imizol is used in Lyme disease. Cycloserine, a drug used as anti-tuberculous medication. They also found Rhinosporidium seeberi is susceptible to some Biocides. Biocides are antiseptics and disinfectants. Some biocides at concentration sused in hospital and laboratory practice proved to have anti-rhinosporidial activity. It has been assessed by modified MTT-reduction method. These are hydrogen peroxide, glutaraldehyde, chlorohexenol, chlorhexidine, cetrimide, thiomerosal, 70 percent ethanol, iodine in ethanol, 10 percent formalin, povidone-iodine, sodium azide, and silver nitrate67,68. Ezeanolue and Odike tried with Fluconazole and found effective69.

These in vitro results were correlated well with the data from clinical studies from the only drugs on which clinical information was available. These drugs include amphotericin B, antimony compounds, ketoconazole, and Dapsone. Dapsone has had most attention with detailed descriptions of the inflammatory and healing responses of the host and the effects on the pathogen. Drugs that were not effective in the MTT reduction test in vitro included penicillin G, streptomycin, gentamicin, ciprofloxacin, metronidazole, pentamidine, pyrazinamide, isoniazid, and rifampin. Rajam et al and Satyanarayana found pentamidine ineffective in the therapy of rhinosporidiosis66,70,71.

Multi-drug therapy using cycloserine, ketoconazole and Dapsone, has recently been recommended for treating disseminated Rhinosporidiosis, not responding to Dapsone monotherapy72.

Amphotericin B

Kutty and Teh found Amphotericin B to have caused arrest of the development of the pathogen, preventing the recurrence of disease during a three year follow-up period, and ultrastructural damage to R.seeberi was marked73. Bhomaj et al found topical amphotericin B on corneal and nasal Rhinosporidiosis have been successful74. Though, Ho and Tay found intravenous drug to be ineffective in the treatment of disseminated Rhinosporidiosis75.

Antimony compounds

Allen and Dave used the antimony compound "Neostibosan" in 18 patients with nasal Rhinosporidiosis, with a satisfactory outcome in only three patients76. In another case report by Atav et al, there was no recurrence noted after

one year after Neostibosan therapy and surgery on nasal Rhinosporidiosis77. Arseculeratne SN et al had some in vitro studies with the pentavalent antimony compound, sodium stibogluconate found anti rhinosporidial activities71.

Ketoconazole

Kunel'skaiaet al in their study found systemic ketoconazole, topical clotrimazole, and surgery effective in the treatment of nasal Rhinosporidiosis78.

Dapsone

Nair noted a significant reduction of recurrence rates from 93 percent to 39 percent in Dapsone untreated and treated patients during three years, respectively64. Job et al concluded in his study with that medical therapy alone could replace surgery. The usual oral dose used was 100 mg/day for durations from 6 months to several years79.

The applicability of anti-rhinosporidial therapy using medication can be considered clinically in two scenarios (a) presurgical or postsurgical and (b) solely medications. These comments relate only to Dapsone since detailed studies on host and pathogen responses to the other drugs shown to be effective in vitro, are not yet available.

A serious complication of surgery in Rhinosporidiosis especially of the nasal and nasopharyngeal sites, is the profuse intraoperative hemorrhage that results from the high vascularity of the growths80. The responses of patients after medical therapy with Dapsone without surgery74 indicate that the disease process is arrested with the increased resolution and fibrosis, which would expect to minimize the intraoperative haemorrhage.

Dapsone used post surgically controls the colonization of normal mucosa by the endospores released from the site of excision. Postoperative use of Dapsone has been the commoner mode of treatment. With Dapsone therapy, recurrences have been reported to have been minimized or prevented64. In view of the danger of dissemination of R. seeberi, especially after surgery, with extensive histolysis of soft tissues including bone and cartilage, it can be considered advisable to commence medications.

In the study of 200 cases in endemic area by Dr T Balasubramanian & Dr R Geetha, in a 5 year period, found all these patients gave history of bathing in ponds which could account for the common etiopathogenic factor. All the cases were managed by surgical resection followed by 9 months course of Tab. Dapsone to minimize risk of recurrence. Despite these measures they got a recurrence rate of about 19% 81. Job et al, Crosara et al and Madke et al in some of their studies stated that dosage of 100 mg/day of Dapsone for several months is recommended in human patient to prevent the recurrence of disease after surgical removal79,82,83.

Adverse effects depend on the dose and they rarely occur at doses less than 100 mg per day. They are mainly shown on skin, nervous system, digestive system, hepatobiliary system, and kidney and hematologic system. The most important adverse effects are hemolytic anaemia and methemoglobinemia. Hemolysis usually occurs at doses of 200 mg and more per day. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis may be provoked by a dose less than 50 mg per day. For prevention, before using Dapsone in therapy, clinical examination with history, blood parameters, liver and renal parameters and determination of glucose-6-phosphate dehydrogenase level are recommended84.

Semaan et al reported in their study that Dapsoneis widely used for a variety of infectious, immune and hypersensitivity disorders including Rhinosporidiosis. However, the use of Dapsone may be associated with a plethora of adverse effects, some of which may involve the pulmonary parenchyma. Methemoglobinemia with resultant cyanosis, bone marrow aplasia and/or hemolytic anemia, peripheral neuropathy and the potentially fatal Dapsone hypersensitivity syndrome (DHS), the focus of this review, may all occur individually or in combination. DHS typically presents with a triad of fever, skin eruption, and internal organ (lung, liver, neurological and other systems) involvement, occurring several weeks to as late as 6 months after the initial administration of the drug. In this sense, it may resemble a DRESS syndrome (Drug Rash with Eosinophilia and Systemic Symptoms). DHS must be promptly identified, as untreated, the disorder could be fatal. Moreover, the pulmonary/systemic manifestations may be mistaken for other disorders. Eosinophilic infiltrates, pneumonitis, pleural effusions and interstitial lung disease may be seen. This syndrome is best approached with the immediate discontinuation of the offending drug and prompt administration of oral or intravenous glucocorticoids85.

Prior hypersensitivity to Dapsone or its derivatives including

agranulocytosis and hypersensitivity syndrome are the absolute contraindications to the use of Dapsone. Deaths from agranulocytosis, aplastic anemia, and other blood dyscrasias have been reported with Dapsone administration. Allergy to sulfonamide antibiotics, significant cardiopulmonary disease, significant liver or renal function impairment, or pre-existing peripheral neuropathy are the relative contraindications to the use of Dapsone. Dapsone is a pregnancy category C drug. Therefore, it should be used with caution only if benefits outweigh risks. According to the American Academy of Pediatrics, Dapsone is listed as a "maternal medication usually compatible with breastfeeding."86

During use of Dapsone, close monitoring is advised. Complete history and physical examinations with emphasis on cardiopulmonary, gastrointestinal, neurologic, and renal systems. Some baseline investigations which includes complete blood count, differential count, liver function tests, renal function tests, G6PD level, and urinalysis should be done. Regular follow-up with complete blood count (CBC) with differential every week for 4 weeks, then every 2 weeks until week 12, then every 3 to 4 months. Reticulocyte count as needed. Liver function tests and renal function tests every 3 to 4 months. Methemoglobin level may be clinically indicated. Toxicity of Dapsone; Dapsone-induced methemoglobinemia typically is the result of acute poisoning, either by accidental ingestion or suicidal intent. Methemoglobinemia may be treated with vitamin E and C, cimetidine, or intravenous (IV) methylene blue86.

Leni George et al found that a case of disseminated Rhinosporidiosis in an immunocompromised individual on antiretro-viral drugs, non-responsive to Dapsone and therefore treated with a multidrug therapy of Cycloserine, Dapsone and Ketoconazole along with ART (Antiretroviral therapy) after surgical excision with good response. The patient had been diagnosed as having Rhinosporidiosis elsewhere and had taken Dapsone for about 10–12 years without adequate response, instead there was progressive increase in the number and size of the mucocutaneous lesions and he was in severe distress. As there is a significant drug interaction between ketoconazole and nevirapine, his antiretroviral therapy was changed to an efavirenz-based regimen. He was started on cycloserine (250 mg) three times a day, ketoconazole (400 mg) twice a day along with Dapsone orally. Higher doses of ketoconazole were given as efavirenz decreases the bioavailability of ketoconazole. There was a significant response to this multidrug regimen in this patient with Dapsone refractory disseminated Rhinosporidiosis at the end of 1 year. Ketoconazole has been used only once in nasal Rhinosporidiosis along with cryotherapy and surgery with complete response47.

At present, there are no data on the development of resistance in R. seeberi to Dapsone. As Dapsone is the single most common drug used in the chemotherapy of rhinosporidiosis, it might be prudent to use combinations of several medications. This could be Dapsone combined with one or more of the drugs mentioned above, that have been recently shown1 to have in vitro anti-rhinosporidial activity. Arseculeratne, 2008 unpublished data, stated that cycloserine might be the additional candidate with Dapsone for the multidrug chemotherapy of Rhinosporidiosis, whether cycloserine is synergistic with Dapsone is yet to be determined. In vitro determinations of the time-course of action of Dapsone revealed more rapid inactivation than clinical responses suggested, probably because of the in vivo pharmacokinetics of Dapsone that delay an access of the drug into the pathogen87.

Regarding Prevention Of Recurrence

Recurrence of disease either due to incomplete excision or from the healthy tissue where sporangium of the disease remains.

The exact cause for its recurrence is yet to be established. Following points are believed for its recurrence:

a. The causative agent not yet identified correctly, debate in taxonomy;

b. Not able to culture in vitro;

c. Sensitivity to antimicrobial agent could not be assessed in vitro;

d. Limited drugs are effective on trial basis in vivo against them pre-surgically or post-surgically;

e. Debate for proper surgery either in method or technique or even incomplete excision;

f. Patient re-expose to that environment responsible for the disease such as bathing in pond or stagnant water.

Drop out in follow up that not allow to detect the recurrence earlier and preventing the measure that could have been taken. At sometimes patient present with extensive and bizarre form of recurrence rarely with disseminated throughout the body where surgical clearance is very difficult or even impossible.

Medical treatment should play role in the treatment, to prevent its recurrence and in recurrent disease.

Further Research

For eradication of the disease, surgery alone is not enough. Effective medical treatment must play a role. But the causative agent is notestablished and culture in vitro is not possible till now. As long as these problems will not be solved, eradication will not be possible. So, researcher must emphasized on these points in their research. Target of research must include to disclose the aetiological agent and of course its culture in vitro.

The etiological agent of Rhinosporidiosis, R. seeberi, has been a riddle from past 9-10 decades. This pathogen cannot be successfully grown over artificial media under laboratory

conditions. Prevention will be the best option to be safe from this organism as the disease takes a chronic course which makes diagnosis difficult. Hence swimmers and persons who are frequent visitors to water bodies should have safety precautions as this organism get transferred through cut wounds.

Hence newer assays should be developed to detect this pathogen early both in human and animal so as to control the disease effectively16.

Raquel Vilela, Leonel Mendoza hopes that the notion of plastid DNA in R. seeberi will ignite a new interest in the subject, which could redirect future research efforts in this and other areas that still need further research7.

Discussion

Iram Khan et al in their study stated that Rhinosporidium seeberi, the causative organism, has a debatable taxonomy as the microorganism is intractable to isolation and microbiological culture, and the morphological features resemble both fungi and protozoa46. But recently a study has classified Rhinosporidium seeberi in a class, the Mesomycetozoea, along with 10 parasitic and saprobic microbes. The controversial spherical bodies have been shown to comprise both lipid-protein nutritive bodies and other spherical bodies. This is supported by a study conducted by Herr et al. group which includes fish and amphibian pathogens in the form of DRIP clade (Dermocystidium, the rosette agent, Ichthyophonus, and Psorospermum)88,89.

The nose has been found to be the predominant site of involvement. Nasal and nasopharyngeal mucosa traditionally is the preferred site of inoculation58,90,91,92, the reason is not known though92. Exposed mucosa with minor epithelial breach could be a possibility, which also explain rhinosporidiosis in less common sites, like oropharynx, lacrimal sac, conjunctiva, upper respiratory tract (the laryngotracheal complex) and the urethral mucosa51.

Mahendra Pal et al stated that Rhinosporidiosis,a chronic granulomatous infection of humans and animals, is caused by an agent of uncertain taxonomy Rhinosporidium seeberi. Recent molecular evidence has indicated that the organism earlier considered as fungus is now a protistan parasite. How the disease is acquired still remains a great enigma. The principal site of infection is usually the nasal mucous membranes, and infrequently the skin, and other tissues of humans, and animals. The natural habitat of R.seeberiis thought to be stagnant water. Many attempts to isolate the pathogen on various cultural media were unsuccessful. Cytological examination of aspirates from lumps or smears of secretions with PAS technique is also very useful to detect R.seeberi. Hence, cytodiagnosis can be recommended as a simple, economical, and reliable method to confirm the disease both in humans and animals in laboratories with no facility for histopathology93.

M. Prakash and J. Carlton Johnny in searching the cause of endemicity of Rhinosporidiosis in India, Sri Lanka, Bangladesh17 and Pakistan they arrive at a hypothesis that the climatic conditions, cultural practice and physiochemical properties of water in this tropical areas are more in favor of the fungal growth when compared to the west. It is essential for any fungi to require humidity and a warm temperature for its sporulation. So these tropical regions are very good breeding grounds for the fungi. The most important of all factors is the cultural habits which lead to the spread of the disease. It is not customary in the west to clean cattle in local ponds or even take bath along with the cattle in the pond94.

Sirshak Dutta et al in their study of 39 cases, the patients were predominantly male (59 %), rural residents (82 %). Almost everyone (97.44 %) was reportedly habituated with pond-bathing. About 54 % belonged to the age-group of 15 years and above. One-third of the study population was engaged in agricultural activities and about 59 % in cattle farming. Nearly 87 % were fresh/new cases56.

Debdulal Chakraborty et al in their study concluded that although recurrence is very common, in their series it is much less because of meticulous and complete removal. It was possible due to use of epinephrine soaked cottonoids along with the guidance of endoscope or microscope whenever needed. They proposed, Dapsone can be used in recurrent cases. The population at risk should be educated to avoid bathing in ponds and rivers open to animals. Regular postoperative follow up with endoscopy is a must to detect and treat early recurrence53.

In some studies indicating some clue that there might be association of blood groups and occurrence of Rhinsopridiosis. Narayanaswamy and Rajendraprasad in their study found that 70% of our patients were O Rh positive group and 30% were AB Rh positive95. Suneer and Sivasankari in their study found majority of their cases were O Rh positive group and B Rh positive, 40% and 36% respectively24.

SN Arseculeratne et al in their article found sera from infected patient had no effect on the morphological integrity or the viability of the endospores, so they suggested that anti-rhinosporidial antibody has no direct protective role against the endospores, the infective stage, in rhinosporidiosis. They concludes that this finding is compatible with the occurrence of chronicity, recurrence and dissemination that are characteristics of rhinosporidiosis despite the presence of high titres of anti-rhinosporidial antibody in patients with these clinical characteristics96.

Recurrent cases usually appear as huge, complex mass with multiple attachments. Suneer and Sivasankari in their study found among the 50 cases, 22% have multiple attachments where 78% cases have single attachment. All the cases with

multiple attachments are recurrent cases24.

Muhammed K and Abdul K L. in their case stated that the previous polypectomy and surgical excision of the cutaneous lesions might have led to the haematological dissemination of the disease, leading to severe disseminated rhinosporidiosis. They concludes that though, surgical excision is the treatment of choice recommended in all standard text books, it should be done with caution, as it can lead on to haematological dissemination.96

David N. Fredricks et al in their study discussed that multiple antimicrobials, including antifungal agents, have been used in the treatment of rhinosporidiosis, based on the belief thatR. seeberiis a fungus. However, no antimicrobial agent is clearly effective. They suggest medical treatment of rhinosporidiosis may be improved through screening antiparasitic drugs for an effect on disease in Dermocystidium-infected fish or infected cell lines. They concludes, phylogenetic analysis of the R. seeberi18S rRNA gene suggests that this culture-resistant organism is not a member of the Eumycota, but rather is the first known human pathogen from a novel clade of aquatic protistan parasites that form a branch in the evolutionary tree near the animal-fungal divergence. R. seeberispecific PCR and FISH (Fluorescence in Situ Hybridization) confirm the association of this unique 18S rDNA sequence with the presence of rhinosporidiosis. This knowledge can be used to further understanding of the natural reservoir of this organism and the risk factors, pathogenesis, and treatment of this disease. This discovery also expands appreciation of the diversity among eukaryotic organisms that are pathogenic to humans and highlights the limitations of basing phylogenetic classification on morphology alone97.

Narayanaswamy and Rajendraprasad in their study trying to find out of the endemicity, they found that all 36 patients were from the same community and had the ritual of taking bath in a small pond located adjacent to their place of worship. A corroborative inference was thus drawn that taking bath in that pond might be the reason for so many people getting infected. Hence a health education programme was conducted to discourage people from taking bath in that particular pond and also a public notice was put up informing the people about the hazards of taking bath in that pond95.

Conclusion

As the aetiology is not clear till now and pathogens are not able to culture in vitro, sensitivity to antimicrobial agent is not established. Bleeding during surgery and recurrence are the major complications of this disease. Recurrence occurs in more bizarre and extensive form. So we should think more about its aetiology and culture in vitro. If we found the sensitive antimicrobial agent then it can be used in both pre and post operatively to minimize the complication.

Recurrence of Rhinosporidiosis is common. So, modern treatment options are not enough to prevent the recurrence of Rhinosporidiosis. We should find out the limitations and pitfall of treatments options. This review will make us thinking in this line.

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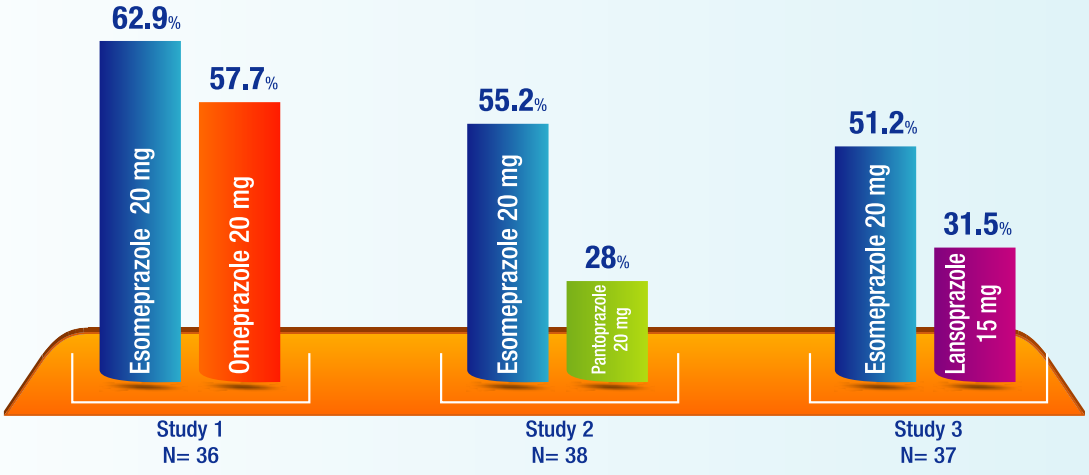
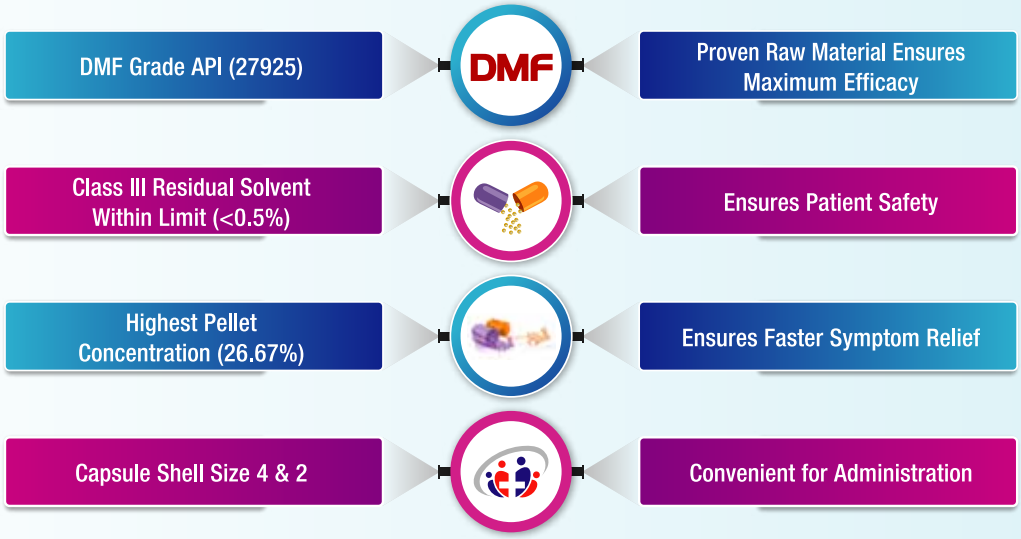


Patients obtained better pH control during daytime



The ORION Medical Journal 2019 September;21-2(47): p06-12

Common Problem Faced By Orthopaedic And Trauma Surgeons An Observation At District Level Hospital, narsingdi For Last Eighteen Years.

Dr Abul Kalam Azad [1], Dr. Md.farhan Azad.badhon [2], Dr.nadia Natasha Ahmed Chowdhury [3], Dr Quazi Abul Azad [4], Dr Siddika Sultana [5],

ABSTRACT

For eighteenen years starting from January 2001 to December 2018, different age group patients referred back from Govt. and Non Govt. Medical Colleges, NITOR or from private clinics were studied due to different complications. Patient came back from the above mentioned site to overcome the rush of over crowding of patientsts. at that level. From this patient I learnt a vast experience and tried to manage the patient with my own experience and my own way. I treated so many patients but I considered six cases which were treated at different clinics, govt and non govt hospital .the patient were initially treated by orthopaedics surgeon and I found all of them problematic and presented to me with complications.

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INTRODUCTION

TO ERR IS HUMAN. The same is true for Orthopaedic Surgeon. Orthopaedic and Trauma Surgeons are very much busy with emergency trauma and orthopaedic patients. Some of the Surgeons are very much busy with either huge number of serial patients that are to be seen in a limited time and some are very much busy due to hurriness of operation. Mistakes that may be seen either due to busy practice, hurriness of operation, gross negligence of private and govt. practice or may be due to other causes. (like patient's general health condition, too early operation, immediate decision, improper decision, lack of knowledge). This observation was done at the district level with the patient in my practice, referred back patients from different medical colleges, NITOR and patients came from abroad (like middle east countries). Finally patients were treated under my orthopaedic supervision in my own way with or without full recovery.

CASE ILLUSTRATION I

A ten year male patient was treated at Dhaka private clinic with Comminuted fracture upper S.O.F (Rt) with D.C.nsitu .patient came from Dhaka admitted at district level under my unit. 2 months after initial treatment. I followed up the patient, for further 2 months. I found no feature of bony union with gradual bowing of femur with shorting of the lower limb 8 inches incomparison with other extremity. Gradually I found radiologically impaction of the proximal implant into the comminuted fracture fragment. Ultimately non union developed, so I decided to remove the implant under spinal anesthesia and corrected the deformity by close osteoclasis and hipspica was done and was kept for further 3 months. calcium and vitamin D preparation was given routinely for initiating healing process. Bony union occurred without major complication and shortening was in a acceptable range.

CASE ILLUSTRATION II

A case of open fracture G-1 of tibia of 40 years male was treated at NITOR with external fixator. patient came to me 1 month after application of external fixator.I do the x-ray of the part and I found schanz screw itself causing distraction of the fracture fragment interfering with close contact & healing.I decided to remove the external fixation 2 month after the application .I removed it under spinal anesthesia and treated the

patient with sterile dressing with application of plaster of parries in the form of long leg full plaster. I followed up the patient for farther 3 months clinically and radio logically .Again I removed the long leg plaster with and replaced with PTB plaster for further 2 months. Associated calcium, vitamin D and antibiotic was given routinely for aiding healing process. I removed the PTB 2 months after application and found the healing of the fracture without complication. Patient was discharged with proper advice.

CASE ILLUSTRATION III :

A young boy of 17 years old with good alignment of supra condylar fracture of Femur was treated by L-plate at Dhaka in a private clinic.Patient was came to me 2 months after operation, in my private practice. I took x-ray of the part showing gross displacement and rotation of the fracture fragment with clinically presented with multiple sinuses. Initially I applied broad spectrum antibiotic with calcium and vitamin D. Finally I decided to remove the L-plate with surgical debridement & curettage of sinuses and correction the rotation and applied long leg plaster cast.i removed the plaster of parise after taking followed up x-ray showing boney union 3 months after operation. ultimately fracture healed up spontaneously within 3 months. Patient was discharged with proper advice.

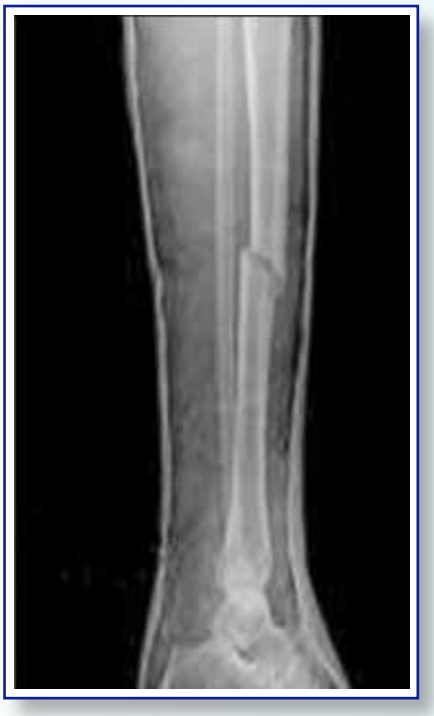

figure 1: showing case illustration of case patient after VI before operation, of Hbsag positive multiple patient with closed fracture tibia and fibula non union

CASE ILLUSTRATION IV:

A forty years female patient was treated by cortical screw with K weire for close supra condylar # of humerus with minimum displacement showed in the initial x-ray. Patient was treated percutaneous K-weire with screw which were interfering the union of boney healing when x-ray was taken .Initially patient was treated somewhere in a private clinic by an orthopadice surgeon. Patient presented to me in my private practice two and half month after operation with severe pain and swelling and asked me to removed the implant by any means .I took X-ray of the part and x-ray showed K weire and screw were interfering healing with displacement of the fracture fragments. I ultimately removed the K weire and screw after 2.5 months of operation under regional anesthesia and treated the patient with L.A.F.P. Antibiotic, calcium and vitamin D preparation was given routinely for initiating healing process and healed up spontaneously one and half months after application of plaster of parise. Plaster was removed and patient was discharged with proper advice.

figure 2: showing same operation with DCP with sinuses with feature of

CASE ILLUSTRATION V :

A case of young boy of 15 years with abdominal injury with fracture humerus with epsilatteral fracture radius & ulna in was treated casualty unit DMCH Dhaka. Patient came to me with deformity of humerus & fore-arm one and half month after initial treatment .Initially the patient was treated by laparatomy at casualty unit.they did not give treatment to the fracture part.patient was presented to me with deformity to the arm and forearm.I took the x-ray of the part and x-ray showed malunit-ing fracture epsilateral radius and ulna.I treated the patient conservatively by closed osteoclasis with long arm full plaster, and kept for 1 and half month. Calcium and vitamin D prepara-tion was given routinely for initiating healing process. Patient was discharged with proper advice.

CASE ILLUSTRATION VI :

A male addicted pt. of 45 years old with close fracture tibia & fibula(minimum displacement). Pt. was treated by ORIF by D.C.P. in a private clinic at Dhaka.patient came to me with infection ofimplant with multiple sinuses one and half months after operation.routine investigation was done to exclude DM and HBV infection. This pt. was found HbsAg Ve+.with proper precaution broad spectrum antibiotic coverage repated surgical toileting was done to aid healing of the wound.xray was taken to see the healing of the fracture but yet not shown any feature of union skin wound and boney union even after 12 months after initial operation. Pt. is still under my orthopaedic treatment & supervision. All precautionary measure were taken for healing of the wound and fracture by giving antiviral drug, vitamin E preparation. c/s done of the sinuses and treated by antibiotics.

DISCUSSIONS :

Secondary treatment of the orthopaedic cases are really a challenging procedures if the 1st (Initial) treatment is inade-quate, improper decision, or infection present. Orthopaedic and trauma surgeons should not operate the pt. where ever the cases found, whatever instrument is available, wherever the fracture found. It may bring money but may lead to dangerous compli-cation even may lead to amputation of the operated part.

CONCLUSION:

Operation is not always good. Surgeon must properly select the patient; should consider the nature of fracture, associated fractures, pt. conditions, type of implant suitable for that fracture, proper time of operation.Surgeon must not forget to take pre-operative proper decision before operation, should not operate upon united fracture, consider anatomy before opera-tion, associated epsilatteral fracture, proper instrumentation, proper route & methodology during procedure, proper tourni-quet time, removal of tourniquet, operation upon normal extremity, associated vessels, nerves, proper way of instrumen-tation, preparation to overcome unavoidable circumstances like impaction and jamming of I.m, Nail, Rush Nail, Broken Nail, fracture during operation, during excision of radial head & femoral head, part of fragment may remain hidden and displaced, introduction of lag screw use during the last part of D.H.S operation, lastly use of drain with eye remain within the wound but not outside and nerves must not mistakes with tendons. Likely in conservative means, should not forget to take proper view, position of X-ray and assessment before procedure and give short brief to pt. guardian regarding sequely of treatment & operation. If we properly follow the procedure we can overcome most of the complication in conservative and operative means. Our target is to make the mistakes Nil or Zero.

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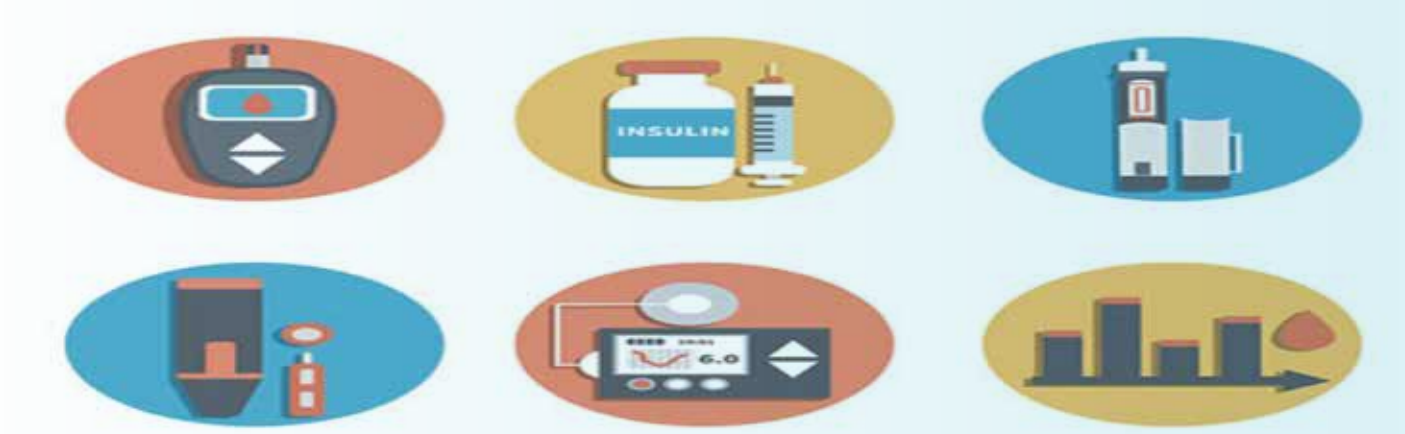
All You Need to Know About Insulin

How a medical breakthrough saved countless lives.
By Helen Cowan



Diabetics were suffering from what is now known as type 1 diabetes. This Before the discovery of insulin, diabetes was a death sentence. Widely regarded as the first true miracle drug, insulin has saved millions of lives. But why do some people need insulin and how does it work?

Diabetes has been recognised as a disease since ancient times, and as early as 1775 physician Matthew Dobson detected the presence of sugar in the urine of diabetics. Diabetic children were thin, listless and pale, with sickly sweet breath, and would inevitably slip into a coma before their untimely death.

In 1797, John Rollo demonstrated that a very low kilojoule diet could prolong the lives of diabetics, but only for a limited period before they died of starvation or complications from malnutrition.

But at the beginning of the 20th century, although the biological mechanism of diabetes was understood, medical science was yet to come up with an effective treatment.

Type 1 Diabetes

means the body cannot make insulin, a deficiency perhaps caused by genetics or an immune response triggered by a virus. Type 2 diabetes is a different disease, where the body has difficulty using insulin. It often begins later in life, and can lead to loss of insulin production. Type 2 diabetes can be triggered by genetics and lifestyle, such as being overweight and having a poor diet.

Insulin is a hormone that unlocks cells, letting glucose in, where it is either used as energy or stored as fuel. Without insulin, glucose remains in the blood and is passed through the kidneys into the urine. Diabetics produce a lot of urine as the glucose draws water out of the body, leading to thirst. Weight loss and a lack of energy result when glucose cannot get into the body's cells.

The Discovery of Insulin

Canadian Dr Frederick Banting, together with medical student Charles Best, building on the work of earlier physicians, isolated insulin from the pancreases of dogs and cows in 1921.

In 1922, the insulin was first tested on 14-year-old Leonard Thompson, a diabetic, and it restored him to health.

No other drug in the history of medicine changed the lives of so many people so suddenly. Banting was jointly awarded the Nobel Prize in 1923 for his work in diabetes.

Insulin Injections

The many types of insulin can be divided into those that act quickly and for a short time (taken just before a meal), and those that act slowly and for a long time (taken once or twice a day to keep glucose levels stable). Many diabetics are prescribed both forms of insulin.

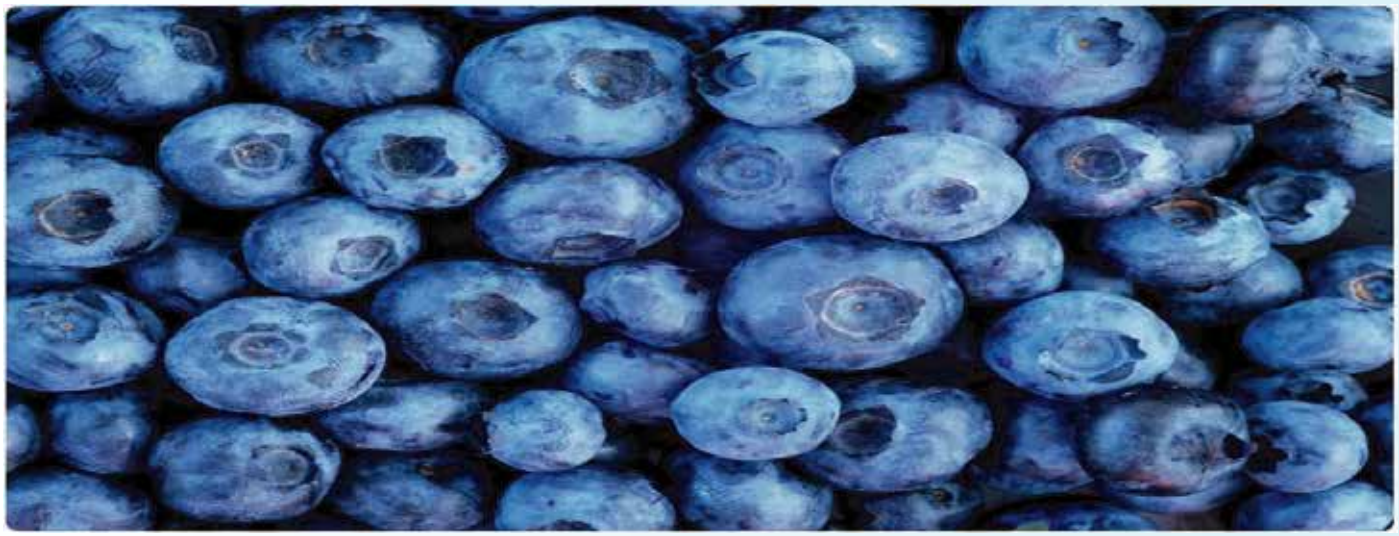
While life-saving, injected insulin is unable to match the body's own insulin for blood-glucose control. When blood-glucose levels fall too low, it can lead to confusion and even coma, and sugar needs to be given by mouth or injection. Chronically raised blood-glucose levels can damage the eyes, kidneys, nerves and heart.

Pumps that constantly monitor blood glucose and adjust the amount of insulin injected are available, and may better control blood-glucose levels. Pancreas transplants are also occasionally available. An insulin pill to replace needles has proved difficult for researchers, as insulin is destroyed in the stomach. For now, insulin injections are indispensable for the health of diabetics across the world.

https://www.rdasia.com/healthsmart/diabetes/All-You-Need-to-Know-About-Insulin

Eating blueberries could reduce your risk of heart disease

Researchers at King's College London have found that eating blueberries may help to lower blood pressure. Daily consumption of the berries over the course of a month was associated with improved blood vessel function and a lowering of systolic blood pressure.



An analysis of the results suggests the beneficial cardiovascular effects are mediated by antioxidants called anthocyanins – the phytochemicals that give blueberries their color.

In the US, high blood pressure (hypertension) is estimated to affect about one in three adults. The National Institutes of Health recommends that people manage the condition by maintaining a healthy diet and weight, not smoking, and engaging in physical activity.

Studies have previously identified foods that appear to improve cardiovascular health including broccoli, pulses, fish, and spinach. Now, Ana Rodriguez-Mateos and team have found that blueberries may also reduce the risk of heart disease due to their antioxidant content.

For the study, the team recruited 40 healthy participants who were randomly assigned to one of two groups. One group consumed a daily drink that contained 200g of blueberries while the other group consumed a control drink that did not contain blueberries.

The researchers measured the participants' blood pressure and flow-mediated dilation (FMD) of the brachial artery, a major blood vessel found in the upper arm. The FMD test shows how much the artery dilates as blood flow increases and is a standard indicator of cardiovascular disease risk.

Next, the team compared drinking the blueberries with drinking a solution that contained purified anthocyanins or a control drink with a vitamin, mineral and fiber content similar to that found in blueberries.

As reported in The Journals of Gerontology, the researchers saw beneficial effects on blood vessel function just two hours after participants had consumed the blueberry drinks. Furthermore, over the course of one month, blood pressure in the blueberry drinking group fell by 5mmHg - a reduction comparable to the effects of anti-hypertensive medication.

The study also found that participants who consumed the drink with purified anthocyanins had improved endothelial function (as measured by FDM), while participants who consumed the control drink saw no such benefit.

"The effects were similar to those of blueberries containing similar amounts of anthocyanins, while control drinks containing fiber, minerals or vitamins had no significant effect," say the researchers.

Source:

Rodriguez-Mateos, A., et al. 2019. Circulating anthocyanin metabolites mediate vascular benefits of blueberries: insights from randomized controlled trials, metabolomics, and nutrigenomics. The Journals of Gerontology: Series A.

https://www.news-medical.net/news/20190225/Eating-blueberries-could-reduce-your-risk-of-heart-disease.aspx

New system for treating colorectal cancer can lead to complete cure

Researchers at Memorial Sloan Kettering Cancer Center in New York City and Massachusetts Institute of Technology in Boston have developed a new, three-step system that uses nuclear medicine to target and eliminate colorectal cancer. In this study with a mouse model, researchers achieved a 100-percent cure rate -- without any treatment-related toxic effects. The study is reported in the November featured article in The Journal of Nuclear Medicine.

Until now, radioimmunotherapy (targeted therapy) of solid tumors using antibody-targeted radionuclides has had limited therapeutic success. "This research is novel because of the benchmarks reached by the treatment regimen, in terms of curative tumor doses, with non-toxic secondary radiation to the body's normal tissues," explains Steven M. Larson, MD, and Sarah Cheal, PhD, of Memorial Sloan Kettering Cancer Center. "The success in murine tumor models comes from the unique quality of the reagents developed by our group, and the reduction to practice methodology, including a theranostic approach that can be readily transferred, we believe, to patients."

Theranostics, a term derived from therapy and diagnostics, is the use of a single agent to both diagnose and treat disease. The theranostic agent first finds the cancer cells, then destroys them, leaving healthy cells unharmed -- minimizing side effects and improving quality of life for patients.

In this study, the glycoprotein A33 (GPA33), an antigen found on over 95 percent of primary and metastatic human colorectal cancers, was targeted with a bispecific antibody for A33 tumor antigen and a second antibody for a small-molecule radioactive hapten, a complex of lutetium-177 (177Lu) and S-2-(4-aminobenzyl)1,4,7,10-tetraazacyclododecane tetra-acetic acid (177Lu-DOTA-Bn).

The DOTA-pretargeted radioimmunotherapy (PRIT) strategy was tested on a mouse model. In randomly selected mice undergoing treatment, serial SPECT/CT imaging was used to monitor treatment response and calculate radiation-absorbed doses to tumors. All the DOTA-PRIT-treated animals tolerated the treatment well, and all 9 assessed mice had no trace of cancer remaining upon microscopic examination. There was also no detectable radiation damage to critical organs, including bone marrow and kidneys.

The 100-percent cure rate in the mouse model is a promising preliminary finding that suggests that anti-GPA33-DOTA-PRIT will be a potent radioimmunotherapy regimen for GPA33-positive colorectal cancer tumors in humans.

According to the Centers for Disease Control and Prevention, colorectal cancer is the third most common cancer affecting both men and women. Each year, approximately 140,000 new cases are diagnosed in the United States and 50,000 people die of the disease.

The applications of this nuclear medicine treatment protocol could extend to other cancers as well. Larson and Cheal state, "If clinically successful, our approach will expand the repertoire of effective treatments for oncologic patients. The system is designed as a 'plug and play' system, which allows for the use of many fine antibodies targeting human tumor antigens and is applicable, in principle, to virtually all solid and liquid tumors in man." They add, "There is a huge unmet need in oncology, especially for the solid tumors, for curative treatments for advanced disease. This includes, colon, breast, pancreas, melanoma, lung, and esophageal, to name a few."

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https://www.sciencedaily.com/releases/2017/11/171102110005.htm

High-Dose Vitamin D: No Help for Bone Health

Surprise in randomized trial: a hint of actual adverse effect from supplementation

by Kristen Monaco, Staff Writer, MedPage Today August 27, 2019

Vitamin D might not be much help for strengthening bones among healthy adults without osteoporosis, Canadian researchers reported, even at doses far higher than recommended daily allowances.

In a clinical trial assessing three levels of daily vitamin D supplementation -- 400 IU, 4,000 IU, and 10,000 IU -- radial volumetric bone mineral density (BMD) was significantly lower among those (ages 55-70) taking higher doses for 3 years, according to Steven Boyd, PhD, of the University of Calgary in Canada, and colleagues:

• 400 IU: reference
• 4,000 IU: -3.9 mg calcium hydroxyapatite (HA)/cm3 (95% CI -6.5 to -1.3)
• 10,000 IU: -7.5 mg HA/cm3 (95% CI -10.1 to -5.0)

No dose of vitamin D supplementation was able to prevent bone loss, as each dose saw a drop in the percentage of radial volumetric BMD over 3 years, they reported in JAMA:

• 400 IU: -1.2%
• 4,000 IU: -2.4%
• 10,000 IU: -3.5%

Boyd's group explained that the findings were unexpected, and that the outcomes were in fact the opposite of what they were anticipating. But they cautioned that "this evidence of high-dose vitamin D having a negative effect on bone should be regarded as hypothesis generating, requiring confirmation with further research. Therefore, the appropriate interpretation of this study is that for maintenance of bone quality in healthy vitamin D-sufficient adults, these results do not support a skeletal benefit of vitamin D doses well above the recommended dietary allowance."

Similar outcomes were noted with tibial BMD, with people on higher doses seeing a larger drop-off after 3 years. Compared with those on a 400 IU/day dose, the 4,000 IU dose group saw a -1.8 mg HA/cm3 (95% CI -3.7 to 0.1) difference in tibial volumetric BMD, while the 10,000 IU group saw a -4.1 mg HA/cm3 (95% CI -6.0 to -2.2) difference.

However, people on every dose saw a drop in average tibial density over the course of the trial compared with baseline values (-0.4% with 400 IU, -1.0% with 4,000 IU, and -1.7% with 10,000 IU).

One possible explanation for these findings could be related to an increase in plasma marker of bone resorption (CTx) paired with suppression of parathyroid hormone. This was particularly true among the highest 10,000 IU/day group who saw sharp decline in parathyroid hormone levels, as well as a sharp increase in plasma CTx levels during the first 18 months of being on high-dose vitamin D, according to the authors.

"High-dose vitamin D without extra calcium supplementation has been associated with increased levels of the active vitamin D metabolite 1, 25(OH)2 vitamin D (calcitriol), and an increase in CTx," they explained. On the other hand, high doses of vitamin D can also suppress parathyroid hormone levels either by directly impacting parathyroid cells or also by bolstering intestinal calcium absorption.

A total of 311 Canadian adults were included in the randomized trial, all of whom were free of osteoporosis at baseline and were ages 55-70. All participants had baseline serum 25-hydroxyvitamin D levels between 12-50 ng/mL (30-125 nmol/L) and baseline serum calcium levels between 8.4-10.2 mg/dL (2.10-2.55 mmol/L).

Vitamin D supplements were provided in the form of drops, and all participants were instructed to take no more than 200 IU of additional vitamin D each day, such as in the form of a multivitamin. Only those who weren't taking in the recommended level of calcium (1,200 mg/day) were provided calcium citrate tablets.

Volumetric BMD was measured with high-resolution peripheral quantitative CT. DXA scans were also used to measure the total hip areal BMD, which showed no changes over time among any of the vitamin D dosage groups.

As for adverse events, people on the highest dose of vitamin D experienced the most instances of hypercalciuria and hypercalcemia -- a serum calcium level more than 10.22 mg/dL (2.55 mmol/L). Other adverse events, such as renal or hepatic dysfunction, falls, low-trauma fractures, and cancer, didn't differ among the dosage groups.

Study limitations included the exclusion of people with osteoporosis or with 25(OH)D levels of <30 nmol/L, who may respond differently to high-dose vitamin D supplementation. Also, the study did not include a placebo control group.

Last Updated August 27, 2019

https://www.medpagetoday.com/endocrinology/osteoporosis/81832

Corporate Social Responsibility: Orion offers 'Orion Medical Scholarship'

As a continuation of Corporate Social Responsibility (CSR), Orion Pharma Ltd. Conducted an inauguration ceremony of "Orion Medical Scholarship" at "Orion Renal & General Hospital" Kalabagan, Dhaka on 27th April, 2019 presided by Director of ORION and Trustee of Orion Pharma Welfare Trust Mrs. Arzuda Karim.

Orion Pharma always appreciates the 'Going-to-be-Doctor' who already got admitted into the medical college and decided to sacrifice their life in exchange of bringing smile to the face of ailing humanity. Orion Pharma Ltd. has decided to be with those masterminds in this voyage towards a noble mission by offering scholarship to those medical students of the country who cannot afford the exorbitant cost of medical education. All together 08 (Eight) students are awarded by Orion Pharma Welfare trust through a random lottery process. These selected students will enjoy all the facilities under the "Orion Medical Scholarship" programme, from their 1st to 5th academic year. All poor and meritorious students from different Govt. Medical Colleges are eligible to apply for this scholarship in the beginning of their first academic year.

Medical students along with their parents were present on this auspicious program and showed heartfelt gratitude to Orion Pharma Management for this noble effort.

Medical Services Department (MSD) of Orion Pharma Ltd. successfully arranged momentous number of Scientific Seminar, Round Table Meeting & Clinical Meeting in different venues of Bangladesh.

SCIENTIFIC SEMINAR

Bangabandhu Sheikh Mujib Medical University, Dhaka

A Scientific Seminar was arranged by the Department of Surgery (Unit-Brown) of BSMMU on 06th July, 2019 in The Cafe Rio Restaurant, Dhanmondi, Dhaka. Dr. Oliul Islam Biplob, RS (Surgery) appeared as the Speaker of the programme.

Dhaka Medical College & Hospital, Dhaka

A Scientific Seminar on "Management of Diabetes in Surgical Practices" was arranged by the Department of Surgery (Unit-II) of Dhaka Medical College & Hospital on 06th April, 2019 in Surgical Conference Room. Dr. Ragib Shahriar, MS (Resident) appeared as the Speaker & Prof. Dr. Tapan Kumar Saha, Head of the Department of Surgery (Unit-II) adorned the seat of Chairperson.

Dhaka Dental College & Hospital, Dhaka

A Scientific Seminar has been organized on 10th April, 2019 by the Department of Dental Pharmacology, Dhaka Dental College & Hospital. "Tooth Preparation" was the key topic of the Seminar which Dr. Syed Faruk Shihab, Associate Professor, Department of Dental Pharmacology discussed on the topic to all the members of the department. Dr. Zahid Rahman, Director, DDCH enlighten the meeting as the Chairperson.

National Institute of Cancer Research & Hospital, Dhaka

A Scientific Seminar was arranged on 15th April, 2019 by the National Institute of Cancer Research & Hospital, Dhaka on "Future Prospect in Cancer Management". Dr. Sharmin Sultana was discussed about the key topic. Prof. Dr. Parveen Shahida Akter, President, Medical Oncology Society of Bangladesh (MOSB) enlightened the seminar as the Chairperson.

Khulna Medical College & Hospital, Khulna

On 16th May, 2019 A Scientific Seminar was arranged by the Gastroenterology Department of Khulna Medical College & Hospital, Khulna at the Conference Room on "Hyperacidity & Its Management". Prof. Dr. Abdul Ahad, Principal & Head, Department of Gastroenterology were present as the Chairperson and he spoke about the management of hyperacidity.

ROUND TABLE MEETING

Kurmitola General Hospital, Dhaka

A Round Table Meeting was arranged on 23th April, 2019 by the Department of Medicine, Kurmitola General Hospital at Fish & Co. Restaurant, Gushan-1, Dhaka. Dr. Md. Abdullah Hel Kafi, Senior Consultant, Department of Medicine adorned the seat of the Chairperson.

Medinova Medical Services, Narayanganj

On 06th September, 2019 A RTM was organized by Medinova Medical Services, Narayanganj in Conference Room. Dr. Shampa Rani Saha, Consultant, Obs & Gynae, Matuail Institute of Child and Mother Health, Dhaka was the Chairperson & Key note speaker of the program. About 120 Doctors attended the session followed by delicious lunch sponsored by OPL.

Centre for The Rehabilitation Of The Paralysed (CRP), Savar

A RTM has been organized on 11th April, 2019 by CRP, Savar. Dr. Sayeed Uddin Helal, Neurosurgeon & Head, Medical Services Wing, CRP, Savar was Chairperson of the Program. 15 (Fifteen) Consultants were present the seminar and enjoyed delicious lunch sponsored by OPL.

Khulna Medical College & Hospital, Khulna

A RTM was arranged on 18th July, 2019 by the Department of Pediatrics of Khulna Medical College & Hospital, Khulna. All members of the departments were present in the program. It was concluded with luscious refreshment sponsored by OPL.

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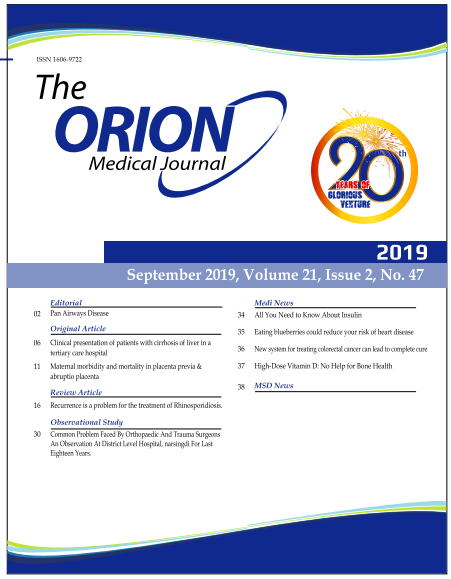
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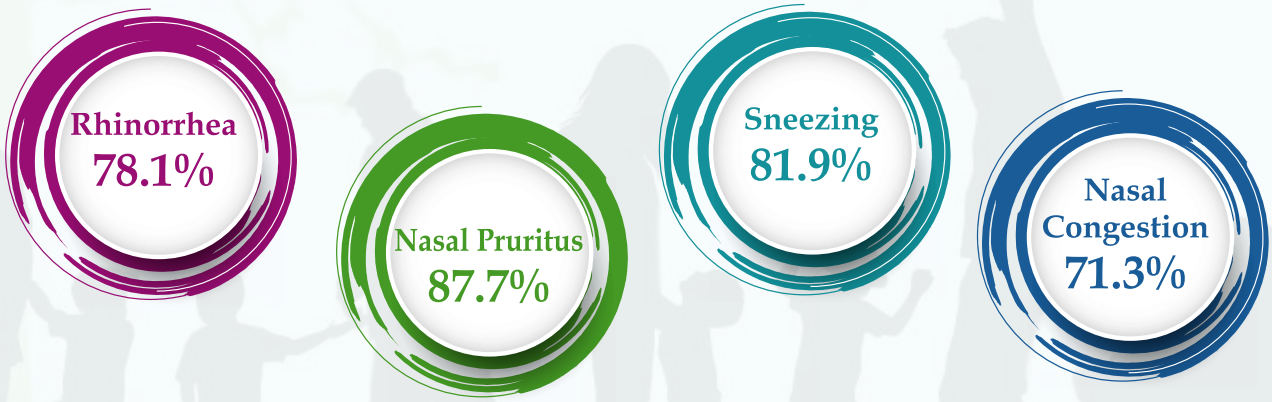

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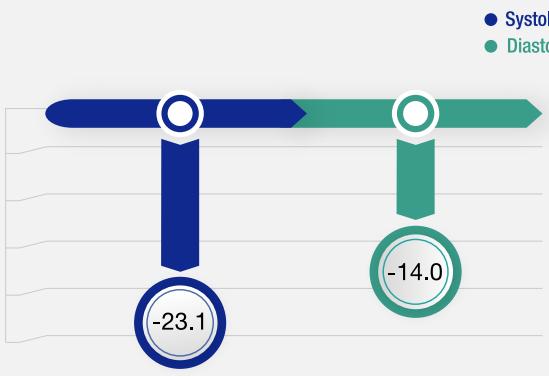

Fig.: Reduction of BP at Day Time with 12 weeks therapy

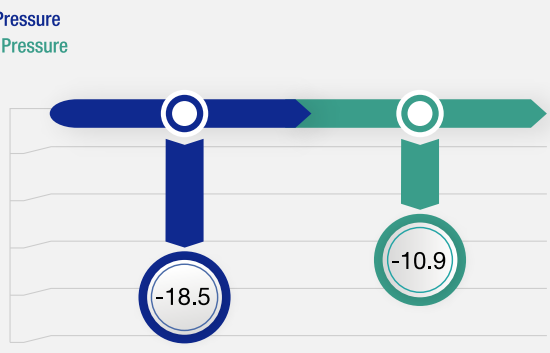

Fig.: Reduction of BP at Night Time with 12 weeks therapy

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