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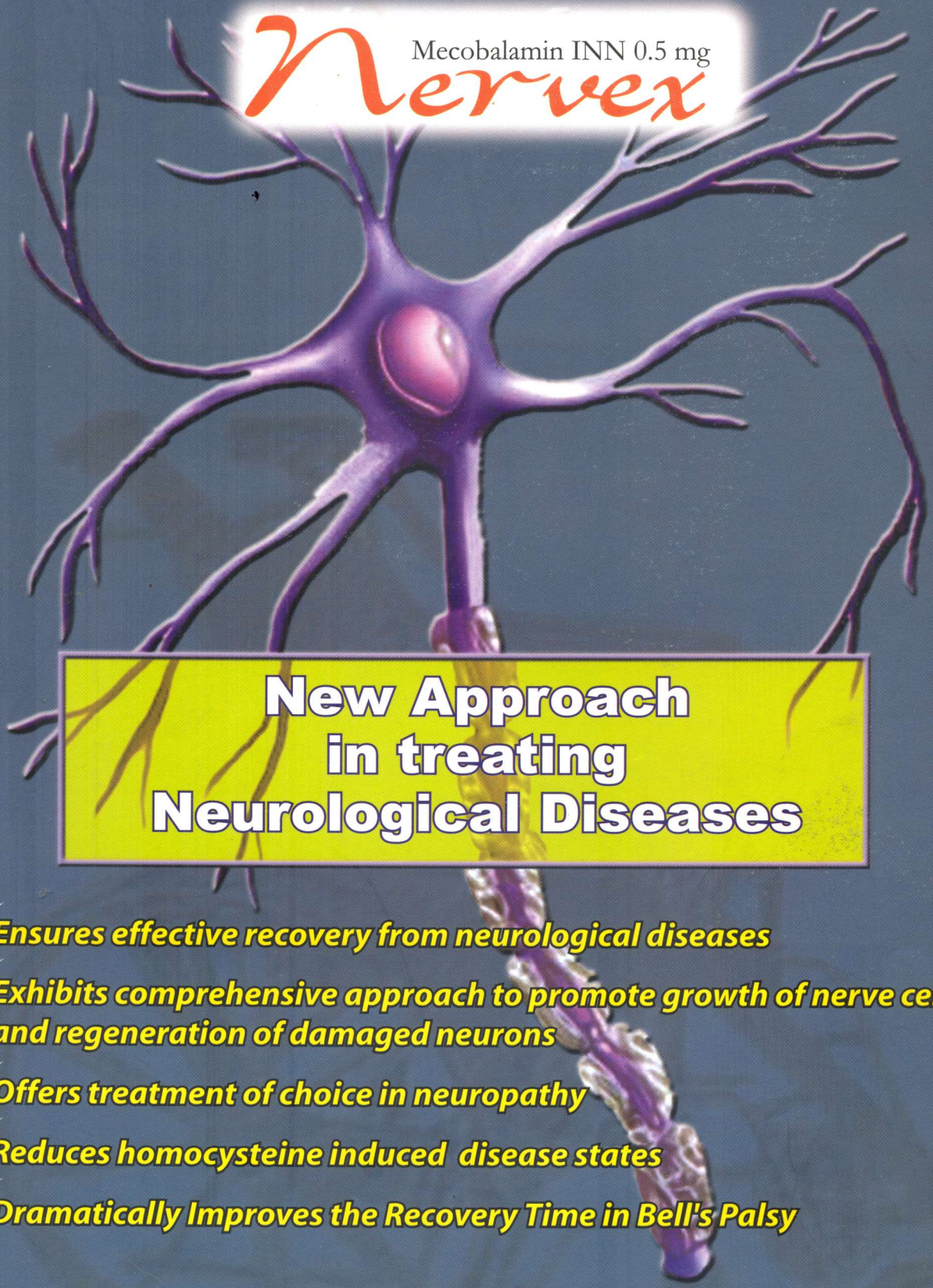

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The ORION Medical Journal

Editor's Choice

New Epoch, The ORION & Oncology

The ORION is enjoying a very elegant animated life since last five years. The journal now unfolds a new era in the spectrum of oncology. Accordingly, this issue is trimmed with two articles of heamatology like 'An overview and treatment advancement of Chronic Myeloid Leukemia' (P-99-103) & 'Prevention and control strategy of Thalassemia in Bangladesh' (P-121-122). The ORION is affirming its cherished readers for further progression in oncology from the next issues.

Apart from this, the editorial of this issue points out a global epidemic of type-2 diabetes in Bangladesh perspective (P- 98).

An original article on ' Prevalence of *Helicobacter pylori* in Bangladesh through rapid urease test (P-104-105) is highlighting the high incidence of *H. pylori* infection in the country. A very interesting article, documenting minimal invasive surgery regarding female stress incontinence (P-119-120), reflects a new treatment hope for the concern population.

A review article on 'smoking in patients with mental disorders: observations in a developing country' (P-106-108) nicely sketches the incidenc of smoking abuse among mental disorder patients. Another article on 'Hypertension: ophthalmologist's perspective' (P-109-111) confers specially on different types of hypertensive retinopathy and the voices of ophthalmologists for hypertension.

The article ' New advancement in the management of post-menopausal osteoporosis' (P-112-114) gives an updated treatment profile for post-menopausal women and another article on 'Anti-lipid measures : An overview ' (P-115-116) clearly correlates the high serum cholesterol level and the risk of atherosclerotic heart disease. Moreover, the article also states the various treatment options for the high risk group.

The review article on 'Perinatal HIV infection' (P-117-118) flushes the global prevalence of AIDS and the treatment option for pregnant HIV infected women & perinatally HIV infected infants. A case report on the use of venlafaxine in the treatment of non-depressed outpatient with generalized anxiety disorder (P-123) delineates the efficacy and tolerability of venlafaxine. Another regular feature of scientific letter (P-124) is focused on Endoscopic Retrograde Cholangio Pancreatogram (ERCP) for managing hepatobilliary and pancreatic diseases.

This issue of 'The ORION' medical journal hopes ameliorating the professional knowledge of the valued readers and also opens a window on heamato oncology in their daily practice.

The opinion and suggestion of the readers are always appreciated to make 'The ORION' medical journal upgraded day by day.

May the Almighty bless all in the spirit of good health.

The ORION wishes a very happy and prosperous life in every moment.

DR. MOHAMMAD ZAKIRUL KARIM
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and Manager,
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Global epidemic of type-2 diabetes : Bangladesh perspectives

Mahtab H[1]

The ORION Vol. 16 Sept. 2003: 98

Increasing trend of diabetes prevalence throughout the world

The recent World Health Organization (WHO) report on the prevalence of diabetes mellitus has presented an alarming picture of a global epidemic of type-2 diabetes (1997). It is posing a serious threat to entire population of the world irrespective of stages of industrialization and development. The increasing prevalence of diabetes mellitus for South East Asian Region (SEAR), was estimated from the observed prevalence in 1995 that projected to 2000 and 2025. This trend observed two folds increase in the developed and almost three folds in the developing nations. Global comparison estimated that highest increase would be observed in SEAR and in Eastern Mediterranean Region (East-Med). Of the total global burden of diabetic patients in 2025, more than twenty percent will be found only in the SEAR.

Increasing trend of diabetes prevalence in Bangladesh

Although there was no large-scale national survey in Bangladesh, several small-scale surveys at intervals have been done over several years. The prevalence of IGT has increase from-0.37% in 1983 to 12.5% in 1996 and that of diabetes from 0.7 in 1983 to 5.2% in 1996. As estimated on the basis of present prevalence rates of (Type 2 diabetes ~ 5.2% and IGT ~12.5%), in the projected population, more than ten million Bangladeshis will suffer form the disease in the year 2005. This is a conservative estimate because the trend of increasing prevalence will make this figure much higher. Diabetes registry in BIRDEM, a referral center, also showed an increasing trend. Only 389 diabetic subjects were registered throughout the year 1960. This figure increased to 1181, 2363, 9641 and 17163 in the year 1970, '80, '90 and 2000, respectively. All these figures indicate that the magnitude of health problems related to diabetes in Bangladesh has been increasing rapidly.

It has been observed that the prevalence of diabetes was significantly higher in the urban than rural community of Bangladesh. So it is likely that the prevalence has been increasing with increasing urbanization. It has also been observed that the complications of diabetes were more frequent among the rural than urban and in poor than rich diabetic population.

Diabetes morbidity and mortality is more prevalent in Bangladeshi population

Although the exact causes or risk factors are not known for increased mortality in Bangladeshis, both genetic predisposition and environmental factors are commonly attributed irrespective of ethnicity.

Genetic factor

Several epidemiological investigations in migrant population observed that diabetes and coronary risk factors are more prevalent in Bangladeshis compared with other South Asian migrants (Indian, Pakistani) settled in United Kingdom and with the native population. It has also been reported that Bangladeshis among the entire South Asians immigrant had highest mortality and attack rate from diabetes and coronary heart diseases. These findings favor the hypothesis that Bangladeshi population is genetically more prone to develop diabetes and its complications than other SEAR population.

Environmental factors

Obesity, physical inactivity, food habit, life-style are known risk factors related to diabetes. Obesity, diabetes, hypertension and dyslipidemia - popularly known as "insulin resistance syndrome or syndrome - X" are the major risk for developing Atherosclerosis that eventually leads to coronary heart disease (CHD) and peripheral vascular disease (PVD). It is well known that CHD is the cause of highest mortality in the world. Likewise, PVD is the leading cause of lower limb amputation. We have no estimate related to such morbidity and mortality for Bangladeshi population.

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Director
Clinical Service, Research & Academy, BIRDEM

In addition to known environmental factors, maternal under nutrition and low birth weight (LBW) is getting more importance as an independent risk factor for developing diabetes and other metabolic diseases. Some studies observed that LBW and malnutrition in infancy or early childhood may lead to diabetes hypertension and CHD. It is hypothesized that under-nutrition either in terms of trace element or vitamin deficiency (micronutrient deficiency) or of chronic energy deficiency (CED) may lead to these disorders. More recent reports are even more important, relevant to disproportionate increase of diabetes, and cardiac diseases in under-privileged communities.

In Bangladesh, low birth weight (LBW), under-nutrition in pregnant mothers, infection and malnutrition in early childhood are very frequent. These environmental insults to the pregnant mother and growing infants and children, resulting in short stature, are so common that these are almost always considered as current problems and never thought of their future consequences. It is important to note that short stature was found to be related to diabetes and the major determinant of short stature is the low birth weight and uneven growth during childhood. In our population too, short stature in women was found to be significantly associated with diabetes.

Bangladesh is one of the least developed countries. A large proportion of its population is exposed to under-nutrition. In this context of nutritional status, it appears that more and more people are likely to develop diabetes and other cardiovascular diseases in future. So, further importance should be given to the fact that the maternal and child health care may be the key to the prevention of diabetes, hypertension and coronary heart disease in Bangladesh.

Increased prevalence poses serious threat to existing health care system in Bangladesh

It is already reported that increasing prevalence of diabetes and its complications in the developing communities would pose a real threat in respect to their existing health care service. As with the increasing number of diabetic patients more and more will need specialized diabetic care, and failure to provide the care they will develop more complications like CHD, diabetic foot, chronic renal failure and blindness.

BIRDEM is a unique referral center for diabetes health care; it has been working as a WHO-collaborating center for diabetes care in South East Asian Region since 1982. This is a unique referral model, not only in Asia but also for the entire third world countries to undertake for the comprehensive care of a non-communicable disease like diabetes. About 1500-2000 diabetic patients attend BIRDEM-OPD everyday either for registration or for follow-up. The objective of follow up is to control glycemia, lipid profiles and hypertension, and to maintain body weight. Effective follow up care prevents most disabling and life threatening complication. Though this center is doing well it can not shoulder the national burden of diabetic care. The capacity of effective follow up system of BIRDEM has already been exceeded. Considering the higher prevalence in our population it may be concluded that the increasing need of diabetic health care at present and in future must be given priority to reduce the ensuing diabetes morbidity and mortality. Therefore, all concerned personnel like health care planners and health care providers must give priority in this regard.

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Chronic Myeloid Leukaemia (CML) : An overview and advancement in the treatment

Yunus A B M[1], Sohel S I[2]

The ORION Vol. 16 Sept. 2003: 99 -103

Background

Chronic myelogenous leukemia (CML) is a myeloproliferative disorder characterized by increased proliferation of the granulocytic cell line without the loss of their capacity to differentiate. Consequently, the peripheral blood cell profile shows an increased number of granulocytes and their immature precursors, including occasional blast cells. The Philadelphia Chromosomes is present in more than 85% cases. This translocation relocates an oncogene called abl from the long arm of chromosome 9 to the long arm of chromosome 22 in the bcr region. The presence of bcr-abl rearrangement is the hallmark of CML, although this rearrangement has also been described in other diseases. It is considered diagnostic when present in a patient with clinical manifestations of CML.

Age & Frequency

In general, this disease occurs in the fourth and fifth decades of life.Younger patients aged 20-29 years may be affected and may present with a more aggressive form, such as in accelerated phase or blast crisis.Uncommonly, CML may appear as a disease of new onset in elderly individuals.

CML accounts for 20% of all leukemia's affecting adults. It typically affects middle-aged individuals. Although uncommon, the disease also occurs in younger individuals. Increased incidence was reported among individuals exposed to radiation in Nagasaki and Hiroshima after the dropping of the atomic bomb.

Mortality/Morbidity

Generally, 3 phases of the disease are recognized. The general course of the disease is characterized by an eventual evolution to a refractory form of acute myelogenous or, occasionally, lymphoblastic leukemia. The median survival of patients using older forms of therapy was 3-5 years.

Most patients present in the chronic phase, characterized by splenomegaly and leukocytosis (see Image 1) with generally few symptoms.

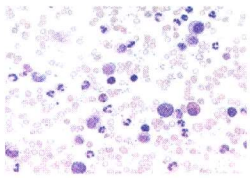

Image-1

This blood film at 400x magnification demonstrates leukocytosis with the presence of precursor cells of the myeloid lineage. In addition, basophilia, eosinophilia, and thrombocytosis can be seen (photographed by U. Woermann, MD, Division of Instructional Media, Institute for Medical Education, University of Bern, Switzerland).

This phase is easily controlled by medication. The major goal of treatment during this phase is to control symptoms and complications resulting from anemia, thrombocytopenia, leukocytosis, and splenomegaly. Newer forms of therapy aim at delaying the onset of the accelerated or blastic phase.

After an average of 3-5 years, the disease usually evolves into the blast crisis, which is marked by an increase in the bone marrow or peripheral blood blast count or by the development of soft tissue or skin leukemic infiltrates. Typical symptoms are due to increasing anemia, thrombocytopenia, basophilia, a rapidly enlarging spleen, and failure of the usual medications to control leukocytosis and splenomegaly. The manifestations of blast crisis are similar to those of acute leukemia. Treatment results are unsatisfactory, and most patients succumb to the disease once this phase develops. In approximately two thirds of cases, the blasts are myeloid. However, in the remaining one third of patients, the blasts exhibit a lymphoid phenotype, further evidence of the stem cell nature of the original disease. Additional chromosomal abnormalities usually are found at the time of blast crisis, including additional Ph chromosomes or other translocations.

In many patients, an accelerated phase occurs 3-6 months before the diagnosis of blast crisis. Clinical features in this phase are intermediate between the chronic phase and blast crisis.

History

The clinical manifestations of CML are insidious and often are discovered accidentally when an elevated WBC count is revealed by a routine blood count or when an enlarged spleen is revealed during a general physical examination.

Nonspecific symptoms of tiredness, fatigue, and weight loss may occur long after the onset of the disease. Loss of energy and decreased exercise tolerance may occur during the chronic phase after several months.

Symptoms related to enlargement of the spleen and/or the liver often are present.

The large spleen may encroach on the stomach and cause early satiety and decreased food intake. Left upper quadrant abdominal pain described as "gripping" may occur due to spleen infarction. The enlarged spleen also may be associated with a hypermetabolic state, fever, weight loss, and chronic fatigue.

The enlarged liver may contribute to the patient's weight loss.

Low-grade fever and excessive sweating related to hypermetabolism may occur in some patients.

The disease has 3 clinical phases, and it follows a typical course of an initial chronic phase, in which the disease process is easily controlled; followed by a transitional and unstable course (accelerated phase); and, finally, a more aggressive course (blast crisis), which usually is fatal.

The majority of patients are diagnosed while still in the chronic phase. The WBC count usually is controlled with medication (hematologic remission). This phase varies in duration depending on the maintenance therapy used. It usually lasts 2-3 years with Hydroxyurea or busulfan therapy and has lasted for longer than 9.5 years in patients who respond well to alpha-interferon therapy.

Some patients progress to a transitional or accelerated phase, which may last for several months. The survival of patients diagnosed in this phase is 1-1.5 years. This phase is characterized by poor control of the blood counts with myelosuppressive medication and the appearance of peripheral blast cells (≥15%), promyelocytes (≥30%) (see Image 3), basophils (≥20%), and platelet counts less than 100,000 cells/µL unrelated to therapy. Usually, the doses of the medications need to be increased; splenomegaly may not be controllable by medications, and anemia can worsen. Bone pain and fever, as well as an increase in bone marrow fibrosis are harbingers of the last phase.

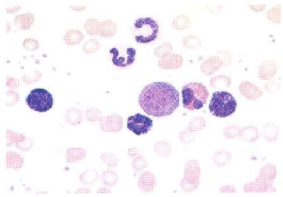

Image-3

Blood film at 1000x magnification shows a promyelocyte, an eosinophil, and 3 basophils (photographed by U. Woermann, MD, Division of Instructional Media, Institute for Medical Education, University of Bern, Switzerland)

Acute phase, or blast crisis, is similar to acute leukemia, and survival is 3-6 months at this stage. Bone marrow and peripheral blood blasts of 30% or more are characteristic. Skin or tissue infiltration also defines blast crisis. Cytogenetic evidence of another Ph-positive clone (double) or clonal evolution (other

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cytogenetic abnormalities such as trisomy 8, 9, 19, or 21, isochromosome 17, or deletion of Y chromosome) usually is present.

In some patients who present in the accelerated, or acute, leukemia phase of the disease (skipping the chronic phase), bleeding, petechiae, and ecchymoses may be the prominent symptoms. In these situations, fever usually is associated with infections.

Physical

Splenomegaly is the most common physical finding in patients with CML.

In more than half of patients with CML, the spleen extends more than 5 cm below the left costal margin at time of discovery.

The size of the spleen correlates with the peripheral blood granulocyte counts (see Image 2), with the biggest spleens being observed in patients with high white cell counts.

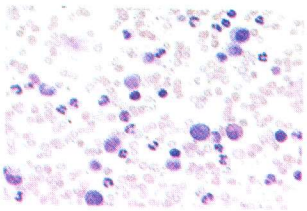

Image-2

This blood film at 1000x magnification demonstrates the whole granulocytic lineage, including an eosinophil and a basophil (photographed by U. Woermann, MD, Division of Instructional Media, Institute for Medical Education, University of Bern, Switzerland

Very large spleen usually is a harbinger of transformation into an acute blast crises form of the disease.

Hepatomegaly also occurs, although less commonly than splenomegaly. Hepatomegaly usually is part of the extramedullary hematopoiesis occurring in the spleen.

Physical findings of leukostasis and hyperviscosity can occur in some patients with extraordinary elevation of their WBC counts, exceeding 300,000-600,000 cells/µL. Upon funduscopy, the retina may show papilledema, venous obstruction, and hemorrhages.

Causes

The initiating factor of CML still is unknown, but exposure to irradiation has been implicated, as observed in the increased incidence among survivors of the atomic bombing of Hiroshima and Nagasaki.

Other agents, such as benzene, are suspected causes.

D/D

Agnogenic Myeloid Metaplasia with Myelofibrosis
Myelodysplastic Syndrome
Myeloproliferative Disease
Polycythemia Vera

Other problems to be considered

Leukemoid reactions from infections (chronic granulomatous, such as tuberculosis)
Myelodysplasia
Tumor necrosis
Essential thrombocytosis/thrombocythemia
Chronic neutrophilic leukemia
Chronic myelomonocytic leukemia
Acute myeloid leukemia

Lab studies

Peripheral blood findings show a typical leukoerythroblastic blood picture, with circulating immature cells from the bone marrow (see Image 4).

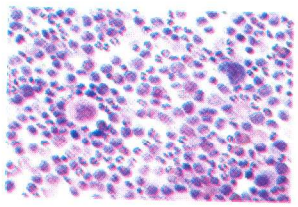

Image-4

This bone marrow film at 400x magnification demonstrates clear dominance of granulopoiesis. The number of eosinophils and megakaryocytes is increased (photographed by U. Woermann, MD, Division of Instructional Media, Institute for Medical Education, University of Bern, Switzerland).

Increase in mature granulocytes and normal lymphocyte counts (low percentage due to dilution in the differential count) results in a total white cell count of 20,000-60,000 cells/µL. A mild increase in basophils and eosinophils is present and becomes more prominent during the transition to acute leukemia.

These mature neutrophils, or granulocytes, have decreased apoptosis (programmed cell death), resulting in accumulation of long-lived cells with low or absent enzymes, such as alkaline phosphatase. Consequently, the leukocyte alkaline phosphatase (LAP) stains very-low-to-absent in most cells, resulting in a low score.

Early myeloid cells such as myeloblasts, myelocytes, metamyelocytes, and nucleated red blood cells commonly are present in the blood smear, mimicking the findings in the bone marrow. The presence of the different mid stage progenitor cells differentiates this condition from the acute myelogenous leukemias, in which a leukemic gap (maturation arrest) or hiatus exists that shows absence of these cells.

A mild-to-moderate anemia is very common at diagnosis, which usually is normochromic and normocytic.

The platelet counts at diagnosis can be low, normal, or even increased in some patients (>1 million in some).

Bone marrow characteristically is hypercellular, with expansion of the myeloid cell line (eg, neutrophils, eosinophils, basophils) and its progenitor cells. Megakaryocytes (see Image 5) are prominent and may be increased. Mild fibrosis often is seen in the reticulin stain.

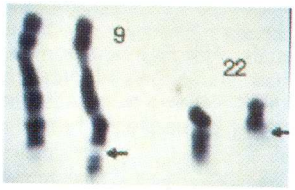

Image-5

The Philadelphia chromosome, which is a diagnostic karyotypic abnormality for chronic myelogenous leukemia, is shown in this picture of the banded chromosomes 9 and 22; showing the result of the reciprocal translocation of 22q to the lower arm of 9 and 9q (c-abl to a specific breakpoint cluster region [bcr] of chromosome 22 indicated by the arrows (photo courtesy of Dr Peter C. Nowell, Department of Pathology and Clinical Laboratory of the University of Pennsylvania School of Medicine).

Cytogenetic studies of the bone marrow cells, and even peripheral blood, should reveal the typical Philadelphia (Ph1) chromosome, which is a reciprocal translocation of chromosomal material between chromosomes 9 and 22. This is the hallmark of CML, found in almost all patients with CML, and is present in CML throughout its entire clinical course.

The Philadelphia translocation is the translocation of the cellular oncogene c-abl from the 9 chromosome, which encodes for a tyrosine protein kinase, with a specific breakpoint cluster region (bcr) of chromosome 22, resulting in a chimeric bcr-c-abl messenger RNA that encodes for a mutation protein with much greater tyrosine kinase activity compared to the normal protein (see Image 5). The latter presumably is responsible for the cellular transformation in CML. This m-RNA can be detected by polymerase chain reaction (PCR) in a sensitive test that can detect it in a few cells. This is useful in monitoring minimal residual disease (MRD) during therapy.

Karyotypic analysis of bone marrow cells requires the presence of a dividing cell without loss of viability because the material requires that the cells go into mitosis to obtain individual chromosomes for identification after banding, which is labor intensive and a slow process. The new technique of fluorescence in situ hybridization (FISH) (see Image 6) uses labeled probes that are hybridized to either metaphase chromosomes or interphase nuclei, and the hybridized probe is detected with fluorochromes. This technique is a rapid and sensitive means of detecting recurring numerical and structural abnormalities.

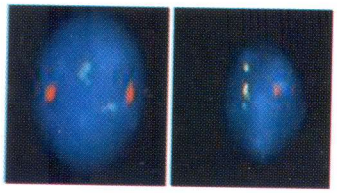

Image-6

This is fluorescence in situ hybridization (FISH) using unique-sequence double-fusion DNA probes for BCR (22q11.2) in red color and c-abl (9q34) gene regions in green. The abnormal BCR/abl fusion present in positive Philadelphia chromosome cells demonstrates the presence of yellow color (right panel) compared to control (left panel) (used with permission, copyright, Emmanuel C. Besa, MD)

Two forms of the bcr-abl mutation are present, depending on the location of their joining regions on bcr 3' domain. Approximately 70% of patients who have the 5' DNA breakpoint have a b2a2 RNA message, and 30% of patients have a 3'DNA breakpoint and a b3a2 RNA message. The latter is associated with a shorter chronic phase, shorter survival, and thrombocytosis.

CML should be differentiated from Ph-negative diseases with negative PCR for bcr-abl m-RNA. These diseases include other myeloproliferative disorders and chronic myelomonocytic leukemia, which now is classified with the MDSs.

Additional chromosomal abnormalities, such as an additional or double Ph+ or trisomy 8, 9, 19, or 21, isochromosome 17, or deletion of Y chromosome, have been described as the patient enters a transitional form or accelerated phase of the blast crisis as the Ph chromosome persists.

Patients with conditions other than chronic-phase CML, such as newly diagnosed acute lymphocytic leukemia (ALL) or nonlymphocytic leukemia (ANLL), also may have a positive Ph chromosome. Some consider this the blastic phase of CML without a chronic phase. The chromosome rarely has been found in patients with other myeloproliferative disorders, such as polycythemia vera or essential thrombocythemia, but these probably are misdiagnosed CML. It rarely has been observed in myelodysplastic syndrome.

Other laboratory abnormalities include hyperuricemia, which is a reflection of high bone marrow cellular turnover and markedly elevated serum B12-binding protein (TC-I). The latter is synthesized by the granulocytes and reflects the degree of leukocytosis.

Imaging Studies

Typical hepatomegaly and splenomegaly may be imaged by using a liver/spleen scan. Most often, these are so obvious that radio imaging is not necessary.

Histologic Findings

Diagnosis is based on the histopathologic findings in the peripheral blood and the Ph1 in the bone marrow cells.

Medical Care

The 3-fold goals of treatment of CML have changed markedly in the past 10 years; they are to achieve a hematologic remission (normal CBC) and physical examination (no organomegaly), to achieve cytogenetic remission (normal chromosome returns with 0% Ph-positive cells), and, most recently, to achieve molecular remission (negative PCR for the mutational bcr-abl m-RNA). The latter is an attempt for cure and prolongation of patient survival.

A new approach to treatment of this disease is to directly inhibit the molecular cause of the disease, ie, using a protein-tyrosine kinase inhibitor that inhibits the bcr-abl tyrosine kinase, the constitutive abnormal tyrosine kinase created by the Philadelphia chromosome translocation abnormality.

STI571 or imatinib mesylate inhibits proliferation and induces apoptosis by inhibiting tyrosine kinase activity in cells positive for bcr-abl and also fresh leukemic cells in CML positive for the Philadelphia chromosome. This drug was approved rapidly by the US Food and Drug Administration because of the following results:

In patients in the chronic phase who were previously treated with interferon and whose treatment failed or who were unable to tolerate therapy, a complete hematologic remission was achieved in 88% (532 patients), with a major cytogenetic response (ie, complete remission was 0%, partial remission was 1-35%, Ph+ metaphases) in 49% of patients.

Among 235 patients in the accelerated phase, the hematologic response was 65% (28% complete remission), and the cytogenetic response was 21%. Patients in myeloid blast crisis (260 patients) achieved a 26% hematologic response (4% complete remission) and a 13.5% major cytogenetic response (5% complete remission).

The decision to choose the initial treatment or primary therapy for chronic-phase CML is difficult since the advent of the tyrosine kinase inhibitor Imatinib (formerly STI571).

For patients with chronic-phase CML, Imatinib at 400 mg/d is the best candidate for primary therapy since it induces complete hematologic response in almost all patients and causes a high cytogenetic response rate, although overall survival data comparing it to interferon are still pending.

Treatment of CML patients in the accelerated phase or in blast crisis has been dismal. However, recent data show that Imatinib can induce hematologic response in 52-82%, but the response is sustained for at least 4 weeks in 31-64%.

Complete response is lower at 7-34%. Karyotypic response can occur in 16-24%, and complete cytogenetic response is observed in only 17%. Higher doses (ie, 600 mg/d) resulted in improved response rates, cytogenetic response, and disease free and overall survival.

Myelosuppressive therapy, which was formerly the mainstay of converting a patient with CML from an individual with an uncontrolled initial presentation to one with hematologic remission with normalization of the physical and laboratory findings, may soon disappear as the new agents prove to be more effective with fewer adverse events and longer survival.

Hydroxyurea, an inhibitor of deoxynucleotide synthesis, is the most common myelosuppressive agent used to achieve hematologic remission. The initial blood count is monitored every 2-4 weeks, and the dose is adjusted depending on the white cell and platelet counts. Most patients enter hematologic remission within 1-2 months. This medication has a short duration for myelosuppression, so even if the counts go lower than intended, stopping or decreasing doses usually controls the blood counts. Maintenance with hydroxyurea rarely results in cytogenetic or molecular remissions.

Busulfan is an alkylating agent that traditionally has been used to keep the white cell counts less than 15,000 cells/µL. However, the myelosuppressive effects may occur much later and persist longer, making maintaining the numbers within normal limits more difficult. Long-term use can cause pulmonary fibrosis, hyperpigmentation, and prolonged marrow suppression lasting for months.

Leukapheresis using a cell separator can lower WBC counts rapidly and safely in patients with WBC counts of higher than 300,000 cells/µL, and it can alleviate acute symptoms of leukostasis, hyperviscosity, and tissue infiltration. Leukapheresis usually reduces the white cell count only temporarily and often is combined with cytoreductive chemotherapy for more lasting effects.

Alpha interferon is the treatment of choice for the majority of patients with CML who are too old or do not have a matched bone marrow donor. This is given at an average of 3-5 million international units (MIU) per day subcutaneously after hematologic remission with hydroxyurea.

The cytogenetic response is monitored every 3-6 months by karyotyping or by FISH to count the percentage of bone marrow cells with Ph-positive cells.

The goal is 100% normal cells after 1-2 years of therapy. Patients with MRD (bcr-abl positive) should be kept on maintenance therapy as long as MRD exists.

Cytogenetic improvement has been observed in 70% of patients treated for longer than 3 months, with the median of Ph'-positive cells declining from 100% to 65% (range 0-95%). Complete suppression of Ph' chromosome was observed in 20% of patients.

Bone marrow transplantation (BMT) should be considered early in young patients (355 y) who have a matched sibling donor.

All siblings should be typed for human leukocyte antigen (HLA) A, B, and DR. If no match is available, the HLA type can be entered into a bone marrow registry for a completely matched unrelated donor.

The mortality rate of BMT is 10-20% or less with a matched sibling and 30-40% with an unrelated donor. The bone marrow registry approximates the cure rate for patients with CML at 50%.

Transplantation is recommended within 1 year of diagnosis or after a 1-year trial of interferon therapy without a complete or significant cytogenetic remission.

Most patients with MRD after transplantation may require interferon maintenance therapy anyway, or they may require reinfusion of T cells collected from the donor.

Treatment decisions involving the use of interferon, BMT, or investigative options for younger patients with CML are extremely complex and in constant flux. Individualized decisions should be made in conjunction with consultation with physicians familiar with the recent literature.

Surgical Care

Splenectomy and splenic irradiation have been used for large painful spleens, usually in the late phase of the disease.

This rarely is needed in patients whose disease is well controlled.

Some authors believe that splenectomy accelerates the onset of myeloid metaplasia in the liver. Splenectomy carries high perioperative morbidity and mortality due to bleeding or thrombotic complications.

Consultations

These patients should be under the care of hematologists and oncologists. Selected patients should be seen by experts in a bone marrow transplantation program in a tertiary care center.

The medications used for patients in chronic-phase CML include a myelosuppressive agent to achieve hematologic remission, which requires 1-2 months of treatment. Once the patient goes into hematologic remission, the goal of treatment is to suppress the Ph-positive hematopoietic clone in the bone marrow for a cytogenetic remission and, hopefully, a molecular remission. This entails the use of alpha interferon or a BMT.

The following factors determine the treatment: (1) age of the patient, (2) HLA-matched donor willing to donate bone marrow, and (3) the Sokal score. The Sokal score falls into 3 categories: (1) low risk is less than 0.8, (2) intermediate risk is 0.8-1.2, and (3) high risk is greater than 1.2.

The Sokal score is calculated for patients aged 5-84 years by hazard ratio = exp (0.011 (age - 43) + 0 .0345 (spleen - 7.5 cm) + 0.188 [(platelets/700)^2 -0563] + 0.0887 (% blasts in blood - 2.1).

The choice of treatment is determined by the prognosis and the age of the patient. Most patients have no matched donor or are too old for BMT; alpha interferon is the drug of choice in these patients.

Drug Category: *Myelosuppressive agents*

To control the underlying hyperproliferation of the myeloid elements, a myelosuppressive agent is necessary to bring down the WBC counts and, occasionally, the elevated platelet counts. The size of the spleen correlates with the WBC counts, and it shrinks as the WBC counts approach normal range. Also, the intermediate and myeloblast cells disappear from the circulation.

Hydroxyurea

Inhibitor of deoxynucleotide synthesis and DOC for inducing a hematologic remission in CML. This agent is less leukemogenic than alkylating agents such as busulfan, Alkeran, or chlorambucil. Myelosuppressive effects last a few days to a week and are easier to control than with alkylating agents; busulfan is associated with prolonged marrow suppression and also can cause pulmonary fibrosis. Adult dose: Initially dose- 30 mg/kg/d at an average of 1000-1500 mg/d PO in 500-mg tablets can be given at higher doses in patients with extremely high WBC counts (>300,000) and adjusted accordingly as counts fall and platelet counts drop; the dose can be given as a single daily dose or divided into 2-3 doses at higher dose ranges Contraindications:Documented hypersensitivity; thrombocytopenia is dose-limiting factor in using hydroxyurea; do not administer if platelet counts <50,000; administer under advisement in patients with counts <100,000/µL; anemia may be aggravated by medications, and concomitant irradiation is contraindicated. Interactions: Neurotoxicity can occur when administered concurrently with fluorouracil. In Pregnancy - Safety for use during pregnancy has not been established. Precautions: Monitor blood counts and adjust doses accordingly; some patients may be sensitive and present with fever, chills, and elevation of liver enzymes, which disappear after stopping drug; skin ulcers may be seen in long-term use of drug; caution in patients diagnosed with renal impairment

Busulfan

Potent cytotoxic drug that, at recommended dosage, causes profound myelosuppression. As alkylating agent, mechanism of action of active metabolites may involve cross-linking of DNA, which may interfere with growth of normal and neoplastic cells. Adult dose: 4-8 mg/d PO; may administer up to 12 mg/d; maintenance dosing range is 1-4 mg/d to 2 mg/wk; discontinue regimen when WBC reaches 10,000-20,000 cells/mm^3; resume therapy when WBC reaches 50,000/mm^3. Pediatric dose: 0.06-0.12 mg/kg/d or 1.8-4.6 mg/m^3/d; titrate dose to maintain WBC >40,000/mm^3; reduce dose by 50% if WBC is 30,000-40,000/mm^3; discontinue if WBC <20,000/mm^3.

Contraindications: Documented hypersensitivity; severely depressed bone marrow function; women who are breast feeding; failure to respond to previous treatment. Interactions: CYP3A3/4 enzyme substrate; acetaminophen, cyclophosphamide, itraconazole, and thioguanine may increase toxicity; phenytoin may decrease levels. In Pregnancy-Contraindicated in pregnancy. Precautions: Regularly examine hematologic profile (particularly neutrophils and platelets) to monitor for hematopoietic suppression; may cause pulmonary fibrosis; if WBC count is high, hydration and allopurinol should be used to prevent hyperuricemia.

Drug Category: *Tyrosine kinase inhibitors*

Imatinib mesylate or STI571 in oral formulation is an agent with strong tyrosine kinase inhibition activity of the bcr-abl abnormality in all phases of CML.

Imatinib mesylate

Specifically designed to inhibit tyrosine kinase activity of the bcr-abl kinase in Ph+ leukemic CML cell lines. Well absorbed after oral administration, with maximum concentrations achieved within 2-4 hours. Elimination is primarily in feces in form of metabolites. Adult dose: In chronic phase- 400 mg/d PO with food and large glass of water; may increase to 600 mg/d if no severe adverse effects or severe non-leukemia-related neutropenia or thrombocytopenia, disease continues to progress (any time), hematologic response is not satisfactory (after at least 3 month treatment), or a loss of previously achieved hematologic response occurs.Accelerated phase or blast crisis: 600 mg/d PO with food and large glass of water; may increase to 800 mg/d (400 mg bid) if no severe adverse effects or severe non-leukemia-related neutropenia or thrombocytopenia, disease continues to progress (any time), hematologic response is not satisfactory (after at least 3 month treatment), or a loss of previously achieved hematologic response occurs. Pediatric dose Not established

Contraindications: Documented hypersensitivity. Interactions: CYP3A4 inhibitors (ketoconazole increases distribution of imatinib); CYP3A4 substrates (simvastin increases maximum concentration of imatinib by a 2-3.5-fold factor); CYP3A4 inducers (phenytoin decreases AUC by approximately one fifth of typical AUC); likely to increase blood levels of drugs that are substrates of CYP2C9, CYP2D6, and CYP3A4/5. In Pregnancy-Contraindicated in pregnancy.Precautions: Dose must be reduced if grade 3-4 neutropenia or thrombocytopenia develops or levels of transaminases or bilirubin become elevated

Drug Category: *Interferons*

Alpha, beta, and gamma are the 3 types known to date. Alpha group has been found to inhibit propagation of Ph-positive hematopoietic clone, allowing return of normal cells in the bone marrow.

Interferon alfa-2a or alfa-2b

Both are recombinant alpha interferons with some minor amino acid differences but are considered equivalent modalities in the treatment of CML. INF alfa2a comes in single (3-MIU, 6-MIU, 9-MIU, 36-MIU strength) or multidose vials (9-MIU, 18-MIU strength). INF alfa2b comes in multidose pens of 18 MIU (delivers 3 MIU/dose), 30 MIU (5 MIU/dose), and 60 MIU (10 MIU/dose) with each pen good for 6 doses.Elderly patients who cannot tolerate adverse effects of alpha interferon may be started at one half the recommended starting dose. Adult dose: Approximately 5 million/m^2/d SC until complete cytogenetic remission (100% Ph-negative BM cells by FISH)Remission can occur within 1-2 years from onset of therapy; an individual maximally tolerated dose can be obtained by starting at 3 million or 1.5 million qd and increasing by 3 million/d each month until tolerance or

cytogenetic remission. Pediatric dose: Not established. Contraindications: Documented hypersensitivity.
Interactions: Theophylline may increase toxicity; cimetidine may increase antitumor effects; zidovudine and vinblastine may increase toxicity. In Pregnancy - Safety for use during pregnancy has not been established. Precautions: Elderly patients do not tolerate treatment as well as younger individuals; caution in brain metastases, severe hepatic or renal insufficiencies, seizure disorders, multiple sclerosis, or compromised CNS; can cause severe mood disturbance in some patients, including clinical depression; caution in history or predisposition to depression; most acute adverse effects are flulike symptoms, which can be alleviated by taking acetaminophen for fever and muscle aches and giving injections at night before bedtime; occasionally, patients may have some psychiatric effects (psychoses) or intolerance due to chronic fatigue; liver function test may be affected with liver enzyme elevation, which is alleviated by decreasing total dose

Further Inpatient Care

Allogeneic bone marrow or stem cell transplantation is the best treatment for cure of this disease
this procedure has a high mortality rate because of the induction and long-term complications. Several types of BMT are available, and most of the data are in allogeneic transplants from an HLA-matched sibling donor and a few syngeneic from an identical twin. The data show that allogeneic transplants have better results than syngeneic transplants because of some graft-versus-leukemia effects.
Allogeneic BMT currently is the only proven cure for CML. Ideally, it should be performed in the chronic phase of the disease rather than in transformation phase or in blast crisis. Candidate patients should be offered the procedure if they have a matched or single-antigen-mismatched related donor available. In general, younger patients fare better than older patients.
Allogeneic BMT with matched unrelated donors has yielded very encouraging results in this disease. The procedure has a higher incidence of early and late graft failures (16%), grade III-IV acute graft-versus-host disease (GVHD) (50%), and extensive chronic GVHD (55%). The overall survival rate ranges from 31-43% for those younger than 30 years and from 14-27% for older patients. Benefits and risks should be assessed carefully with the patient.
Autologous BMT is investigational, but, recently, chemotherapy combinations or interferon have been found to induce a cytogenetic remission and allow harvesting of Ph-negative CD34 hematopoietic stem cells from the patient's peripheral blood.
Other attempts to collect specifically normal stem cells currently are being investigated.

Prognosis

Historically, the median survival of patients with CML from time of diagnosis was 3-5 years, and no known therapy was shown to alter this survival rate until the onset of new modes of treatment. As treatment improved, the need to stage patients according to their prognosis became necessary to determine justification of procedures with high morbidity and mortality, such as BMT.
Staging of patients comes from several analyses using multiple variate analysis between the association of pretreatment host and leukemic cell characteristics and their corresponding patient's survival. The findings from these studies classify patients into good, intermediate, or poor-risk groups, with an average survival of 5-6 years, 3-4 years, and 2 years, respectively. A combined prognostic model, incorporating previous models such as Sokal score, has been devised using the number of poor-prognosis characteristics; stage 1 is for 0 or 1+, stage 2 is for 2+, stage 3 is for 3 or more, and stage 4 is for diagnosis at blastic phase.
Poor prognosis in patients with CML is associated with several clinical and laboratory factors, including older age, symptomatic presentation, poor performance status, African-American descent, hepatomegaly, splenomegaly, negative Ph chromosome or bcr-abl, anemia, thrombocytopenia, thrombocytosis, decreased megakaryocytes, basophilia, or myelofibrosis (increased reticulin and/or collagen).
Several therapy-associated factors may indicate poor prognosis in patients with CML, including longer time to hematologic remission with myelosuppression therapy, short duration of remission, total dose of hydroxyurea or busulfan, or poor suppression of Ph-positive cells by chemotherapy or interferon alfa therapy.
Recently, the prognosis of patients with CML has improved from an expected median survival of 3 years and a 5-year survival rate of less than 20% to a median survival of 5 or more years and a 5-year survival rate of 50-60%. The improvement is due to early diagnosis, improved therapy with interferon and BMT, and better care.
A German study of 139 low-risk patients with CML, according to the Sokal index, shows that the median survival with busulfan is 6 years (50 patients), with hydroxyurea is 6.5 years (55 patients), and with alpha interferon is approximately 9.5 years (34 patients), indicating improvement in survival with new therapy.
Some patients with molecular remissions from alpha interferon may be cured, but this will only be established over time.
The new and active tyrosine kinase inhibitor, Imatinib, is associated with a higher response rate and better tolerance of adverse effects. It may replace interferon as first-line therapy. Long-term remissions remain to be seen, and Imatinib will be reevaluated in the near future to determine its role in the treatment.

Miscellaneous

Medical/Legal Pitfalls:
Failure to diagnose and treat early with new modalities may be a cause for malpractice charges.

Conclusion

The discovery of new agents presently under study, such as tyrosine kinase inhibitor therapy, may prove valuable in prolonging the survival of this group of patients and may provide them with an eventual cure. Physicians should refer their patients to tertiary care and specialized centers for clinical trials involving these therapies under the guidance of Haemato-Oncologists. Currently in Bangladesh all kinds of facilities for CML (except ABMT) is present. The Government should come forward to fulfill these measures for the overall benefit of the patients.

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Prevalence of *Helicobacter pylori* in Bangladesh: Rapid urease test

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Abstract

H. pylori infection is common in developing countries which show very high prevalence. We studied the prevalence of *H. pylori* in Bangladesh subjects with dyspepsia. *H. pylori* was looked for in biopsy specimens taken from the antrum by rapid urease test[Campylobacter-like organism(CLO) test]. Two hundred forty one subjects with dyspepsia were studied. Overall 168(69.7%) of the subjects studied were CLO positive. *H. pylori* was found in 63.9% of patients with gastritis, 77.8% of patients with duodenitis, 80.7% of patients with gastric ulcer, 85.2% of patients with duodenal ulcer, 14.3% of patients with GERD(gastresophageal reflux disease), 66.7% of patients with gastric polyp and 62.5% of normal control subjects. No significant age specific increase in the prevalence of *H. pylori* infection was noted in the age groups. No significant difference was observed in relation to sex (male: female=68.4%: 70.1%, P>0.1). However, subjects with duodenal ulcer disease had significantly increased prevalence of *H. pylori* compared with normal controls (P=0.01). Subjects with GERD had significantly decreased when compared to normal controls (P=0.02).

Key words- *H. pylori, Rapid urease test(CLO test), Duodenal ulcer, GERD*

Introduction

H. pylori is one of the most important pathogens for a wide spectrum of gastroduodenal diseases including acute and chronic active gastritits, peptic ulcer diseases, gastric mucosa-associated lymphoid tissue lymphoma and gastric malignancy[1-7]. It may be acquired at any age but once acquired, the infection persists for years and often for a life time[4].

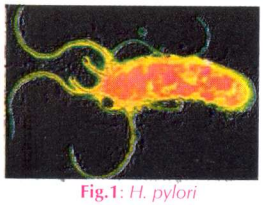

Fig.1: *H. pylori*

H. pylori prevalence varies according to ethnic groups significantly[1]. *H. pylori* can be identified in gastric mucosal samples by histologic examination, culture and detection of urease activity. A urea breath test using ^{13}C or ^{14}C also has been developed for identifying *H. pylori* on the basis of urease production with release of labeled CO_2[4-6]. Antibodies (IgG and IgA) to *H. pylori* have been identified in sera of individuals with *H. pylori* colonization[2,3]. *H. pylori* produces large amounts of urease. The rapid urease test of gastric biopsy material is a relatively simple and reliable method for presumptive identification of *H. pylori*. A positive test result from an increase in pH, with the phenol red indicator turning from light orange to red. The test is inexpensive, with a sensitivity of at least 90 percent and a specificity approaching 100 percent[8,9].

Until now, some studies have tried to show the prevalence of *H. pylori* infection by serological methods and urea breath test in Bangladesh. But there has not been yet any study to do endoscopic biopsies to determine *H. pylori* infection in this country. So we carried out a prospective study to determine for the first time, the incidence of *H. pylori* infection in Bangladesh by rapid urease test in endoscopic biopsies.

Materials and methods

This was a prospective study on the patients with gastrointestinal symptoms in Bangladesh, performed in the Department of Internal Medicine of Bangladesh Korea Friendship Hospital during the period from August, 2001 to May, 2003.

Two hundred forty one subjects were included for this study as shown in table 1. Most of the patients came to check endoscopy because of dyspepsia. One or two mucosal biopsies were taken from the gastric antrum of each patient using a disinfected endoscope. These biopsy tissues were used for CLO test. After endoscopic examination, 201(83.4%) of 241 were found to have definite disease as shown in table-2 and 40(16.6%) were found to have normal endoscopic examination, which were regarded as controls. Gastritis was considered present when there was erythema and erosion of the gastric mucosa. Duodenitis was considered present when there was definite erythema and erosion of the duodenal mucosa.

CLO test

During the gastrointestinal endoscopy, one or two biopsy specimens were taken from the gastric antrum at the lesser curvature. The antral biopsy specimen was immediately inserted in CLO test(Ballard Medical Products, Utah 84020 U.S.A.) which detects the urease enzyme of *H. pylori*. Results were read for up to 24h for a CLO test. Positive results in urease tests were read according to the manufacturer's instructions.

Statistical Methods

This data was examined by Chi-square test (including Fisher's exact test where appropriate). We considered a P value of 0.05 or less to indicate statistical significance.

Results

A total of 241 subjects with upper gastric symptoms were included for this study. Main symptoms were epigastric pain (preprandial or postprandial), upper abdominal dyscomforts, nausea, indigestion etc. One hundred forty-four (144) were male and ninety seven (97) were female. The average age of these subjects was 35.6 years (range 15 to 69).

Table- 1 shows *H. pylori* prevalence and age group of subjects attending endoscopy. Overall 168(69.7%) of the subjects studied were CLO positive. About 64% of the subjects were found to be infected by the age of 20 but no significant age specific increase in the prevalence of *H. pylori* infection was noted in the age groups(Figure). No significant difference was observed in relation to sex (male:

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female=68.4%: 70.1%, P>0.1).

Table-1. Age & sex related *H. pylori* prevalence by CLO test

Age* group (years)	n	CLO* Positivity No. (%)	n	Male CLO Positivity No. (%)	n	Female CLO Positivity NO. (%)	p-value**
10~19	11	7(63.3)	9	5(55.6)	2	1(100)	0.52
20~29	61	45(73.8)	37	27(73.0)	24	19(79.2)	0.58
30~39	80	52(65.0)	44	27(61.4)	36	25(69.4)	0.22
40~49	55	39(70.9)	30	23(76.7)	25	16(64.0)	0.30
50~59	29	21(72.4)	20	15(75.0)	9	6(66.7)	0.64
60~69	5	4(80)	4	4(100)	1	0(0)	0.02?
Total	241	168(69.7)	144	101(70.1)	97	67(69.1)	

Table-2 shows the *H. pylori* prevalence according to endoscopic diagnosis. Our classification of endoscopic diagnosis was gastritis, duodenitis, gastric ulcer, duodenal ulcer, GERD, gastric polyp and normal, which was considered as a control. However among subjects with duodenal ulcer disease the prevalence of *H. pylori* was significantly increased when compared with normal control (P=0.01). Subjects with GERD was likely to have significantly decreased *H. pylroi* when compared to normal control (P=0.02). No significant difference was observed in relation to sex in each disease.

Table-2. Endoscopic Diagnosis related *H. pylori* prevalence by CLO test

Endoscopic* Diagnosis	n	CLO* Positivity No. (%)	n	Male CLO Positivity No. (%)	n	Female CLO Positivity NO. (%)	p-value**
Gastritis	97	62(63.9)	49	30(55.6)	48	32(66.7)	0.57
Duodenitis	9	45(73.8)	6	5(73.0)	3	2(66.7)	0.57
Gastric Ulcer	31	52(65.0)	24	20(61.4)	7	5(71.4)	0.48
Duodenal Ulcer	54	39(70.9)	42	35(76.7)	12	11(91.7)	0.47
Normal	40	21(72.4)	18	10(75.0)	22	15(68.2)	0.21
GERD	7	4(80)	4	0(0)	3	1(33.3)	0.38
Gastric polyp	3	168(69.7)	1	1(100)	2	1(50.0)	
Total	241	168(69.7)	144	101((70.1)	97	67(69.1)	

GERD(Gastroesophageal Reflux Disease)
Nor vs gastritis : 0.87
Nor vs duodenitis: 0.38
Nor vs gastric ulcer: 0.09
Nor vs duodenal ulcer: 0.01
Nor vs GERD: 0.02 (Fisher exact test)
Nor vs gastric polyp : 0.8 (Fisher exact test)

Discussion

There are several methods to detect *H. pylori* infection. Among them, we used rapid urease test to detect *H. pylori* infection in the stomach. It is a very simple and reliable method for a quick diagnosis of *H. pylori* infection in the endoscopy unit[9]. Early diagnosis of *H. pylori* infection enables the physician to initiate therapy before histological results are available[8,9]. The rapid urease tests with high sensitivity and specificity are commonly used in adults and children[8,9]. We studied the prevalence of *H. pylori* by CLO test for the first time in Bangladesh.

Our results showed that no significant age specific increase in the prevalence of *H. pylori* infection was noted in the each age group. And no significant difference was observed in relation to sex (male: female=68.4%: 70.1%, P>0.1). But there was a significant disease specific association between duodenal ulcer disease and CLO positive (P=0.01). Namely, the prevalence of *H. pylori* in duodenal ulcer disease is more common than normal subjects as a control. No significant difference was observed in relation to sex in each disease. These results show that *H. pylori* may be a main cause for important gastrointestinal disease in Bangladesh. Clinically, we experienced, if we eradicate the *H. pylori* in peptic ulcer patients, most patients were improved in their symptoms.

Ahmad *et al.*[2] reported that the prevalence of *H. pylori* in Bangladesh subjects was 92% in their serological study. And Miah *et al.*[3] reported that the prevalence of *H. pylori* in diabetes patients was 84.8% in their serological study. Mahalanabis *et al.*[4] also reported that the prevalence of *H. pylori* is 63% in infant aged 1-3month, 33% in 10-15months old children, 84% in 6-9year olds. Two of them were studied serologically, another one was by ^{13}C-urea breath test.

Our results show low percentage when compared to former several studies. In this regard, we think that there is a time interval more than 6 years between our study and former studies. Another reason is the different method of study. In addition we took only one or two biopsy tissue from gastric antrum during endoscopy, so we think that this is also a contributing factor to the low prevalence of our results.

This study showed the correlation between gastric disease by endoscopic diagnosis and *H. pylori* infection for the first time in Bangladesh. Especially, we showed that *H. pylori* infection is significantly increased in the duodenal ulcer patients, so we can recognize *H. pylori* as a main cause for duodenal ulcer disease. This study also showed that GERD has significantly low incidence of *H. pylori* infection. This results support the assumption that *H. pylori* may protect the gastroesophageal reflux.

However, the data of the current study may not be an exact estimate of the prevalence of *H pylori* in Bangladesh because the sample we studied was small. Association of *H pylori* infection with dyspepsia and rapid urease test in Bangladesh needs further large scale study.

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Smoking in patients with mental disorders : Observations in a developing country

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Abstract

Tobacco smoking is a form of substance abuse. Studies on smoking mainly from the developed countries noted higher rates of smoking by psychiatric patients, especially those with schizophrenia, when compared to the general population. Some studies indicated that smoking could have some positive effects on the clinical state in schizophrenia and depression through neurotransmitter mechanisms. Such observations could be misinterpreted if one does not consider the enormous morbidity and mortality associated with smoking. Studies on smoking by psychiatric patients are few from developing countries where social and cultural and familiar factors influence smoking behavior. This study in Bangladesh on an urban population of 510 male psychiatric patients (Schizophrenia = 286, Major affective disorders = 84, Nonpsychotic disorder = 140) showed that the prevalence of smoking in psychiatric patients is no greater, if not lesser, than a control group of medically ill patients with no psychiatric disorder (n=177) and the general population. More number of psychiatric patients had quit smoking than the medically ill. The resons for absence of higher smoking rates in the psychiatric group could be purely socio-economic and cultural. The study suggests that smoking is not invariably high or purposive in psychiatric disorders. Caution should be exercised in understanding results emerging from nicotine research in psychiatric patients.

Key Words : *Smoking-Psychiatric disorders - Developing country Prevention*

Introduction

An association between substance abuse and major psychiatric illness, mainly schizophrenia and affective disorders, is increasingly recognized (Lawrie et al, 1995; Jeste et al, 1996). There is compelling evidence that tobacco-smoking represent a form of drug addiction to nicotine, now classified as a psychoactive substance (Nissel et al, 1995). Smoking tobacco has been found to be common among patients with major psychiatric disorders like schizophrenia and affective disorders (Diwan et al, 1998; Breslau et al, 1998) higher than that in the general population (Goff et al, 1992; De Leon et al, 1995; Forchuk et al, 1997). Smoking was highest (50% to as high as 93%) among those with schizophrenia (Hughes et al, 1986; Diwan et al, 1998)

Research indicated that nicotine directly regulates the dopaminergic transmission in the mesolimbic and nigrostriatal systems through nicotinic receptors (Lohr & Flynn, 1992). It has been suggested that nicotine could control psychiatric symptoms especially the negative ones and reduce extrapyramidal side effects of antipsychotic drugs in patients with schizophrenia (Adler et al, 1993; Glassman et al, 1993; Sandyk et al, 1993). In these patients smoking had been described as a form of self-medication by the patient to experience its beneficial effects on psychotic symptoms (Nissel et al, 1995). Smoking has been related to clinical status in major depression also by the observation of relapse following withdrawal from smoking (Covey et al, 1997).

The relationship between smoking and psychiatric status may not be as simple as it is made to appear. Education and social class are powerful predictors of the likelihood that a person will smoke (Desjarlais et al, 1995). Several sociocultural and economic factors could influence smoking behaviour. Most reports on smoking in schizophrenia have come from the developed west where the general social attitude to smoking is different from cultures where smoking is not so permissible and affordable. In countries like India smoking is often prohibited by familial, cultural and religious practices. For example less that 3% of Sikh men living in urban Delhi were found to be smokers compared to 45% of men in general (Venkatanarayan et al, 1996). In a common Hindi family smoking is looked down upon and disliked. Smoking in women is low in India. Only 7% of women were found to be smokers in a survey in Delhi (Venkatanarayan et al, 1996) compared to the west, and it more common among illiterate. Usually smoking by a female in a common Hindi family is considered blasphemous. The mass media in India are restricted from depicting smoking by women. The cost factor is another important one that determines the frequency and severity of smoking, especially among the poor. A severely disabled psychiatric patient with little or no independent source of income may not be able to afford smoking when the family refuses to oblige him.

The significance of smoking in psychiatric disorders would be clearer if the phenomenon is studied under circumstances like in India where non-clinical factors influences smoking behaviour. This information would help to understand better the relationship between smoking and psychopathology smoking. This study on Indian male population was done with the aim to measure the prevalence of smoking behaviour in patients with psychiatric disorders compared with a control group medically ill patients who had no psychiatric disorder. The prevalence of smoking by men in the general population in urban India has been placed at 40 to 45% (Khor, 1996; Venkatanarayan et al, 1996; Chaturvedi et al, 1998).

This report pertains to only male patients. Hence they were not included for detailed analysis. Chewing tobacco is a form of nicotine use widely prevalent in Bangladesh. The data on this behavior was not analyzed for sake compatibility in comparing with other studies on smoking.

Methodology

Patient selection

The study group consisted of psychiatric patients with

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schizophrenia (SCZ) affective disorders (AD-major depression, biporal disorders) and non-psychotic disorders (NPD-dysthymia, anxiety disorders and somatoform disorders). Diagnosis was made by clinical interview using DSM IV criteria (American Psychiatric Association, 1994). Medically ill patients (MI) seeking treatment with a general practitioner and who were evaluated not to have a psychiatric disorder formed the control group.

The outpatients were a consecutive sample taken over a period of 6 months. Patients with AD and NPD were consecutive sample during the same period from the consultation practice AHMF The medically ill patients were studied in the outpatient consultation facility of EK a general practitioner working in the same city. Diagnosis of the medical condition was made by EK. Exclusion of psychiatric disorder in them was done by AHMF through a semi-structured clinical interview. All the patients lived with their families in the city or its suburbs. All the patients and families were explained the nature of the study and included into the study with their consent.

Smoking behaviour

Information of smoking was elicited by interviewing the study subjects. One relative living with them was also interviewed. This was possible for all the psychiatric our patients and nearly 80% of the medical patients. The respondents were asked the following three questions.

1. Was the subject ever a smoker?
2. Is he currently smoking or smoked only in the past?
3. Number of cigarettes of bidis (a native form of tobacco leaves) smoked per day.

The details of age, education, employment, economic status, marital status of the patient were also recorded.

Smokers were divided into two groups- "Current smokers" who were smoking currently and "Past smokers" who smoked in the past but abstinent at the time of study. These two together formed the "Ever smoked" group. The "Quit rate" indicated the number of smokers who had given up smoking at the time of the study and calculated as the percentage of past smokers among ever smokers. Information from the patient and the family member on the exact number of cigarettes/bidis smoked per day and was taken for analysis. Current smokers smoking 20 cigarettes/bidis or more per day were labelled as 'Heavy' smokers.

Analysis

SPSS program version 5.0 (Norusis, 1992) was used for compilation and analysis of data. Analysis was done to compare thenumber of current and ever smokers in each study group. Chi-square test, odds ratio and t test were performed for statistical comparison.

Results

Patient population

The total number of patients assessed were 687. The study group consisted of 510 patients with psychiatric disorders and the control group was made up of 177 medically ill with no psychiatric disorder.

In the psychiatric group there were 286 with schizophrenia, 84 with major affective disorders and 140 with non psychotic disorders. The psychiatric patients were of the same age as the MI (mean age=37, standard deviation (sd) = 11 vs 38, sd = 14; t = 0.86, p = not significant).

The number of MI who had less than 5 years of schooloing (n=50, 28%) was significantly more than the psychiatric group (n=68, 13%; x2=20.55, p<0.0001). More of the psychiatric patients (n=240, 47%) were unemployed than the MI (n=24, 14%; x2=62.32, p<0.001).

Unemployment was more in SCZ (n=190, 66%) than AD (n=27, 32%; x2=31.48, p<0.0001 and CMD (n=23, 16%; x2=94.01, p<0.0001. Psychiatric patients were more often poor (n=104, 20%) than the MI (n=19, 11%; x2 = 8.34, p<0.01).

The marital status of the psychiatric patients (341/510, 67% were married) was similar to the MI (125/177, 71% were married).

Prevalence of Smoking

The comparison of the study and contron groups is shown in table 1 and figure 1. Among the psychiatric patients 235 (46%) had ever smoked that was not significantly different from the non-psychiatric MI patients (n=77, 44%)

Table1: Comparison of psychiatric and control groups

Variable	Psychiatric patients N= 510	Medical patients Control Statistics N=177	Odds ratio (95% confidence interval)	
Mean Age	37 (sd=11)	38(sd=14)	t=0.86 NS	
<5 years schooling	68(13%)	50 (28%)	chi- squared= 20.55 p<0.001	0.4 (0.3-0.6)
Unemployed	240(47%)	24 (14%)	chi- squared= 62.32 p<0.001	5.7 (3.5-9.3)
Poor	104 (20%)	19 (11%)	chi- squared= 8.34 p<0.01	2.1 (1.2-3.7)
Married	341 (67%)	125 (71%)	chi- squared= 0.82 p<0.36	1.2 (0.9-1.8)
Smoking Status				
Current smoker (CS)	161 (32%)	73 (41%)	chi- squared= 5.48 p<0.02	0.7 (0.5-1.0)
Past smoker (PS)	74 (15%)	4(2%)	chi- squared= 18.39 p<0.001	7.3 (2.7-28)
Ever smoked(ES)	235 (46%)	77 (44%)	chi- squared= 0.35 p<0.55	1.1 (0.8-1.6)
Never smoked (NS)	265(54%)	97 (55%)		
Quit rate (ES/PS)	74/235 (31%)	4/97 (5%)	chi- squared= 20.01 p<0.001	8.4 (3-32.6)
Heavy smoker	33/161(20%)	13/73(18%)	chi- squared= 0.23 p<0.63	1.2 (0.6-2.6)

The number of psychiatric patients who were currently smoking (161, 32%) was significantly less than the MI (73, 41%).

The number of current smokers in Schizophrenia (109/286) was significantly higher than Affective Disorder (20/84, x2=5.59, p<0.02) and NPD (32/140, x2=6.86, p<0.01 but same as the MI group (x2=0.45, NS) Smoking quit rate was

significantly more among the psychiatric patients (74/235, 31%) than the MI (4/77, 5%). NPD had the maximum quit rate of 45%. The number of heavy smokers among psychiatric patients (33/161 current smokers, 20%) was not significantly higher than the MI patients (13/73, 18%).

Discussion

It was evident from this study in Bangladesh on a fairly large number of psychiatric patients that the prevalence of smoking by the mzale psychiatric patients was not significantly greater than non-psychiatirc population or the general population of urban India. In fact the number of current smokers were significantly less in those with psychiatric disorders when compared to medically ill control group.

Among psyciatric patients those with schizophrenia smoked more often that others but not more than the medically ill controls or the general population. The number of heavy smokers was also similar in the psychiatric and control groups. The significantly high 'quit rates' among the psychiatric patients indicated that they were able to give up smoking more readily than those without a psychiatric disorder. It seems the repeated observations of higher rates of smoking in patients with schizophrenia and other psychiatric disorders than others may not always be true. This raises the issue whether the observation that increased smoking in psychiatric patients has some 'therapeutic' relevance mediated by biochemical mechanisms needs a fresh look. The reasons why psychiatric patients we studied did not smoke more could be predominantly socioeconomic and cultural. More of them were unemployed and poor and had no independent source of income. The patients were dependent on the family to give money to buy cigarettes of bidis. As all the patients studied were living with their families that gave the family a better control over smoking by the patients. Moreover, in India the patients do not receive any disability assistance from the state that could be spent on smoking as it happens in the developed contries where such assistance is available. The economic factor along with the cultural restrictions mentioned earlier could have curbed smoking behaviour by the patients. The benefits of quiting as well as the hazards of continuing smoking are clearly demonstrated. Tobacco use causes far more deaths than all other psychoactive substances combined. About three million people die each year from smoking-related diseases and this is estimated to reach 10 million by the year 2025. Smoking has been increasing in the developing countries whereas it has been falling in the developed countries. In has been noted that a major obstacle faced in reversing this upward trend is the aggressive sales promotion of cigarette companies that have shifted their focus from the developed countries to the poorer ones. The success of propaganda is greater among those who have fewer independent sources of information and who are under greater social stress. A vulnerable group is the patients with severe psychiatric disorders like schizophrenia living in poor countries. The trend in nicotine reasearch in psychiatry, especially schizophrenia, could have serious consequences to the overall health care of psychiatric patients if one fails to consider the entire picture. Reports mentioning 'relief of psychiatic symptoms' 'lessening of drug-induced side effects' attributed to smoking, even if true in some instances, could tempt one to propose that smoking might be therapeutic to people with serious mental disorders. These half-truths emerging from nicotine research could be exploited by vested interests towards prompting smoking by such patients.

Limitations of the study

Smoking leads to increased morbidity and higher utilisation of health services. Hence selection of medically ill patients as a comparison group may not be ideal as the prevalence of smoking could be higher in them.

This study however found the prevalence of smoking in the medically ill was comparable to the general population. Hence use of this group for comparison is acceptable. Chewing of tobacco is a frequent alternative mode of tobacco use in Bangladesh and in India (Gajalakshmi et al, 1996). This paper did not report on this through we found that chewing was indulged in by only 3% of psychiatric patients, half of who were also smokers. Hence it was not the case that psychiatric patients indulged in other forms of tobacco use.

Conclusion

This study showed that smoking in schizophrenia and other psychiatric disorder is not necessarily high as depicted by studies done in the west. Socioeconomic and cultural factors in developing countries like India could influence the smoking by person with psychiatric disorder. With information available from nicotine research, the mental health professionals, public health personnel and, most importantly, the psychiatric patients themselves should not be misled to believe that smoking is inevitable and purposeful in psychiatric disorders like schizophrenia. Social, cultural and family influences that curb smoking could be utilized to prevent and reduce smoking by psychiatric patients.

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Hypertension : Ophthalmologist's perspective

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Introduction

Among the vascular diseases affecting the eye hypertension is an important concern for the Ophthalmologists. It is one of the leading causes of ocular morbidity. Ocular changes induced by hypertension may be the initial finding in an otherwise asymptomatic patient necessitating a primary care referral. On the other side, a symptomatic patient may be referred to the Ophthalmologist for visual changes caused by hypertension.

Purposes of this article

To arouse interest about the ocular involvement in Systemic diseases in general & Hypertension in particular.

To highlight the importance of meticulous eye examination in all situations.

To stimulate the Non ophthalmologists in realizing the role of fundus examination in the diagnosis and confirmation of their clinical findings.

To urge the Ophthalmologists to examine the eye not treating it an isolated organ but as a part of the whole system.

In this context, we can remember **William B. Bean,** a renowned medical scholar who described "The Eye as the Gateway to Medical Wisdom."

Peter Mayer Latham, an ancient English clinician used to teach his students -

"If you desire to make pathological knowledge the ground work of your credit and usefulness through life, let me advice you not to allow the period of your pupilage to pass by without making a special study of "Diseases of Eye". Here you see almost all disease in miniature; and from the peculiar structure of the Eye, you see them as though through a glass; and you learn many of the little wonderful details in the nature of the morbid processes, which, but for the observation of them in the eye, would not have been known at all. Let every one of you who has a few months to spare give them to the Eye Infirmary".

Basis of ocular manifestations of hypertension

- Thrombosis
- Embolism
- Vasospasm

→ Vascular occlusion resulting in ischaemia & its consequences

- Mechanical effects of arteriolosclerosis on veins.
- Release of local mediators

Hypertension may follow diversification in its presentation or straightforward it may cause some oculopathies. Here, few of its common presentations are being discussed.

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Hypertensive retinopathy

- **Vascular changes :** Persistent hypertension causes - arteriolosclerosis, hyalinization & vasospasm.

Consequently

a. **Light reflex change**

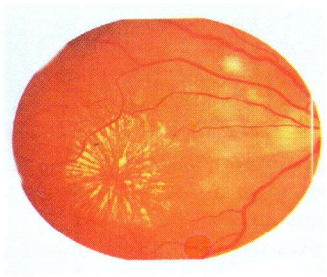
Broadening of light reflex, copper wiring, silver wiring.

b. **Arterial attenuation**

Focal or generalised. Vascular spasm leads to narrowing which can become permanent by fibrosis.

Fig. 1

Arterial attenuation macular star and cotton wool spot



c. **AV nicking**

Due to compression of hard artery an veins (sharing common adventitia) - **Salus' sign:** deflection of Veins at crossing site. **Bonnet's sign:** Banking of Vein (dilated) distal to the crossing site. **Gunn's sign:** Tapering of vein on either side of crossing.

- **Extravascular changes**

a. **Microaneurysms**

Most visible by FFA (Fundus Fluorescin Angiogram). Occur at localized areas of capillary wall weakness. Stasis engorgement of the capillary lead to anoxia, poor nutrition contributes to microaneurysm formation.

b. **Retinal haemorrhages**

Streak hges in the nerve fiber layer (predominate) & blot hge in the deeper layer.

c. **Retinal & macular oedema**

Either of transudation of choroidal fluids after breakdown of RPE (Retinal pigment epithelium) or failure of autoregulation of retinal capillaries.

d. **Retinal lipid deposits (hard exudates)**

Either in a scattered pattern or a macular star (Predominant) (due to the radially oriented nerve fibre layer of Henle).

e. **Cotton wool spots**

Due to focal nerve fibre infarcts.

f. **Focal intra-retinal periarteriolar transudates (FIPT)**

Punctate, white opacities, round or oval, alongside major arterioles in deep retinal areas and on disc. They may appear and disappear in crops, leave no permanent change.

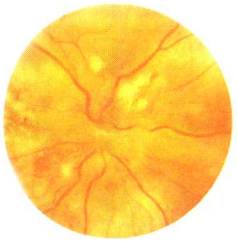
g. **Retinal macroaneurysm,** rarely.

- **Changes in malignant hypertension**

Necrosis and fibrinoid deposition in the vessel wall occurs, (more in choroidal than retinal arteries). Oedema occurs from breakdown of barrier at RPE and failure of auto regulation of retinal capillaries. Papilloedema develops.

Fig. 2

Malignant hypertension, reflecting papilloedema, retinal oedema, cotton wool spots, haemorrhages



Hypertensive choroidopathy

Choroidal arteries run a relatively short course, hence, systemic pressure is felt stronger than in retinal arteries.
Pressure and flow is higher in macula than periphery.
Acute and severe hypertension alters chorio-capillaries, resulting in-choroidal ischaemia, Retinal oedema, CME (Cystoid macular oedema), Serous RD (Retinal detachment), RPE changes.
It occurs more prominently in young patients with- severe acute hypertension, pheochromocytoma, eclampsia, etc.
Elschnig's spot : Focal infarcts in the choriocapillaries cause yellow spots in the overlying RPE. They are completely obstructed terminal choroidal arterioles and fibrin and necrotic tissue. They are also known as acute focal RPE lesions and window defects.
Siegrist's streaks: Radially oriented chains of pigmented spots along sclerosed choroidal vessels representing linear foci of RPE disruption, an indicative of malig. hypertension.
Serous RD: Decompensation of the RPE in hypertensive choroidopathy leads to breakdown of the outer blood-retinal barrier, leading to subretinal accumulation of protein-rich exudates –> Serous RD.

Vascular occlusive disorders

A. **Retinal artery occlusion**

CRAO (Central retinal artery occlusion)

It is usually the result of atheroma, although may be caused by emloli.
It results in infarction of the inner two-thirds of the retina, reflex constriction of the whole retinal arterial tree, stasis in retinal capillaries.
The central infarct is ischaemic; therefore unlike RVO, hge is minimal.
The retina appears white as a result of cloudy swelling caused by intracellular oedema. Fovea is devoid of this change.
Normal orange reflex of choroid seen through fovea in contrast to surrounding opaque retina, gives rise to a 'Cherry-red spot' appearance.
FFA shows exrtreme delay in arterial filling and masking of choroidal background fluorescence by retinal oedema.
Usually patient has painless. total or near total loss of vision unless the pt. retains central vision via a clioretinal artery (present in 15–30%eyes) supplying the papillomacular bundle.

BRAO (Branch retinal artery occlusion)

It presents with an acute and severe altitudinal visual field defect. Whitish appearance due to retinal infarction in the distribution of the affected vessel.

Ophthalmic artery occlusion

Vision of no light perception indicates choroidal ischaemia, due to OA (Ophthalmic artery) occlusion in addition to CRAO. Intense retinal whitening is seen. FFA shows marked defect in choroidal & retinal perfusion.

B. **Retinal vein occlusion**

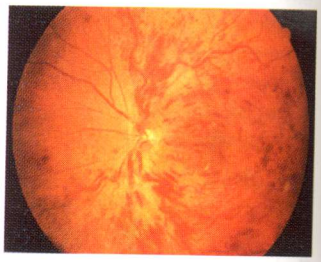
CRVO (Central retinal vein occlusion)

Non- ischaemic CRVO

Mild tortuosity & dilatations of veins. Hges seen throughout the fundus. (not massive). Mild disc swelling. Little or no cotton wool spot. FFA-shows venous stasis, good retinal capillary perfusion. Mild reduction of V/A.

Fig. 3

Non ischaemic CRVO



Ischaemic CRVO

Marked reduction of V/A, marked tortuosity & dilatations of veins. Massive hges all over the fundus. Cotton wool spots are common. Disc markedly swollen. FFA-after disappearance of hge-reveals extensive areas of capillary nonperfusion.

BRVO (Branch retinal vein occlusion)

It may occur near the optic disc and the AV (Artero-venous) crossing site. Blockage of superior temporal vein frequently involves the macula.

Prognostic factors in RVO (Retinal vein occlusion)

Macular oedema - Retinal ischaemia - Neovascularization - Neovascular glaucoma.

C. **Carotid occlusive disease**

Amaurosis Fugax

Emboli that temporarily obstruct the Ophthalmic or central retinal artery may produce sudden, severe, painless, transient loss of vision. It is called amaurosis fugax. The attack usually lasts for few minutes, then returns to normal as the embolus travels away. Most common source of emboli is fibrin and cholesterol from ulcerated plaques in the wall of the carotid artery.

Ocular ischaemic syndrome

Significant carotid stenosis can result in ocular ischaemic syndrome. Rarely develops in young pts. Males are at greater risk. Bilateral involvement in 20% cases .

Presentations

Vision loss, ocular pain – secondany to ischaemia of the globe or NVG (Neovascular glaucoma), robeosis iridis, ocular hypotony (sometimes).
Retina shows -
arterial constrictions, venous dilatations, hges, oedema, cotton wool spots, neovascularization, etc.

Hypertensive neuropathy

A. **Non arteritic AION (Anterior ischaemic optic neuropathy)**

Infarction of ON(Optic nerve) head results from occlusion of the post. ciliary arteries produces ischaemia → reduced axoplasmic flow → disc swelling. It is followed by optic atrophy.

B. **Neuro- ocular palsy**

There may be isolated nerve palsy or may be associated with other neurological deficits. Cranial nerve palsy presents with :

Ocular malalignment, diplopia, exposure keratopathy. neurotropic keratopathy, ptosis, etc.

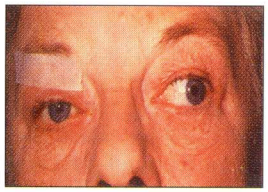


Fig. 4

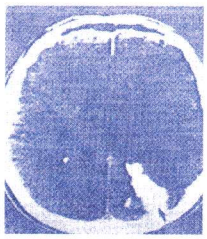
Right sided ptosis and failure of adduction indicating right 3rd nerve palsy

Vascular accidents of brain & brain stem

It may present with various types of neurological field defects according to involvement of various part of visual pathway upto visual cortex (due to vascular accident).

Visual problems may be associated with other motor or sensory neurological deficits.

According to neurological deficit actual site of vascular accident can be localized.



CT-scan showing occipitalhaematoma producting homonymous hemianopioa

Rupture of Aneurysms

Hypertension may be the cause of formation and rupture of aneurysms. Rupture of carotid aneurysm may present as bilateral pulsatile proptosis due to carotid-cavernous fistula

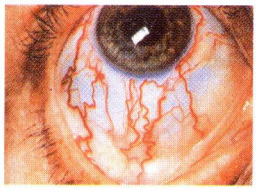


Fig. 5

Corkscrew conjunctival vessels in carotid- cavernous fistula.

Surgical complications due to hypertension

If hypertension is not managed well pre-operatively, surgery may be complicated with excessive haemorrhage (DCR operation), subconjunctival hge., hyphaema in intraocular surgery. Per-operative hypertensive encephalopathy, even cardiac complication is not unusual.

Conclusion

'Act locally, think globally' - like this modern concept of global village, an ophthalmologist, though working in ophthalmic field, should always think to correlate an ocular problem with the whole system and be familiar with the systemic examinations. Side by side, a non-ophthalmologist while dealing with any systemic problem should give emphasis on ocular examination as in most instances eye is the mirror of the whole system. Again I am to quote from W.B. Bean -

"Nobody has ever really worked out the geography of the Great Republic of Medicine - If he would have, he would definitely realize that the eyes have a head, and the head has a body and the body has a head, and the head has eyes, and these are all part of a greater unity".

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Executive Director of ORION Laboratories Limited accorded 'The Financial Mirror Businessmen Award-2002'

Mr. Ebadul Karim, Executive Director of ORION Laboratories Limited received 'The Financial Mirror Businessmen Award-2002' in recognition to his outstanding achievement in the pharmaceutical sector of Bangladesh and also played a significant contribution in the Government treasury.

ORION Laboratories Limited has been enjoying phenomenal growth through the last 5 years under the direct care of Mr. Ebadul Karim. He expressed his wholehearted thanks and gratitude to the doctor's community for their continuous support to ORION products.

The Executive Director of Orion Laboratories Limited Mr. Ebadul Karim received 'The Financial Mirror Businessmen Award-2002' from Barrister Moudud Ahmed, Minister for Law, Justice and Parliamentary Affairs.

Source: *www.financial express-bd.com*

New advances in the management of post-menopausal osteoporosis

Ikram Z[1]

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Introduction

Osteoporosis is characterized by a decrease in bone mass and a deterioration in skeletal microarchitecture, which lead to increased fragility and susceptibility to fractures. In the aging population throughout the world, this is a disease that is important not only for the morbidity and mortality it causes, but also for the enormous burden it puts on the health care system. The aim of treating osteoporosis is to prevent further skeletal deterioration, and to increase bone mass and improve bone microarchitecture to reduce the risk of vertebral and peripheral fractures. One of the major causes of skeletal fractures is bone loss that occurs after menopause.

In the past, estrogen replacement was considered a primary therapy for the prevention of postmenopausal osteoporosis. Estrogen had the additional advantages of controlling menopausal symptoms and presumptive prevention or delay of cardiovascular disease. However, data from the Women's Health Initiative (WHI) revealed that estrogen-progestin therapy does not reduce the risk of coronary heart disease, and increases the risk of breast cancer, stroke, and venous thromboembolic events. However, primary prevention of osteoporosis initiated in the immediate postmenopause is not yet considered a public health priority by most. Most phycisians are faced with situations in which women seek treatment at later stages of the disease, after the diagnosis of osteoporosis has already been made on the basis of random radiographs, bone densitometry or a clinical fracture.

None of the available medications (such as, estrogens, calcitonin, and early-generation bisphosphonates) has unequivocally demonstrated its ability to fully prevent the occurrence of new vertebral or peripheral osteoporotic fractures once the disease is established. Some of these agents have potentially severe toxicity or prohibitive cost, discouraging their widespread or prolonged use.

This review will focus on the new drugs that provide a better preventive and therapeutic approach to postmenopausal osteoporosis - selective estrogen receptor modulators [SERMs], second- or third-generation bisphosphonates and parathyroid peptides.

Raloxifene

SERMs are defined as compounds that produce estrogen agonism in 1 or more desired target tissues (eg, bone, liver) together with estrogen antagonism and/or minimal agonism in the breast or uterus. Raloxifene was initially investigated as a treatment for advanced breast cancer. It was also shown to inhibit the hypertrophy of the uterus in response to estrogens, to reduce serum cholesterol levels, and to increase BMD. On a molecular basis, raloxifene activates the gene encoding transforming growth factor beta (TGF beta3), which, together with other growth factors and cytokines, induces production of osteoblasts and inhibits the activity of osteoclasts and shortens their life span.

The Multiple Outcomes of Raloxifene Evaluation (MORE) Trial

The MORE trial was a randomized, placebo-controlled study of Raloxifene 60 or 120 mg/day vs placebo (all women received calcium 500 mg and vitamin D 400 IU/day) involving 7705 women who were at least 2 years postmenopause. This study was conducted at multiple centers throughout 25 countries. The primary end point of MORE was the determination of the percentage of women taking Raloxifene who had at least 1 new vertebral fracture, as compared with the control group. Secondary end points were the relative risk (RR) of nonvertebral fractures, breast cancer, and cardiovascular events.

All women enrolled met the World Health Organization (WHO) criteria for osteoporosis (T-score </= -2.5). Approximately one third had prevalent vertebral fractures.

At 36 months, of radiographs in 6828 women, 503 (7.4%) had at least 1 new vertebral fracture, including 10.1% of women receiving placebo, 6.6% of those receiving 60 mg/day of Raloxifene, and 5.4% of those receiving 120 mg/day of Raloxifene. Risk of vertebral fracture was reduced in both study groups receiving Raloxifene (for 60 mg/day group: RR 0.7; for 120 mg/day group: RR 0.5). Frequency of vertebral fracture was reduced in women who did not have prevalent fracture. In women with prevalent vertebral fractures who received 60 mg/day of Raloxifene, RR for new vertebral fractures was 0.7; it was 0.5 in those with low BMD but no prevalent vertebral fractures at inclusion. Compared with placebo, the 60-mg/day and 120-mg/day dosages of Raloxifene increased BMD in the femoral neck by 2.1% and 2.4%, respectively, and in the spine by 2.6% and 2.7%, respectively ($P < .001$ for all comparisons).

At 1 year, Raloxifene 60 mg/day decreased the risk for new clinical vertebral fractures by 68% compared with placebo in the overall study population and by 66% in women with prevalent vertebral fractures, who are at greater risk for subsequent fracture. The risk for clinical vertebral fractures in the Raloxifene 60-mg/day group was decreased by 46% at 2 years and by 41% at 3 years. The cumulative incidence of new clinical vertebral fractures was lower in the group receiving Raloxifene 60 mg/day compared with placebo ($P < .001$).

In the overall cohort, the risk of nonvertebral fractures for Raloxifene (60 mg/day and 120 mg/day) vs placebo did not differ significantly (RR 0.9). However, when assessing separately women whose fracture severity grades, at baseline, corresponded to an estimated decrease in vertebral height of > 40% (grade 3), Raloxifene 60 mg/day significantly decreased the risk of new vertebral fracture (RR 0.73) and nonvertebral fracture (RR 0.53) at 3 years.

Thirteen cases of breast cancer were confirmed among the 5129 women assigned to Raloxifene vs 27 among the 2576 women assigned to placebo (RR 0.24; $P < .001$). To prevent 1 case of breast cancer, 126 women would need to be treated. Raloxifene decreased the risk of estrogen receptor-positive breast cancer by 90%, but not estrogen receptor-negative invasive breast cancer.

Raloxifene also significantly reduced the risk of cardiovascular events in a subset of women with increased cardiovascular risk (determined by the presence of multiple cardiovascular risk factors or prior coronary events or revascularization procedure). In the overall cohort, there were no significant differences between treatment groups in the number of combined coronary and cerebrovascular events: 96 (3.7%) with placebo, 82 (3.2%) with 60 mg/day of Raloxifene, and 94 (3.7%) with 120 mg/day of

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Raloxifene. Similar results were obtained when coronary and cerebrovascular events were analyzed separately.

Among the subset of 1035 women with increased cardiovascular risk at baseline, however, those assigned to Raloxifene had a significantly lower risk of cardiovascular events compared with placebo (RR 0.6). Hot flashes were the most common nonserious adverse event, prompting withdrawal in 0.1%, 0.7%, and 0.5% of the women in the placebo, Raloxifene 60 mg, and Raloxifene 120 mg groups, respectively. Leg cramps were also reported more frequently in the women given Raloxifene (7.0% in the 60 mg and 6.9% in the 120 mg groups) than in the placebo group (3.7%).

After 3 years, Raloxifene increased the risk of venous thromboembolic disease (RR = 3.1) but did not increase the risk of endometrial cancer.

Bisphosphonates: Alendronate

The cornerstone of the development of Alendronate for osteoporosis was the Fracture Intervention Trial (FIT), a 3-year randomized, controlled trial investigating the effects of Alendronate on the risk of fractures in 2027 women with prevalent vertebral fractures and in 4432 women with low femoral BMD but no prevalent fractures. The dose of Alendronate (initially 5 mg daily) was increased to 10 mg daily at 24 months. In the fracture arm of the study, 8% of women in the Alendronate group had 1 or more new morphometric vertebral fractures compared with 15% in the placebo group (RR = 0.53). For clinically apparent vertebral fractures, the RR was 0.45. In this arm of the study, a significant reduction in the risk of any clinical fracture (RR = 0.72), hip fracture (RR = 0.49), and wrist fracture (RR 0.49) was also reported for Alendronate users.

In the patients without prevalent spinal fractures, who were treated for a mean duration of 4.2 years, Alendronate increased BMD at all sites but did not reduce significantly the incidence of clinical fractures (RR = 0.86) in the whole population. However, Alendronate significantly decreased the risk of radiographic vertebral fractures by 44% overall (RR = 0.56) and the risk of clinical fractures by 36% (RR = 0.64) in women with baseline osteoporosis at the femoral neck. When analyzing the results of the FIT study of Alendronate administration for 3-4 years in 3658 women with osteoporosis (with existing vertebral fractures or BMD in the osteoporotic range), the estimate of the effect of Alendronate on RR of fracture was 0.47 for the hip, 0.52 for radiographic vertebral, 0.55 for clinical vertebral, and 0.70 for all clinical fractures.

Increases in spinal BMD with Alendronate continued for up to 7 years (0.8% per year after the initial 18 months with the 10-mg/day dose), whereas other skeletal benefits (ie, increases in BMD at other skeletal sites and decreases in biochemical markers) remained stable during the same period. Reduction of fracture risk with Alendronate was also shown to be consistent within fracture risk categories, with more fractures being prevented by treating women at highest risk due to advanced age or severe osteoporosis.

Esophageal erosion and ulcerative esophagitis were reported in association with the use of oral alendronate. However, particular recommendations for Alendronate intake (swallowing Alendronate with 180-240 mL water on arising in the morning, and remaining upright for at least 30 minutes after swallowing the tablet and until the first food of the day has been ingested) reduce the risk of esophagitis.

Dose-ranging studies suggest that the potential for esophageal irritation, observed with daily oral bisphosphonates, may also be substantially reduced with less frequent dosing. Less frequent dosing with any medication may enhance compliance, thereby maximizing the effectiveness of therapy. Therefore, a once-weekly (70-mg) formulation of Alendronate was developed, which fully satisfied equivalence criteria (lumbar spine, hip or total body BMD, and rate of bone turnover assessed by biochemical markers) relative to daily therapy.

Risedronate

Risedronate is a pyridinyl bisphosphonate with high antiosteoclastic potency because of a nitrogen atom in its cyclic structure. In women with a mean lumbar spine T-score of </= -2, Risedronate (5 mg/day) has been shown to increase BMD after 24 months, by 4% at the lumbar spine, 1.3% at the femoral neck, and 2.7% at the femoral trochanter. All these changes were significantly different from the evolution observed in the placebo group. The evidence for an antifracture efficacy of Risedronate came from 3 randomized controlled clinical trials. In 2458 postmenopausal women who had at least 1 prevalent vertebral fracture, treatment with 5 mg/day of Risedronate, compared with placebo, decreased the cumulative incidence of new vertebral fractures by 41% over 3 years.

In another study, 1226 postmenopausal women with 2 or more prevalent vertebral fractures were also exposed to the same protocol (Risedronate 5 mg/day vs placebo) for 3 years. In this cohort, Risedronate reduced the risk of new vertebral fractures by 49% after 3 years.

In a cohort of 9331 women older than 70 years, the incidence of hip fracture among all women assigned to Risedronate was significantly reduced compared with that of women assigned to placebo (RR = 0.7). However, this effect was manifest only in women aged 70-79 years who had vertebral fractures at baseline (n = 1703) (RR = 0.4); whereas no significant effect was observed in women aged 70-79 years with low BMD but no prevalent spinal fractures (RR = 0.6) or in women over 80 years of age with at least 1 clinical risk factor for hip fracture (RR = 0.8). The risk for clinically important gastric irritation with Risedronate was reported to be very low even at the highest available doses.

New Bisphosphonates: Ibandronate and Zoledronate

[1-hydroxy-3-(methylpentylamino) propylidene] bisphosphonate (Ibandronate) and [1-hydroxy-2-(1H imidazole-1-yl) ethylidene] bisphosphonate (Zoledronate) are interesting new compounds, currently in phase 3 development for the treatment of postmenopausal osteoporosis.

Ibandronate

Oral Ibandronate was compared with placebo in 2946 women who had BMD T-score < -2.0 in at least 1 lumbar vertebra and 1 to 4 prevalent vertebral fractures. Two dosage regimens of Ibandronate, either given daily (2.5 mg) or on alternate days for 12 doses every 3 months (20 mg), for 3 years, were investigated. Daily and intermittent oral ibandronate significantly reduced the risk of radiologically confirmed vertebral fractures by 62% and 50%, respectively, compared with placebo and showed a sustained effect over the trial period.

This study demonstrates for the first time significant fracture efficacy for intermittent bisphosphonate treatment with a dose-free interval of more than 2 months. Significant reductions in clinical vertebral fractures were also shown in the 2 treatment groups. In a subgroup of women from this trial whose BMD T-score of the femoral neck was < 3 standard deviations at baseline, daily and intermittent oral Ibandronate administration reduced the incidence of clinical fracture by 66% and 50%, respectively, and nonvertebral fractures by 69% and 37%, respectively. These results confirm previous preclinical findings indicating that the efficacy of Ibandronate is a function of the relationship between

loaded dose and the dosing frequency. This obviously supports development of new flexible dosing regimens targeted to minimize the frequency of dosing, which are expected to improve convenience and lead to enhanced long-term patient compliance. Oral once-weekly Ibandronate (20 mg) and daily administration of Ibandronate (2.5 mg) induced almost identical increases in lumbar spine BMD after 48 weeks, and the once-weekly regimen was proven to be statisticially noninferior to daily administered oral Ibandronate. Three-monthly (2 mg) intravenous Ibandronate bolus injections were related to even larger increases of lumbar spine BMD after 1 year (5%). Significant benefits were also reported at the femoral neck or at the trochanter.

Zoledronate

In a similar prospective study assessing the effects of the dose and dosing interval on changes in therapeutic effects of bisphosphonates, zoledronate was evaluated in a 1-year randomized controlled trial of 351 postmenopausal women with low BMD. Women received placebo or intravenous Zoledronic acid in doses of 0.25 mg, 0.5 mg, or 1 mg at 3-month intervals. In addition, 1 group received a total annual dose of 4 mg as a single dose, and another received 2 doses of 2 mg each, 6 months apart.

Similar increases in BMD were recorded in all the Zoledronic acid groups to values for the spine that were 4.3% to 5.1% higher than those in the placebo group and values for the femoral neck that were 3.1% to 3.5% higher than those in the placebo group, suggesting that an annual infusion of zoledronate might be an effective treatment for postmenopausal osteoporosis.

Parathyroid Hormone

In order to assess the effects of 1-34 amino-terminal fragment of PTH on fractures, 1637 postmenopausal women with prior vertebral fractures were randomly assigned to receive 20 or 40 mcg of PTH(1-34) or placebo, administered subcutaneously daily by the women. Vertebral radiographs were obtained at baseline and at the end of the study (median duration of observation, 21 months), and serial measurements of bone mass were performed by dual-energy x-ray absorptiometry. New vertebral fractures occurred in 14% of the women in the placebo group and in 5% and 4%, respectively, of the women in the 20-mcg and 40-mcg PTH groups; the respective relative risks of fracture in the 20-mcg and 40-mcg groups, as compared with the placebo group, were 0.35 and 0.31. New nonvertebral fragility fractures occurred in 6% of the women in the placebo group and 3% of those in each PTH (RR = 0.47 and 0.46). As compared with placebo, the 20-mcg and 40-mcg doses of PTH increased BMD by 9% and 13%, respectively, in the lumbar spine and by 3% and 6%, respectively, in the femoral neck; the 40-mcg dose decreased BMD at the shaft of the radius by 2%. Both doses increased total body BMD by 2% to 4% more than did placebo. PTH had only minor side effects (occasional nausea and headache). The authors concluded that treatment of postmenopausal osteoporosis with PTH(1-34) decreases the risk of vertebral and nonvertebral fractures; increases vertebral, femoral, and total-body BMD; and is well tolerated. The 40-mcg dose increased BMD to a greater extent compared with the 20-mcg dose but had similar effects on the risk of fracture and was more likely to have side effects. Human recombinant PTH(1-34) (Teriparatide) was approved for treatment of osteoporosis by the US Food and Drug Administration at the end of November 2002. Two years is the maximum recommended treatment duration.

Conclusion

New therapeutic approaches have emerged during the past 5 years that significantly improve the daily management of osteoporosis. Alendronate and Risedronate have unequivocally shown their ability to reduce fractures of the axial appendicular skeleton. Their weekly formulations reduce the discomfort generated by the requirements for its oral ingestion without compromising the activity of the drug, hence improving the potential for patient compliance. Intermittent regimens with the new agents Ibandronate and Zoledronate may substantially modify the perspective of bisphosphonate treatments by offering efficient, more user-friendly, and safer therapeutic regimens. Raloxifene has a rapid and sustained antifracture efficacy both in women with prevalent vertebral fractures and those with low BMD. Although its effect on spinal fractures is undisputed, further studies are required to show if it prevents hip fractures as well. In the choice between bisphosphonates and Raloxifene, the collateral benefits reported with the SERM, ie, the significant reduction in estrogen receptor-positive breast cancer incidence in older osteoporotic women and the decrease in the rate of cardiovascular events, in a high-risk population, may be important considerations. A potent anabolic action on bone is mediated by the parathyroid hormone fragment PTH(1-34). This compound has demonstrated ability to reduce the risk of vertebral and nonvertebral fractures. In Bangladesh, we have seen a major change in the osteoporosisscene, with the advent of reliable ways to measure bone density, and the availability of Alendronate, Risedronate, Ibandronate, Zolendronate and Raloxifene. All that is needed now is for us to increase our awareness of osteoporosis so that we can offer our patients a better postmenopausal life.

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Anti-lipid measures : An overview

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Introduction

Epidemiological studies showed that there is a positive correlation between high serum cholesterol level & risk of atherosclerotic coronary heart disease. Raised level of LDL & triglyceride (TG) is also positively correlated with CHD. Low density lipoprotein (LDL) is popularly known as bad cholesterol; on the other hand high level of high density lipoprotein (HDL) is negatively related to the development of CHD. So HDL is known as good cholesterol.

Combination of high total cholesterol, high LDL & TG & low HDL are considered as atherogenic. Through other factors such as smoking, hypertension, central obesity, insulin resistance & procoagulant in blood will also act to induce atherosclerotic coronary heart disease.

Lipoprotein

Cholesterol, triglyceride (TG) & phospholipid being insoluble in water circulate in plasma making it soluble after binding with complex protein called lipoprotein complex. They are -

(a) High density lipoprotein (HDL)
(b) Low density lipoprotein (LDL)
(c) Intermediate density lipoprotein (IDL)
(d) Very low density lipoprotein (VLDL) & chylomicron.

Apo- lipoprotein is protein constituents of lipoprotein & is called Apo-B, Apo-E & Apo-C. Chylomicron & chylomicron remnants contain exogenous lipid, e g: those from diet.

VLDL, IDL, LDL all contains endogenous cholesterol. HDL cholesterol contains minimum amount of cholesterol & more protein. HDL is not atherogenic & on the other hand removes cholesterol from tissue so it is called good cholesterol.

LDL contains highest amount of cholesterol & is atherogenic. It is called bad cholesterol.

Triglyceride is present mainly in chylomicron, chylomicron remnants, low density & intermediate lipoprotein. TG is also atherogenic.

Is cholesterol always harmful???

This is a very common query in the mind of high risk group and the solution of that type of query is negative. Because, normal cholesterol is essential components of cell membrane. It is used for the synthesis of steroid hormone & bile salt. So cholesterol is essential for the body.

Cholesterol Homeostasis

Tissue has receptor for LDL. It recognizes apo B & binds it thus cholesterol is endocytosed. In steady state cholesterol enters & leaves the cell. When cholesterol leaves the cell HDL absorbs it for clearance.

Cholesterol Synthesis

Normally cholesterol is synthesized from acetate. It is converted into acetyl CoA & to betahydroxy beta methyl-Co A (HMG-CoA). HMG- CoA reductase converts it into cholesterol by several steps.

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HMG-CoA is the rate-limiting enzyme for cholesterol synthesis. Statins (cholesterol lowering drug) acts on this enzyme.

Stable & unstable atherosclerotic plaque

Lipid rich plaque is unstable because it can be ulcerated. Thrombus can be deposited on the plaque producing myocardial infarction if the occlusion of the vessel is complete & unstable angina if occlusion is incomplete and intermittent.

Fibrous rich plaque is stable & does not ulcerate easily.

Value of anti-lipid measures

There are experimental and clinical evidences that by lowering cholesterol atherosclerotic plaque regresses. Cholesterol from tissues goes to circulation by binding with HDL and then cleared. When treated by anticholesterol drugs lipid rich atherosclerotic plaque converted into lipid poor fibrous plaque. Fibrous plaque is stable in contrast with lipid rich plaque that is unstable and can ulcerate.

Exogenous source of cholesterol

It is present in red meat, whole milk & milk product. Fats containing saturated fatty acid if taken with food are converted into cholesterol in the body.

Diet and cholesterol

Cholesterol level is elevated if diet is rich in saturated fatty acid. But diet rich in unsaturated fatty acid such as olive oil, plant seed oil such as soybean, sunflower, corn oil mustered oil etc tends to reduce serum LDL cholesterol & increase HDL cholesterol. Such diet though high in fat is not atherogenic.

Sea fish oil has negative correlation with atherosclerosis. Japanese people take more sea fish; as a result incidence of coronary heart disease is not high in Japanese as compared to other developed countries.

Dietary fiber

Both soluble and insoluble from cereals, vegetables & fruits lower LDL cholesterol probably by decreasing absorption of fatty acid. Such diet also lower blood pressure.

Drugs to reduce cholesterol

1. Statin
2. Fibrate
3. Others: Niacin, Resins, and fish oil.

Statins

Simvastatin, fluvastatin, lovastatin, crevastatin, provastatin, atrovastatin.

These are the most widely prescribed drugs to reduce cholesterol. They reduce synthesis of cholesterol by acting on HMG Co-A reductase. They also increase HDL & decrease triglyceride to some extent.

Statins also reduce smooth muscle cell proliferation & migration & stabilizes atherosclerotic plaque.

It is said "the effects of statins are beyond LDL cholesterol reduction".

Fibrates

Gemfibrazil, benzafibrate, fenofibrate, ciprofibrate, clofibrate (not used).

They decrease synthesis & increase catabolism of VLDL. VLDL is rich in triglyceride. Fibrate are used in hypertryglyceridaemia.

Niacin

It reduces TG. Because of its adverse side effects it is used only when other drugs fail to reduce TG.

Resins

They bind bile acid in intestine & increase bile acid synthesis from cholesterol in liver. They are not widely used because of the undesirable gastrointestinal side effects.

Fish oil

Omega 3 Fatty acid found in sea fish decrease TG & thereby reduce atherosclerosis. It has anti -inflammatory properties also.

Role of anti oxidants

Recent clinical trials showed no benefit of antioxidants drugs use in reduction of atherosclerosis. Taking natural vitamins , betacarotine, Vit E & C from dietary sources are recommended.

Garlic oil

There is no statistical benefit of garlic oil use in cholesterol reduction & thereby atherosclerosis. So routine use of garlic and garlic oil are not recommended.

Guideline for cholesterol lowering for LDL

	LDL	Therapeutic goal
No CAD & < 2 risk factor	≥ 190 mg%	< 160mg%
NO CAD but > 2 risk factor	≥ 160mg%	< 130mg%
CAD	≥130mg%	< 100mg%

Life style modification

1. **Tobacco:** Stop smoking or use of tobacco in any form such as **"Jarda"," Sada",** " **Gul"** etc.
2. **Fat:** Reduce total fat intake. Replace saturated fat for mono & poly unsaturated fatty acid from vegetable & fish.
3. **Fiber:** Increase intake of fresh fruits, cereals, & green vegetables.
4. **Physical Activity:** Walking or exercise.
5. **Body weight:** Reduce body weight if you are overweight. Do not increase body weight.
6. **Alcohol:** It is to be avoided.

Conclusion

Dyslipidaemia having high LDL cholesterol, low HDL cholesterol and high TG are the main factors for atherosclerotic coronary heart disease. Lowering of LDL cholesterol and TG and raising of HDL is important in primary and secondary prevention of coronary heart disease. Dietary modification should be first approach. If it fails drug treatment should be given.

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Perinatal HIV infection

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The ORION Vol. 16 Sept. 2003: 117 - 118

Human immunodeficiency virus (HIV) infection causes a broad spectrum of disease and a varied clinical course. Acquired Immunodeficiency Syndrome (AIDS) represents the most severe end of the clinical spectrum. HIV is human RNA retrovirus, HIV type - 1 and less commonly, HIV - 2.

The established modes of HIV transmission are (1) Sexual contact (homosexual and heterosexual), (2) Percutaneous (from needles or other sharp instruments) or mucousmembrane exposure to contaminated blood or other body fluids with high titers of HIV (3) Vertical (Mother to infant) transmission before or around the time of birth and (4) Breast feeding.

Causes of AIDS in children have accounted for 2% of all reported cases in the United States. Of the 16,236 AIDS cases reported in Canada upto December 1998, 75% of AIDS cases were amongst women[1]. The proportion of AIDS cases amongst women of child bearing age has steadily increase in the western countries; from 6.2% of the AIDS cases before 1990 to 13.6% in 1998. It is estimated that across Africa over 5,00,000.00 women are living with HIV[2]. Almost all of the infected women are of child bearing age. More than 90% of infected children in the United States acquired their infection from their mothers. As of December 1998; across Canada, 942 babies have been identified as born to HIV infected women, 325 have been confirmed as infected and 107 have died of AIDS[3]. So, Perinatal HIV infection not only threatens the under developing countries, it also becomes a major health hazard in developed countries also.

The exact timing of transmission from an infected mother to her infant is uncertain, but evidence suggests that about 30% of transmission occurs before birth and 70% occurs around the time of delivery. Available evidence suggest that two third of the infections occurring before delivery are due to transmission of virus within the last 14 days before delivery. In several prospective studies and a meta-analysis, mode of delivery has been found to affect the transmission rate[4]. The European Mode of Delivery Study was a randomized controlled trial comparing the transmission rates for elective caesarean section versus vaginal delivery. The transmission rates for delivery vaginally, by emergency caesarean and elective caesarean section were 10.2%, 8.8% and 2.4%, respectively (P=0.009)[5]. The lowest rate, 2.1%, was in mothers on Zidovudine delivering by ceasarean section. In vaginal deliveries a first born twin is a greatest risk of HIV infection than a second born twin. In a prospective observational study of 522 deliveries, it was found that the duration of rupture of membranes was a major factor in the risk of perinatal transmission of HIV[6]. If the membranes were ruptured for more than 4h compared with less than 4h, the odds ratio was 1.82 and P=0.02. Prolonged rupture of membrane even in the presence of antiretroviral therapy is associated with an increased risk of transmission and must be considered with evaluating the mode of delivery and transmission. Post partum transmission occurs through brest feeding. World wide, as estimated 1/3rd to half of mother to child transmission of HIV may be through breast feeding. Human immunodeficiency virus genomes have been detected in cellular and cell free fractions of human milk.

To prevent vertical transmission of HIV, it is essential to identify the maternal infection. Even the most thorough history and physical examination will identify only fewer than half of HIV positive women. Therefore, routinely offering HIV resting to all pregnant women is now recommended[7]. In a randomized controlled trial, therapy with the antiviral agent, ZIDOVUDINE, in three phases (during pregnancy, during labour and delivery and to the newborn) reduced the proportion of HIV - infected infants from 25% to 8%.[8] In practice, ZIDOVUDINE therapy have been effective, with a reduction of vertical transmission rates to 5% of less.[9, 10] Studies are continuing to determine the efficacy of ZIDOVUDINE.[11]

Although the median age of onset of symptoms is estimated to be (12 - 18) months for untreated perinatally infected infants, increasing number of children are being now identified who have remained asymptomatic for more than 5 years. Infants born to HIV infected women have transplacentally acquired antibody and therefore, become seropositive from the time of birth. This transplacentally acquired antibody complicates the diagnosis of infection.

The American Academy of Pediatric (APP) recommends the following HIV serologic testing.

1. HIV nucleic acid detection by PCR (Polymerase chain of reaction) at DNA extracted from peripheral blood mononuclear cells is the preferred test for diagnosis of HIV infection in newborn and results can be available within 24 hours of obtaining a blood sample. About 30% of infants with HIV infection will have a positive DNA PCR results; from samples obtaining before 48 hours of age. About 93% of infected infants have detectable HIV DNA by 2 weeks of age and almost all by a month of age. DNA PCR is more sensitive on a single assay than is virus culture. A single DNA PCR assay has a sensitivity of 95% and specificity of 97%. Infants born to HIV infected women should be tested by HIV DNA PCR during the first 48 hours of life. Because of possible contamination with maternal blood, umbilical cord blood should not be used for this determination. A 2nd test should be performed at (1 - 2) months of age; a third test at (3 - 6) month of age. Any time an infant test positive, testing is repeated on a 2nd blood samples as soon as possible to confirm the diagnosis. An infant is infected if 2 separate samples are positive. Infection can be excluded when 2 HIV DNA PCR assay performed at or beyond 1 month of age are negative.

2. Virus isolation by culture is expensive and requires upto 28 days for results.

3. Detection of the P_{24} antigen is specific but less sensitive than DNA PCR.

4. Enzyme immune assays are used most widely as the initial test for serum HIV antibody.

5. Another is finding of high viral load by RNA PCR, it does not decline during the first year of life unless antiretroviral therapy is initiated.

Because all babies will be HIV antibody positive due to a passive transfer of antibodies from their mother, the diagnosis of HIV infection must be confirmed by testing for viral antigen (p^{24}), HIV

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DNA sequences using polymerase chain reaction (PCR) or HIV culture. Selected laboratories for a region perform these tests. Viral load testing dose use PCR testing; however, this is not the standard diagnostic test for HIV. A larger volume of blood is required for viral load testing than for the diagnostic test using HIV DNA PCR testing. It is hypothesized that infants who are infected peripartum do not have a measurable viremia until a few days after birth and that most infections occur peripartum. Therefore, the sensitivity of available diagnostic tests for perinatal HIV infection in the first 48 h of life is less than 50%. However, because there is increasing evidence that supports early combination antiretroviral therapy, identification of infection as early as possible in recommended[12]. Cord blood should not be used to test the infant's HIV status because of the risk of contamination with the mother's blood.

Antiretroviral Therapy

The only antiretroviral agent that has been licensed for use in pregnancy is zidovudine. However, antiretroviral therapy is such a rapidly evolving area that an expert should be consulted for appropriate therapy for an HIV-positive pregnant woman.

Antiretroviral therapy for an HIV-infected woman should be chosen to offer the best therapy for the woman's health while weighing the benefits and risks of the drugs for the fetus[13]. The major benefit to the fetus is the reduction of HIV transmission and the major risk is potential drug toxicity. The literature on the toxicity of antiretroviral agents in pregnancy is sparse. The most experience is with the use of zidovudine and so far, no long term adverse effects have been observed[14].

There are no clinical features that distinguish infected from non-infected infants at birth. HIV-exposed infants should receive prophylaxis for HIV from birth. Treatment with ZIDOVUDINE in the three periods-prenantal, intrapartum and neonatal is recommended, but there is potential benifit even if given in one or two periods. In siutuations, where maternal HIV therapy has been sub-optimal, HIV managment of the infant must be individualized so the opinion of an expert should be sought. Usually, the infant is premature the dose may need to be modified. One of the most common side effects of ZIDOVUDINE prophylaxis is anemia; therefore, hemoglobin should be checked at birth and at one month of age. Doctors should encourage giving hepatitis B vaccine to all infants of HIV-infected women and if the mother is a hepatitis B virus carrier, then in addition, the infant should be giving hepatitis B immune globulin. It is recommended that an HIV-positive mother not breastfeed because of potential HIV transmission through breast milk[15].

With current therapy that dramatically reduce the rate of mother-to-child transmission, almost all infants followed should serorevert, that is, lose maternal HIV antibodies and become negative by all HIV tests. One goal of care is to determine, as efficiently and safely as possible, which infants are not infected. In an infected infant, the viral load increases rapidly over the first few weeks of life and by 14 days of age, the sensitivity of the DNA PCR reaches 93% [16]. It has been shown that two sequential samples tested for HIV by either PCR or culture have a negative predictive value of more than 90%[17]. The sensitivity and specificity of virological test in detecting HIV-1 in exposed infants whose mothers where taking zidovudine is similar to that of tests in untreated mother-infant pairs. The sensitivities of DNA PCR, RNA PCR and cell culture are 81.9%, 99.6% and 85.3%, respectively, and specificities are 97.6%, respectively [18]. Therefore, if an infant has all negetive HIV tests by PCR or culture on two specimens, one at one month and another at two to four months of age, that infant is very likely not infected. To confirm and document that an infant is not infected, he or she should be followed to at least 18 months of age, at which time he or she should have no physical findings to suggest HIV and an HIV antibody test that has become negative.

Pneumocystis cainii pneumonia (PCP) occurs most frequently in infants with HIV infection between two and eight months of age, and there is a high mortality rate associated with PCP. Prophylaxis with trimethoprim/sulphamethoxazole (TMP/SMX) is recommended for all infants until their HIV status is determined[19]. If the infant is known not to be infected, TMP/SMX should be stopped. For infants who have been confirmed to be infected, TMP/SMX should be used as previously recommended [20].

Referral to a pediatric HIV program should be offered because the multidisciplinary teams in such programs have the resources to deal with the complexity of medical and psychosocial issues that face many of these families. Even after tests show that an infant is not infected, that child should still be followed annually because of the psychosocial issues that may affect the health of a child living in a family with other members infected with HIV. Some of the long-term issues for an affected child are disclosure of the sibling and death of a parent or sibling.

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Review Article

Recent advance treatment of female stress incontinence : Tension free vaginal tape procedure-A minimally invasive surgery

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The ORION Vol. 16 Sept. 2003: 119 - 120

Introduction

Urinary loss which occurs with sudden elevation of intra-abdominal pressure without detrusor contraction is called stress incontinence. Stress incontinence is a common problem in both developed and developing countries. Postmenopausal women are especially prone to develop stress incontinence. Continence is the result of rotation of the urethrocervical junction against the pubocervical fascia and compression of the bladder neck on stress. At the same time the mid-urethra is kinked to occlude the bladder neck. The causes of stress urinary incontinence (SUI) are hyper mobile urethrocervical junction, intrinsic sphincture deficiency (ISD) or both. Goal of surgery for stress incontinence is to 1) Re-establish the pubocervical hammock under the urethrocervical junction without occluding the urethra 2) Re-establishing the fixation of mid-urethra (Pubourethral ligaments) in order to allow kinking of the mid-urethra on stress. Many procedures are at practice to overcome the distressing problem like as Burch retropubic colposuspention, Needle urethropexy, Suburethral slings but the Tension Free Vaginal tape (TVT) is a new and effective procedure to correct the SUI. The surgery could be done under local anesthesia. It is less traumatic, simple, quick and repeatable. Less skilled surgeon also could perform the procedure. Associated pelvic floor pathology could be corrected simultaneously. Tension free vaginal tape was developed by Ulmster et al and reported first in 1996.[1]

TVT procedure is based on the integral theory according to which the female urethra is closed off in its mid-portion and not at the bladder neck.[2,3] The procedure is aimed at reinforcing the urethrocervical fascia at its mid-urethral level using a polypropylene tape. The tape is inserted vaginaly around the mid-urethra with the help of a special needle instrument. Polypropylene mash is tissue friendly, facilitates tissue growth and provides rapid tissue fixation without suturing. The operative procedure is minimally invasive, time tested and safe. 3 to 5 years follow-up reports from multiple centers are encouraging with cure rate of 85%.[4, 5, 6]

Patient selection criteria

Before surgery preoperative urodynamics study to be done, i.e.

1. Stress test (cough provocation) in lying and standing position with a bladder volume of approximately 300 ml.
2. A 24-hour pad weighing test.
3. 2 days voiding diary and residual urine measurement.
4. Urethrocystometry and urethral profilometry in the sitting and /or semilithotomy position.
5. Urine analysis and
6. Gynecological examination.

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Indication of TVT

1. Genuine stress incontinence.
2. Mixed urinary incontinence.
3. Intrinsic sphincter deficiency.

Exclusion criteria

1. Prior incontinence surgery.
2. Urge incontinence.
3. Detrusor instability.
4. Pregnancy or desire for future pregnancy.
5. Current anticoagulant therapy.
6. Acute urinary tract infection.
7. Severe ISD unresponsive to TVT.
8. Previous lower abdominal surgery?

Procedure

The operation may be done under local anesthesia using lignocain with adrenaline. Patient to be placed on lithotomy position. Urinary bladder to be emptied with 18F Foley's catheter. Total number of incision will be three. All the area will be infiltrated with adrenaline containing lignocain. Two similar 1 cm incisions made on the anterior abdominal wall 4 to 5 cm apart just above the symphysis pubis. One 1.5 cm vertical vaginal incision made on the midline and 1 cm bellow the urethral orifice. Blunt dissection was done on the periurethral region. The TVT set consist of two 6 mm needles connected to a handle (introducer) and a specific polypropylene mash covered with thin plastic sheath and fixed with the needles. Cystoscopy to be performed twice after each time the needle passed around the urethra. After the tape had passed around the urethra tension test to be done. The patient asked to cough after placing 250-300 ml saline in the bladder through catheter. The tape should not be fully occluding as there might be chance of post operative retention.

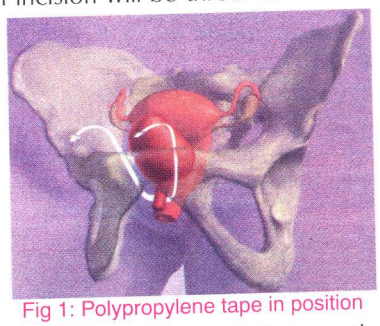


Fig 1: Polypropylene tape in position

Criteria for cure

1. Post-operative negative stress test.
2. A negative pad weighting test for 24 hours.
3. A significant reduction of urinary loss as measured by 24 hours pad weighing test (>50%) reduction.

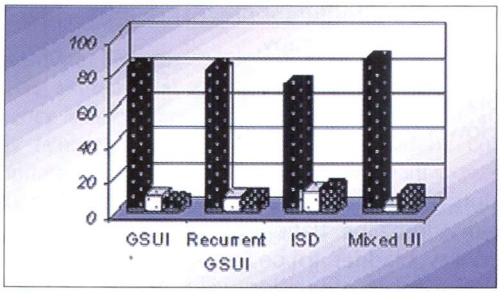
Discussion

Tension free vaginal tape procedure could be performed successfully under local anesthesia. The patient can be discharged from the hospital on the same day. Three years follow up shows an encouraging cure rate of 86% and five years follow-up shows a long term cure rate of 84%.[7] The polypropylene tape usually does not relate to local irritation or any sign of tape rejection. Minimum incision and minimum tissue dissection dose not interfere with blood

Table-1: Complications of TVT Operation.

TVT- Australian Registry Complications n = 2795	%
Bladder perforation	2.70
Post operative UTI	17.00
Re-operation	2.40
30-Loosening the tape	
24-Bleeding hematoma	
1-Small bowel perforation	

Table-2: Follow up of TVT Operation.



(4-5 years follow up of TVT in women with stress urinary continence)

supply. Post-operative retentions could be prevented by allowing escape of few drops of saline during cough test per operatively. Success rate depends upon careful evaluation of patients in both objective and subjective parameters, such as the stress test, the pad weighing test and quality of life assessment, with these strict criteria for cure the TVT procedure compares very well in the long term with the most effective traditional and more invasive surgical procedures, such as the fascial slings and the colposuspension operations.[8,9]

Conclusion

TVT is fast, minimally invasive procedure which may be performed in the out patient department setting.

Approximately ninety percent of patients void spontaneously following the procedure. Cure rate in 1-5 years is 74 to 90% in different set up. Complications are rare but may be significant.

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Review Article

Prevention & control strategy of thalassemia in Bangladesh

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The ORION Vol. 16 Sept. 2003: 121 - 122

Introduction

Thalassemia is the most common inherited gene disorder in the world and varies in different population groups in the world[1]. With global improvement in childhood diseases, due to prevention and treatment with targeted programs to prevent mortality from malnutrition, diarrhoea & acute respiratory infections, thalassemia will become a major issue in developing countries like Bangladesh in this millennium. World Health Organization (WHO) estimates that at least 6.5% of the world populations are carries of different inherited disorders of Hemoglobin[2]. It is predicted that when the world population finally stabilizes, at least 8.0% of the world population will be the carrier or trait of different types of Thalassemia syndromes & hemoglobinopathies[2].

The world population of carriers of beta thalassemia trait is reported to be more than 100 millons worldwide and about 100,000 children with thalassemia major are born each year[2]. Abnormal hemoglobin, called hemoglobin-E, which is quite common in Bangladesh no definite data regrading carrier status of hereditary hemoglobin disorder exist. No screening programme had ever been taken in any population group. A conservative World Health Organization (WHO) report estimates that about 3.0% of populations are carriers of Beta Thalassemia and 4.0% are carriers of Hb-E in Bangladesh, which means that there are about 3.6 millions carriers of beta thalassemia and 4.8 millions carriers of Hb-E and affected birth per thousand of Beta thalassemia is 0.106 & 3.000 of Hb-E/Beta thalassemia and affected birth per thousand of Beta thalassemia is 0.106 & 0.300 of Hb-E/Beta thalassemia[4]. It is presumed that approxmately six thousands thalassemic children are born each year in Bangladesh[1].

The birth of a thalassemic child could place a considerable health and economic strain not only on the affected child and its family but also on the whole community and country. Since it is a severe and incurable disease, emphasis must shift from treatment of the affected child prevention of such births in future. All forms of thalassemia are transmitted only through hereditary. Identification of carriers of the thalassemia gene plays an importment role in preventing this fatal but preventable disease.

All over the world efforts are being made to prevent the birth of thalassemic child and to improve the quality of life those who are being suffering. Thalassemia needs to be recognized, as an important health issue in this country and steps need to be taken to control the birth of thalassemic children. The following steps to be recommended and which are being followed in many countries :

1. Creating awareness

Creating awareness about thalassemia to the general population, government and medical communities by holding seminars, workshops and writing articles in the daily newspapers, broadcasting in television and radio is of prime importance. Thalassemia day is observed on the 8th May all over the world. On this day various activities has to be arranged and media should be utilized for dissemination of information and recent advances about thalassemia. The government must also take steps to create awareness among the rural populations by involving thana health complexes and other different local organizations through different activities like seminars, symposium, publications etc. It is very much painful that other than Dhaka city, no facilities are exists for the diagnosis of thalassemia in any other parts of the country.

2. Population screening

Population screening of such a vast problem in such a huge population and hence it is reasonable to select a cohort for screening e.g. pregnant women. They are usually accessible to the health system and information on reproductive risk is of immediate relevance to them. Screening of close relatives of the couples of affected child also is aggressively pursed.

A cheap, easily reproducible & simple screening test "NESTROF (Naked Eye Single Tube Red Cell Osmotic Fragility) has been developed along with the morphology of red cells & red cell indices (MCV, MCH, RWD) for detection of beta-thalassemia trait & other hemoglobinpathies like Hemoglobin-E trait which is most common abnormal hemoglobin in Bangladesh and showed to be very effective in mass population screening. It is being done in India, Iran, Thailand and Iraq[5]. In Iraq this screening method was applied in national survey to detect the carrier-state all over the Iraq [6]. We are doing this screening test for carrier detection in our countries. A practical approach would be to perform NESTROF on an accessible way to unmarried cohort of peoples like adolescents at school leaving or before starting college, or young adults starting a job or going to marry, must perform this screening HbA2 or Hb-E [7]. By diagnosing and counseling thalassemia carriers, it becomes feasible and attractive alternative for preventation of thalassemic birth in our country.

3. Genetic counseling

Genetic counseling needs to be given to thalassemia carriers and parents who have a thalassemic child. It should be not-directive and the counselor's mail role is to provide people at risk with full information; give them time for consideration and support them in making decisions. Genetic counseling without prenatal diagnosis has not been very successful in Greece and Cyprus but in Iran where

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10,000 people preparing for marriage were screened for the thalassemia trait using CBC (Complete Blood Count) and Hb-A2 level measurement showed that the average of high risk couple initially deciding not to marry was 90% and no new cases of thalassemia was detected in the children of the screened population and the conclusion was that where both members of the couple were trait positive for their preferred choice was not to marry than to marry[6]. We have no experience in genetic counseling and work need to be done to assess the attitude and results of genetic counseling in our country.

4. Prenatal diagnosis

Prenatal diagnosis in being carried out in our neighboring countries like India, Pakistan, Thailand & also in countries like Indonesia, Malaysia & Jordon. It is a well-established procedure in developed countries. There is need for religious and legal scrutiny of prenatal diagnosis and therapeutic abortion in our society.

With the introduction of first trimster diagnosis by chorionic DNA techniques, specfically PCR methods chorionic villi sampling (CVS) has become the simplest and most acceptable method for prenatal diagnosis and most suitable method for use in developing countries. As a result prenatal diagnosis, which was initially limited to North America, Europe, Australia has spread to many developing countries. Training for collection of chorinic villi samples and villous sampling and DNA analysis that represents a major advance in preventation of genetic disorders like thalassemia. With the simplification ofDNA analysis needs to be given to our doctors & DNA centres need to be set up for giving facilities for diagnosis of thalassemia and its prevention.

Thalassemia needs to recognized as an important health problem and plans need to set up to reduce the number of cases born by development of population screening programme, awareness creating by using mass media like radio, television, leaflets, booklets, poster, festoons & improving treatment strategy those who are being suffering from thalassemia within our limited resources.

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Continuation of MSD NEWS from page no.-126

Scientific meeting on 'Selective estrogen receptor modulator (SERMs) in management of osteoporosis and Role of fibric acid derivatives on diabetic dyslepidamia'

Venue: BIRDEM auditorium, Shabag, Dhaka

From left to right: Dr. S.M. Ashrafuzzaman, Assoc. Prof. Dr. Nurul Islam, Prof. Zafar A. Latif, Prof. Hajera Mahtab, Dr. Zahid Ikram.

A scientific meeting was organized by Orion Laboratories Ltd on Thursday, 29th May, 2003 at Auditorium of BIRDEM on "Selective Estrogen Receptor Modulator (SERMs) in management of Osteoporosis (Ralox) and Role of Fibric Acid Derivatives (Fenocap) on diabetic dyslipidaemia." Prof. Zafar A Latif, Head of the Endocrinology Department of BIRDEM was present as Chairperson of the session. Prof. Hajera Mahtab, Director, Clinical service, Research & Academic & Dr. Nurul Islam, Assoc. Prof. of Nephrology, BIRDEM was also present as chief guest and special guest respectively. Dr. Md. Zakirul Karim, Manager, MSD, Orion Lab. Limited welcomed the participants. Dr. Zahid Ikram, Consultant diabetologist & endocrinologist, BIRDEM & Dr. S.M. Ashrafuzzaman, Specialist on diabetes & endocrinology, lit their views on role of SERMs (Raloxifen) on postmenopausal osteoporosis and management of diabetic dyslipidaemia with special emphasis on fibric acid derivatives (Fenocap) respectively.

Scientific seminar on 'Advanced management for post - menopausal osteoporosis, Drug of first choice for the management of benign prostatic hyperplasia (BPH), Management of depression: Pharmacological aspect'

Venue: Zilla Parishad Auditorium, Gaibandha

A Scientific seminar was jointly arranged by Orion Lab. Ltd. and BMA, Gaibandha on "Advanced management (Ralox) of Post - menopausal Osteoporosis, Drug of first choice (Tamlosin) for the management of Benign Prostatic Hyperplasia (BPH), Management of Depression: Pharmacological Aspect (Venlaf)" on Tuesday, 29th July, 2003, at Zilla Porishad Auditorium, Gaibandha. Dr. A. K. M. Shamsuzzoha Khandaker, President, BMA, Gaibandha chaired the session. Dr. Md. Abdul Kuddus, Civil Surgeon, Gaibandha and Dr. Md. Shahadat Hossain, Director (Rtd.) were also present as chief guest and honorable guest respectively. Dr. Md. E.K. Shafique, Secretary, BMA, Gaibandha, welcomed the participants.

Scientific seminar on 'Recent management of dyslipidaemia, Modern management of BPH, Modern management of postmenopausal osteoporosis'

Venue: Lecture Gallery, Faridpur Medical College, Faridpur.

A scientific seminar was jointly arranged by Orion Lab. Ltd. and BMA Faridpur branch on "Recent Management (Fenocap) of Dyslipidaemia, Modern Management (Tamlosin) of BPH, Modern Management (Ralox) of Postmenopausal Osteoporosis." on Sunday, 27th July, 2003 where Dr. Md. Enamul Karim, Principal, Faridpur Medical College chaired the session. Dr. A.T.M. Mahfuzul Haque Shaheen, Medical Officer, FMCH conducted the program & Dr. A. K. M. Rafiqule Islam, Joint Secretary, BMA, Faridpur welcomed the participants. Dr. Sk. Yunus Ali, Asstt. Prof. of Cardiology, FMCH, presented his paper on Recent Management of Dyslipidamia, Dr. J. C. Saha, Asstt. Prof. of Surgery, FMCH, presented his paper on Modern Management of BPH and Dr. Zebunnesa Parvin, Consultant (Gyne & Obs) General Hospital, Faridpur, presented her paper on Modern Management of Postmenopausal Osteoporosis. Dr. Md. Mostafizur Rahaman Shamim, Present, BMA, Faridpur branch thanked the participants for their active participation.

Use of venlafaxine in the treatment of non-depressed outpatient with generalized anxiety disorder : A case report

Mohit M A[1]

The ORION Vol. 16 Sept. 2003: 123

Introduction

Anxiety is a normal response to threat or stressful events, and is usually short-lived and controllable.[1] It probably functions as an 'alarm' mechanism to prepare an individual for physical response to perceived danger, and is therefore common in patients undergoining examination, investigation or treatment in medical settings. Anxiety symptoms are considered clinically significant when they are: abnormally severe, usually prolonged, occur in the absence of stressful circumstances.[1]

It has been accepted that Generalized anxiety disorder (GAD) is a chronic disorder that is associated with debilitating psychic & somatic symptoms.[2] The symptoms are persistent and are not restricted to as strongly predominating in any particular set of circumstances. It is free floating & unvaring and persist more then 6 months.[3] I am reporting here a case where use of venlafaxine in nondepressed outpatient with GAD showed improvment in debilitating psychic & somatic symptoms.

Material & Method

A 22 year unnamed female university student of urban area & of middle class who met the DSM-IV criteria for GAD[4] attended by herself at the OPD of NIMH, Dhaka.

She had excessive anxiety & apprehensive expectation worries about future misfortune, which she found difficult to control. She had also following associated symptoms: restlessness, headache, inability to relax, difficulty in concentrating, irritability, sleep disturbence like restless unsatisfied sleep, difficulty falling or staying asleep.

The symptoms were not caused by organic brain disease, not confined to feature of Axis-1 disorder & the disturbence was not due to the abuse of a substance. The anxiety, worry or physical symptoms caused clinically significant distress in academic & social life functioning. Her symptoms were free floating unvaring & not related to any particular situations.

Her father was educated, in service, mother was also educated, school teacher. She had one younger brother only. They had very good home atmosphore, economically of middle class and their interpersonal relationship within family member was healthy. But her father was dominating with ill temperd, impulsive. She had no family history of phychiatric illness. But her father was hypertensive.

Personal history reveled that her early development was normal, she had a bit shyness. Her academic life started at age 5, performance was fluctuatine in school results. She had fews friends, used to avaid social situations.

She had no experience in sex but her menstrual cycle was normal. She had no history of drug abuse and premorbid personality revealed that her predominant prevaling mood was worrying, self depreciating, fluctuating.

Relevant all investigations were done. After the confirmation of diagnosis she was prescribed Tab. venlafaxine (venlaf) 37.5 mg twice daily. For the initial three weeks tab Clobazam (10mg) was also given. She was also involved in psychological treatment like training in applied relaxation & problem solving tecnique. She was also taught to understand her thinking patterns by cognitive behavioural therapy approaches.

Result

After two weeks, in first follow up session the patient was improved in sleep disturbence. Restlessness was also reduced to 50% (according to her statement). On mental state examination her facial expression of anxiety features were also reduced & mood was less anxious. According to her statement, she performed relaxation technic regularly & also applied problem solving strategies. She was also educated about her negative cognitions in 1st follow up session.

After 4 weeks, in 2nd follow up session, it was observed that, there was no further improvement as observed in session.[1] By the time Clobazam was gradually withdrawn. Valafaxine was increased to dose 75mg at night & 37.5 mg at morning. Her negative cognitions were also challenged.

After 6 weeks, in 3rd follow up session, there was significant improvement in academic performance & social functioning. Her concentration was also improved. Sleep pattern changed to neary smooth life, excessive apprehension about her misfortune was also reduced almost to normal level.

She regularly attended the followup session and dose of venlafaxine was continued. Behavioural & cognitive strategies were also applied in each session.

After 6 months, gradual withdrawl of vanlafaxine was attempted & reduced to 37.5 mg twice daily. In the next subsequent session again there were complaints of excessive anxiety & worry about the misfortune. She was also less concentrating & more irritable. Again the dose changed to 75mg at night & 37.5mg at morning. Patient was observed in improvement with the dose.

Discussion

Vanlafaxine extended release is an effective, rapidly acting safe, once daily agent for both the short & long term treatment of anxiety & may provide an improtant alternative to currently available anxiolytic.[2] In this case study, it has also observed that venlafaxine as a simple agent is safe & effective. When anxiolytic (clobozam) was withdrawn, there was no relapse of the symptoms. Instead increased dose of venlafaxine along with behavioural strategies was associated with significant improvement. This finding is also supported by the statement that other drugs found efficacious in randomized controlled trials in GAD include venlafaxine.[1]

Venlafaxine XR is an effective, safe & well tollerated once daily anxiolytic agent in patients with GAD without combined major depressive disorder.[5] Their finding also supports the result of the case study mentioned here. In this case study, it was clearly observed that venlafaxine was well tolerated effective safe & there was no comorbidity with depression in patient GAD. Althrough drug treatment of GAD is sometimes prescribed as 6-12 month course of therapy, some evidence indicates that it should be long-term, perhaps life long. About 25% of patients relapse in the first month after the discontinuation pharmacologic therapy 60% - 80% relapse over the course of the next year.[6] In this case study it has been observed that reduction of dose of venlafaxine after 6 months was also associted with relapse of symptoms the two weeks.

Limitation

Hamilton Rating Scale for Anxiety (HAM-A) was not applied for score. Cognitive behaviour therapy (CBT) was also not canducted properly & effectively.

Conclusion

Venlafaxine is effective in improvement of GAD. It is safe & tolerable, but gradual withdrawl is also associated with the relapse of symptoms.

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1. **Dr. M. A. Mohit (Kamal)** MBBS, MPhil (Psychiatry),Fellow WPA(USA)
Assistant Professor
National Institute of Mental Health, Dhaka

Imaging hepatobiliary and pancreatic system by ERCP

Alam T[1], Khan Z R[2], Rabbi A N M A[3]

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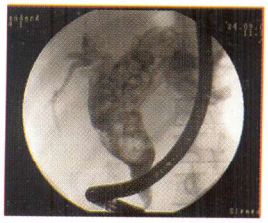
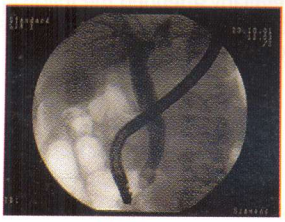
To
The Editor

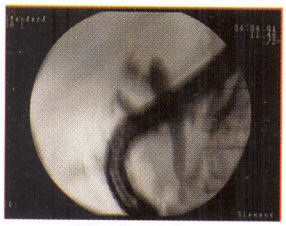
We would like to report our experience in Imaging hepatobiliary and pancreatic system by ERCP (Endoscopic Retrograde Cholangio Pancreatogram) to find out the cause of surgical jaundice, to investigate abdominal pain thought to be biliary in origin and in the management of chronic calcific pancreatitis. 201 ERCP is done during the last 2 years time. Pre-ERCP relevant investigations are done in all cases.



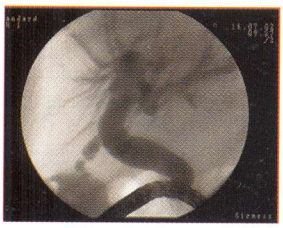
Hepatolithiasis



CBD stone

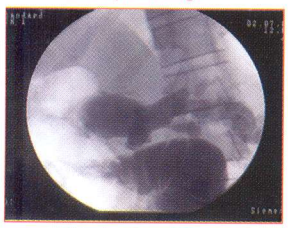


Bile duct injury

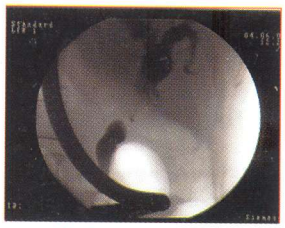


Biliary Leakage

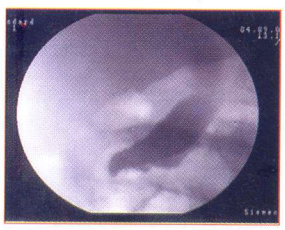
Chledochoal Cyst



Chledochoal Cyst



Cholangiocarcinoma



Ca- Head of the pancreas

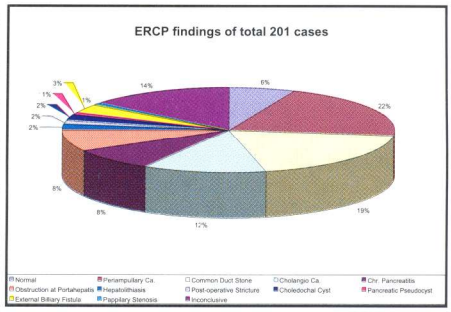
1. **Dr. Towhidul Alam,** MBBS, FCPS (Surgery)
Asstt. Prof. of Surgery, BSMMU

2. **Dr. Zulfiqur Rahman Khan,** MBBS, FCPS, FRCS
Asstt. Prof. of Hepatobiliary and Pancreatic Surgery, BSMMU

3. **Prof. A.N.M Atai Rabbi,** FCPS(S), FICS(USA), FCPS (Pak)
Professor & Chairman, Department of Surgery, BSMMU

Table 1: ERCP findings of 201 cases

Normal	12
Periampullary Ca.	40
Common duct stone	37
Cholangio Ca.	32
Chr. pancreatitis	16
Obstruction at porta.	16
Hepatolithiasis	4
Post-operative stricture	3
Choledochal cyst	4
Pancreatic pseudocyst	2
External biliary fistula	6
Papillary stenosis	2
Inconclusive	27
Total	201



In relation to stone disease in biliary tree ERCP helps us in showing number, size and site of stones, similarly in biliary obstruction due to other benign and malignant conditions ERCP helps by showing the site and extent of obstruction. In relation to chronic pancreatitis ERCP shows the extent of pancreatic duct dilatation which is needed for operative management. All these information that we get from ERCP is not possible from other investigations like USG or CT scan.

Surgical problem related to hepatobiliary and pancreatic system are still managed by two different specialty in our country. With an intension to manage these patient under one specialty we are going to start therapeutic ERCP very soon. So ERCP is still an important tool for managing hepatobiliary and pancreatic disease. It can be mention here that many therapeutic procedures like papillotomy, stone extraction, stenting can also be done.

Launching of New Products

Orion Laboratories Limited and Orion Infusion Limited has recently introduced the following seven new products in the market

Nervex

Mecobalamin INN 0.5 mg tablet

New Approach in treating Neurological Diseases

Nervex (Mecobalamin) is a cobalamin with an active methyl base that can directly participate in nerve regeneration by enhancing nucleic acid and protein synthesis in the nerve cells. It promotes myelination by enhancing lecithin synthesis and also helps axonal regeneration and axonal transport. It is indicated for the treatment of peripheral neuropathies, diabetic neuropathy, Bell's palsy, Parkinson's disease, Alzheimer's disease, diabetic retinopathy, lumbago, multiple sclerosis, drug induced neuropathy, entrapment neuropathy and vertebral syndrome. It is presented in the form of 0.5 mg tablet. The usual adult dose is one tablet 3 times a day. MRP TK. 4.00/tab.

Eprel

Eperisone HCl INN 50 mg tablet

Multifunctional muscle relaxant

Eprel (Eperisone) is a centrally acting, multifunctional skeletal muscle relaxant which provides multifarious actions like relaxation of hypertonic skeletal muscles, analgesia and inhibition of the pain reflex and increase blood flow by vasodilation. It is indicated in the treatment of hypertonic conditions caused by neck-shoulder arm syndrome, scapulohumeral periarthritis, low back pain, and spastic paralysis caused by cerebrovascular accident, spastic spinal paralysis, cervical spondylosis, post-operative sequelae, sequelae of trauma, infantile cerebral palsy, spinocerebellar degeneration, spinal vascular disorders, subacute myelo-optic neuropthy and other encephalomyelopathies. Eprel is presented in the form of 50 mg tablet. The usual adult dosage is 3 tablets daily in 3 divided doses after meal. MRP TK 3.00/tab.

Stimulin

Glimepiride INN 1 & 2 mg tablet

A truly once daily antidiabetic

Stimulin (Glimepiride) is an oral hypoglycemic drug of the sulphonylurea class. It is indicated as monotherapy as an adjunct to diet and exercise for the management of Type-2 (non insulin dependent) diabetes mellitus (NIDDM) in patients whose hyperglycemia can not be controlled by diet and exercise alone . Stimulin is also indicated as combination therapy with Ormin (metformin) when diet, exercise and stimulin or Ormin (metformin) alone do not result in adequate glycemic control. It is cardioprotective and controls blood sugar with virtually no risk of hypoglycemia. Stimulin is presented in the form of 1 and 2 mg tablet. The usual initial adult dosage of stimulin is 1-2 mg once daily administered orally with breakfast or the first main meal. The maintenance dosage of stimulin for the management of Type 2 diabetes ranges from 1- 4 mg once daily by mouth. The maximum recommended dosage is 8 mg once daily. MRP Stimulin 1: TK. 3.00/tab. and Stimulin 2: TK. 5.00/tab.

Nicor

Nicorandil INN 10 mg tablet

A mighty protection for Ischemic Heart

Nicor (Nicorandil), a potassium channel opener with nitrate moiety, is an anti-anginal agent. It is indicated for the prophylaxis and treatment of angina pectoris. Nicor provides better efficacy than other anti-anginal drugs by virtue of its dual mode of action. It also shows headache and nitrate tolerance free anti-anginal activity. It is suitable for patients with hypertension, diabetes mellitus, heart failure (in the absence of pulmonary edema), COPD and cardiac conduction disorders. Nicor is presented in the form of 10 mg tablet. The recommended adult therapeutic dose for Nicor is 10 to 20 mg twice daily. The usual starting dose is 10 mg twice daily (preferably in the morning and in the evening); up to 30 mg twice daily may be used. MRP TK. 3.00/ tab.

Flegnil DS

Carbocisteine BP 250mg/5ml suspension

The only expectorant suspension available in Bangladesh

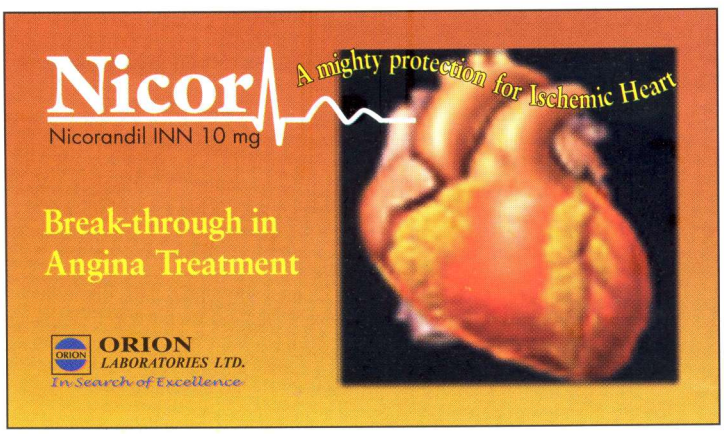
Flegnil DS has been launched for the adult which is the brand extension of Flegnil. It is indicated for the treatment of chronic respiratory conditions like bronchitis, bronchial obstruction as in asthma, bronchiectasis, respiratory tract congestion, glue ear, otitis media, cattarrah, rhinopharyngitis. Flegnil DS is presented in the form of suspension 250 mg/5ml. The usual dosage of Flegnil DS is 2 spoonfull 3 times a day . MRP TK. 40.00/phial

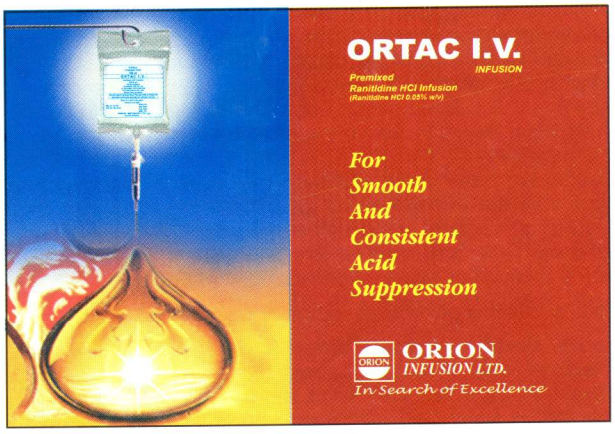
Ortac I.V infusion

Ranitidine HCl 0.05% w/v

For smooth and consistent acid suppression

Ortac I.V infusion (Ranitidine) is a sterile pyrogen free, isotonic formulation of ranitidine for intravenous administration. It is indicated in intractable duodenal ulcer, prophylaxis of hemorrhage from stress ulceration of GIT, prophylaxis of recurrent hemorrhage in patients with bleeding peptic ulcer, before induction of general anesthesia in surgical and obstetrical patients requiring urgent operation (prevention of Mendelson's syndrome), hematemesis and melena, pathological hypersecretory conditions (such as Zollinger-Ellison syndrome), erosive gastritis etc. Ortac I.V is presented in the form of 100ml PVC bag containing 50mg of ranitidine. The usual adult dose of Ortac I.V 100 ml containing 50 mg ranitidine, to be administered 6 to 8 hourly over a period of 15 to 20 minutes @ 5 to 7 ml per minute. MRP TK. 60.00/bag.





MSD NEWS

MSD personnel of ORION Laboratories Limited spent an busy schedule in middle quarter of the 2003, in organizing scientific seminars/clinical meetings in various venues as a part of their Continued Medical Education (CME) Program.

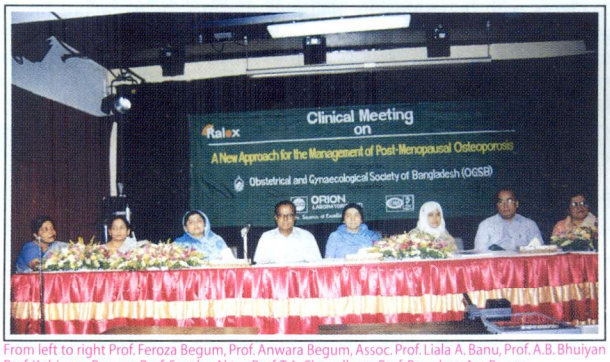
Seminar on '4th generation fluoroquinolone'

Venue: ENT department, BIRDEM, Dhaka.

A scientific seminar was sponsored by Orion Laboratories Ltd on 'Moxifloxacin: A New Fast Acting 4th Generation Fluoroquinolone'. on 20th April Sunday, 2003 at ENT department BIRDEM, Dhaka. Dr. Zaheer - Al - Amin, Consultant, department of ENT, BIRDEM, chaired the session and presented the scientific paper on the occasion.

Clinical meeting on 'Management of post -menopausal osteoporosis' with OGSB.

Venue: BIRDEM Auditorium, BIRDEM, Dhaka.



From left to right Prof. Feroza Begum, Prof. Anwara Begum, Assoc. Prof. Liala A. Banu, Prof. A.B. Bhuiyan Prof. Kohinoor Begum, Prof. Sayeba Akter, Prof. T.A. Chowdhury, Prof. Rowshan Ara Begum

A clinical meeting was jointly organized by Orion Laboratories Ltd. and Obstetric and Gynecological Society of Bangladesh (OGSB) on 'Ralox: A new approach for the management of post - menopausal osteoporosis' on Wednesday, 30th April, 2003 at BIRDEM Auditorium, BIRDEM where Prof. A. B. Bhuiyan, President OGSB, chaired the session. Dr. Farhana Dewan, Scientific Secretary of OGSB conducted the meeting and elected president Prof. Anwara Begum welcomed the participants. Dr. Feroza Begum present the scientific paper on 'An overview on Menopause and Osteoporosis ' and Dr. Zakirul Karim , Manager, MSD, Orion Lab. Ltd. present the scientific paper on "Ralox: in preventing the osteoporosis of post menopausal women and also in decreasing the risk of breast and uterine cancer."

A very interactive panel discussion was moderated by Prof. T. A. Chowdhury along with other panel members like Prof. Sayeba Akter, Prof. Kohinoor Begum, Prof. Rowshan Ara Begum and Assoc. Prof. Laila A. Banu were also present. "Raloxifene (Ralox) prevent the osteoporosis of post menopausal women and reduce the risk of breast and uterine cancer too" said Prof. T. A. Chowdhury as a moderator during panel discussion. He expressed his view as Raloxifene (Ralox) is double breast friendly drug for post - menopausal women.

Venue: Memon Maternity Hospital, Chittagong

A clinical meeting was arranged by Orion Laboratories limited on "Ralox: A new approach for the management of post- menopausal osteoporosis" on Monday, 19th May, 2003 at Conference room, Memon maternity hospital, Chittagong. Dr. Sorforaj Khan Chowdhury, Chief health officer of Chittagong City Corporation chaired the session. Dr. Priti Barua, Senior Consultant of Memon Hospital and Dr. Nurul Islam, in charge of Memon Hospital were also present as co-chairperson on the occasion. Dr. Zakirul Karim, Manager MSD, Orion Lab. Ltd. presented the scientific paper on 'Ralox'-highlighting its role in preventing the osteoporosis of post- menopausal women and also decreasing the risk of breast and uterine cancer.' A very live interactive discussion was conducted by Dr. Nazrul Islam and Dr. Priti Barua, who thanked all participants to make the program fruitful.

Clinical meeting on '4th generation fluoroquiolone and Fenofibrate'

Venue: Department of Medicine, BIRDEM, Dhaka.

A clinical meeting was sponsored by Orion Laboratories Ltd. on 'Moxifloxacin: A New Fast Acting 4th generation fluoroquiolone and Fenocap: A super lipid regulator to prevent the cardiac events' on Monday 28th April, 2003 at BIRDEM, Dhaka. Dr. Khawza Nazimuddin, Consultant, department of medicine, chaired the meeting and Dr. A.K.M. Musa, Consultant, department of medicine, was present as the special guest of the session and presented their scientific papers on the occasion.

Scientific meeting on 'Diagnosis and management of BPH, Management of hyperlipidaemia with special emphasis on fibric acid derivatives and An overview on menopause & osteoporosis'

Venue: Auditorium, Regional Diabetic Hospital, Comilla

From left to right: Dr. Md. Zakirul Karim, Manager, MSD, OLL, Dr. Md. Iqbal Anwar, Dr. Md. Sirajul Haque, Dr. Md. Mizanur Rahman, Dr. Karuna Rani Karmakar.

A Scientific meeting was jointly organized by Orion Laboratories Limited & Bangladesh Medical Association (BMA), Comilla on "Diagnosis and management of BPH (Tamlosin), Management of hyperlipidaemia with special emphasis on fibric acid derivatives (Fenocap) and Menopause & Osteoporosis (Ralox) - An overview " at the auditorium of Regional Diabetic Hospital, Comilla on Tuesday 27th May, 2003. Dr. M. S. Alam, Chairman, scientific sub committee, BMA, Comilla chaired the session & the programme was conducted by Dr. Md. Harun-or-Rashid, scientific secretary BMA, Comilla. Dr. Golam Mohiuddin Dipu, General Secretary, BMA, Comilla welcomed the participants and Dr. Md. Sirajul Haque, Assoc. Prof. of Surgery,CoMCH, expressed his view on diagnosis and management of BPH. Dr. Md. Mizanur Rahman, Asstt. Prof. of Cardiology, CoMCH & Dr. Karuna Rani Karmakar, Asstt. Prof. of Obs & Gynae also lit their views on Management of hyperlipidaemia with special emphasis on fibric acid derivatives and an overview on Menopause & Osteoporosis respectively. Dr. Md. Iqbal Anwar, President, BMA, Comilla thanked the participants for their active participation.

Scientific meeting on 'Combination of diuretics for congestive heart failure & Fibric acid derivatives to manage the hyperlipidaemia'

Venue: Nuclear Medicine Centre, auditorium, SSMC&H.

A Scientific meeting was arranged by Orion Laboratories Ltd. on "Frulac - A logical combination of diuretics: Right choice for congestive heart failure & Fenocap: Super lipid regulator to prevent the undue cardiac events" on Thursday, 24th May, 2003 at Nuclear Medicine Centre, auditorium, SSMC&H. Prof. Dr. Abdul Kashem Khondoker chaired the session & expressed his view on Diuretics and lipid lowering agents. Dr. Azizul Kahhar, Assoc. Prof. of medicine & Dr. Razibul Alam, Assoc. Prof. of medicine, SSMC&H were also present as special guest and lit their views on Role of Diuretics in congestive heart failure and Fenofibrate(Fenocap): the lipid regulator that prevent the undue cardiac events respectively.

Seminar on 'Management of depression and Social anxiety disorder (SAD)

Venue: Bonanza restaurant, Chittagong.

A clinical meeting was organized by Orion Laboratories Ltd. on "A new approach (Venlaf) for the treatment of depression" on Wednesday 21st May, 2003 at Bonanza restaurant, Chittagong. Prof. Dr. Sayed Mahfuzul Huq, Prof. of psychiatry (Retd.) was present as chief guest on this occasion.

Venue: Langthu - Rai Restaurant, Sylhet.

A clinical meeting was arranged by Orion Laboratories Ltd. on "A new approach (Venlaf) for the treatment of depression" on Wednesday 18th June, 2003 at Langthu - Rai restaurant, Sylhet. Prof. Dr. Md. Rezual Karim, Principal, SMAGOMCH, chaired the session and Dr. Gopal Shankar Dey, Assoc. Prof. & Head, department of psychiatry, SMAGOMCH, presented his scientific paper on 'An overview of depression & Social anxiety disorder (SAD).

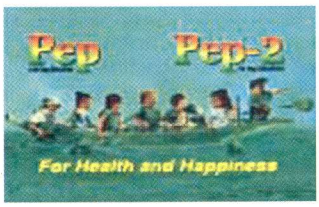
The rest of the MSD NEWS is given on page ...122

Medi News

ZINC
The 'Superstar' of Minerals

Zinc – why it is important to our health

Zinc is needed in our bodies in trace amounts, for a multitude of important functions. In fact the incredible value of this mineral is continuing to grow as more and more evidence comes to light. At least ninety of the body's metabolic enzymes require zinc to function properly.[1] Zinc can be found in all body tissues, but especially in the eye, liver, brain, muscle and reproductive organs. It may be of immense value to the immune system, and is thought to play an important role in regulating insulin activity. But just as fast as zinc is becoming recognised as a vitally essential mineral, studies are also showing many children and adults are suffering from zinc deficiency. Common signs of zinc deficiency are a poor sense of taste and smell, wounds that are slow to heal, excessive hair loss, impotency, growth impairment and the appearance of white flecks on the fingernails.



Deficiencies who is at risk?

Almost everyone may be at risk of becoming zinc deficient. Worldwide, zinc is the mineral most depleted from soil used to grow food.[2] The refining techniques of the modern world actually take out valuable zinc from many of our grains.[3] This may result in two of our most staple foods, bread and cereals being seriously lacking in nutritional value. Even canned, frozen and dried foods contain almost negligible levels of zinc. Populations of countries where the climate is extremely hot are at a greater risk of becoming zinc deficient through the loss of this mineral in sweat. Also particularly prone to this type of deficiency are pregnant women, teenagers and the elderly, as well as heavy drinkers and those who consume a nutritionally poor diet.

Zinc – of special importance to men

Zinc is essential to the entire male reproductive system. The male prostate gland contains more zinc than any other gland in the human body. Male sperm and seminal fluids are also very high in zinc. Deficiencies may cause prostate problems, retarded genital development, impotence or infertility. A recent study of Iranian and Egyptian youths, who showed signs of retarded sex organ development and overall growth, found their diets to be lacking in the mineral zinc. When zinc supplementation was begun, the problem immediately rectified itself and the boys continued to develop normally. The most important discovery to come from this study was that the male hormone cannot be produced without zinc!

When wounds are slow to heal

The Ancient Egyptians knew about the healing properties of zinc. They used it in balms to treat skin irritations. Zinc is the healing ingredient in calamine lotion and over the years has been added to various creams and ointments to relieve skin problems such as sunburn and rashes. But zinc may be even more effective to the healing process from within. When wounds occur zinc is drawn to the site to help rebuild collagen. It also helps to prevent an outbreak of infection. Extra zinc intake may be beneficial to the proper healing of surgical incisions, bed sores, canker or cold sores and chronic leg ulcers as well as other everyday injuries where the skin tissue is damaged.

Acne – a common affliction

As many as 80 percent of all teenagers are affected by acne.[4] Studies show that it may be a lack of zinc, caused by a diet high in refined carbohydrates, that is the main cause in many cases of acne. Supplementation with zinc, usually of the chelated type to ensure better absorption, has been shown to correct the acne problems of some teenagers. Zinc might also be useful in relieving other minor skin irritations such as eczema.

Zinc in the treatment of anorexia

Eating disorders such as anorexia nervosa, bulimia, obesity and pica may be helped by extra zinc in the diet. Although zinc deficiency does not cause anorexia, the starvation diet of those suffering the condition can lead to a shortage of zinc. Loss of appetite is a classic symptom of anorexia nervosa, as it is of zinc deficiency.[5] The sense of taste and smell are also affected. Without these important senses it would be very difficult to break the starvation cycle. Research shows zinc supplementation may effectively restore the appetite and sense of taste and smell, and thereby assist those suffering eating disorders to rediscover healthy eating habits. The importance of zinc in the health of the human body is sure to grow as more research comes to light. Zinc truly is the 'superstar' of minerals.

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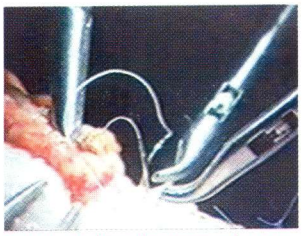
Robot heart surgery success

A British man has left hospital just four days after major heart surgery - performed on him by a robot.

Retired physicist John Cast, 72, is one of the first people in the UK to undergo the procedure, called totally endoscopic robotic coronary artery bypass (TECAB). Normally, a heart bypass requires surgeons to crack the rib cage open so they can gain access. But in Mr Cast's case the only incisions needed were four holes the width of pencils. The procedure is controlled by a surgeon, but instead of operating directly on the patient, he uses an instrument console several feet away. I can't believe how quick my recovery has been John Cast This allows him to orchestrate the highly precise movements of a pair of robotic arms.These arms are designed to mimic the dexterity of a surgeon's forearm and wrist - but in fact they actually have a greater range of motion, and are less susceptible to tremours, allowing surgeons a finer degree of precision than ever before. By watching a monitor linked to a miniature camera, the surgeon is able to manipulate the arms even when they are inside the chest, and out of sight. Mr Cast's surgery, which took place at St Mary's Hospital, Paddington, London, was performed by consultant cardiothoracic surgeon Roberto Casula. As in traditional surgery, a healthy blood vessel was removed and used to bypass a blocked artery to the heart. Mr Casula said: "TECAB surgery is unique because, unlike a traditional bypass operation, there is no need to open up the chest. "This provides a huge number of benefits for the patient including just a small amount of scarring, less pain (and use of pain killers), a reduced chance of post-operative infection and blood transfusion, and importantly, quicker mobilisation speeding along a good physical and emotional recovery."



Robots cut down the trauma of surgery

bbc.com/health

Leukemia pill shows promise against stomach cancer

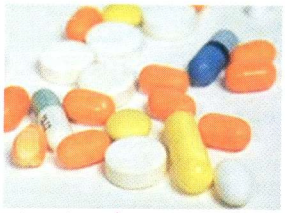
Researchers reported Sunday that a new cancer pill approved by the U.S. Food and Drug Administration for a common type of adult leukemia showed encouraging results when used on stomach cancers like gastrointestinal stromal tumor, or GIST – a type of stomach cancer that affects as many as 5,000 Americans each year. The pill was approved for use against leukemia last week and has been hailed as a major breakthrough. It is taken once a day and causes virtually no side effects. "It turns out that GISTs, or gastrointestinal stromal tumors, have a target that is very closely related and also drives their malignant behavior," said Dr. Charles Blanke, a researcher at Oregon Health Sciences University. Unlike traditional chemotherapy, which attacks all cells randomly, this drug blocks the action of an enzyme that causes stomach tumors while leaving healthy cells untouched. And as with leukemia, researchers often saw results in GIST patients within days. A study of 148 GIST patients showed 59 percent went into remission, and the results were even better in those with the most common type of mutation. A second, smaller study had similar results. The results were to be discussed Sunday at the American Society of Clinical Oncology's annual convention in San Francisco.

Because Imatinib mesylate has been approved for the treatment of chronic mylogenous leukemia and since studies show the pill also works in GIST, theoretically doctors could prescribe for so-called off-label use for treating GIST. "Giving it to patients with gastrointestinal tumors or other kinds of cancers that might work would be a reasonable situation if it was done with full knowledge of the patient and doctor," said Dr. Harmon Eyre of the American Cancer Society.

CNN.com/Health

Warning over food supplement

The supplement beta-carotene may increase the risk of bowel cancer, researchers have warned. The substance has been linked to an increased risk of lung cancer in smokers and people exposed to asbestos. Now a study suggests that in some people it can double the risk of benign tumours known as adenomas that can lead to colorectal cancer. The finding relates to those who smoke cigarettes and have more than one alcoholic drink a day. "Supplementation [with beta-carotene] was beneficial among subjects who did not drink or smoke but, if anything, increased risk among those who drank and/or smoked," said study author Dr John Baron, of the Dartmouth Medical School in the United States.The conclusion is based on a study of 864 patients who had had previous adenomas removed. However, Dr Tim Key of Cancer Research UK at Oxford University, said there was no evidence of benefits for beta-carotene and more evidence of harm. "The advice is you should not take supplements of beta-carotene to prevent cancer," Dr Key told BBC News Online. The warning comes after experts from the UK's Food Standards Agency said that high levels of supplements like beta-carotene over a long period may have irreversible harmful effects. Beta-carotene is a substance from plants that the body converts into vitamin A. Natural beta-carotene is found in food such as fruit and vegetables.



An estimated 10m Britons take vitamin supplements

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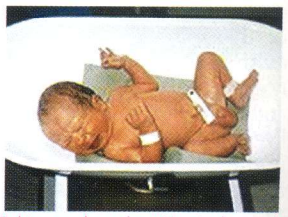
Boy babies 'boost appetite'

Pregnant women carrying boys tend to eat more than those carrying girls, research has found. The finding supports the theory that a developing male foetus demands more energy from its mother -and may be more likely to develop problems if it does not receive an adequate supply of nutrition. This is a phenomenon that continues after birth - men are more vulnerable than women to most diseases and environmental risks throughout life. Researchers analysed the diets of 244 pregnant women attending a large hospital in Boston, US. They found that overall those carrying boys had a 10% higher energy intake. On average, they had an 8% higher intake of protein, a 9% higher intake of carbohydrates, an 11% higher intake of animal fats, and a 15% higher intake of vegetable fats. The researchers, from the Harvard School of Public Health, suggest that a male foetus may secrete a chemical from its developing testicles that stimulates its mother to step up her energy intake. Lead researcher Professor Dimitrios Trichopoulos said the reason for the difference appeared simply to be that male babies tend to grow bigger in the womb. Boys, on average, tend to weigh abut 100g more than girls at birth. Professor Trichopoulos said: "Sad to say, but there is discrimination in nature. "For evolutionary reasons - such as having to compete among themselves to gain the favours of women - males have to be bigger than females and this phenomenon has its origins in the womb." He added that all pregnant women should try to eat a balanced diet.



Babies need good nutrition in the womb

bbc.com/health

Cradling phone can cause 'mini-stroke'

People who cradle the telephone between their head and shoulder could be putting themselves at risk of a "mini-stroke", leading to temporary loss of vision and speech problems. Scientists say a 43-year old psychiatrist in France spent an hour on the telephone talking to a patient, cradling the receiver between his left ear and shoulder so he could keep his hands free. Shortly afterwards he experienced a temporary blindness in his left eye, together with a ringing in his left ear and a difficulty in speaking. An angiogram of the patient's brain showed he had ruptured the carotid artery, a vital blood vessel supplying the brain, eyes and other parts of the head.

Cradling the phone can damage your health

The psychiatrist had no predisposition to arterial disease, but a CT scan showed a bony structure was directly in contact with his internal carotid artery. This was his styloid process, a slender, pointed bone which runs from both sides of the skull under the ears and behind the jaw. Although everyone has two, the man's was unusually long, and was the cause of the rupture. In this case, the psychiatrist's symptoms disappeared within a few hours.

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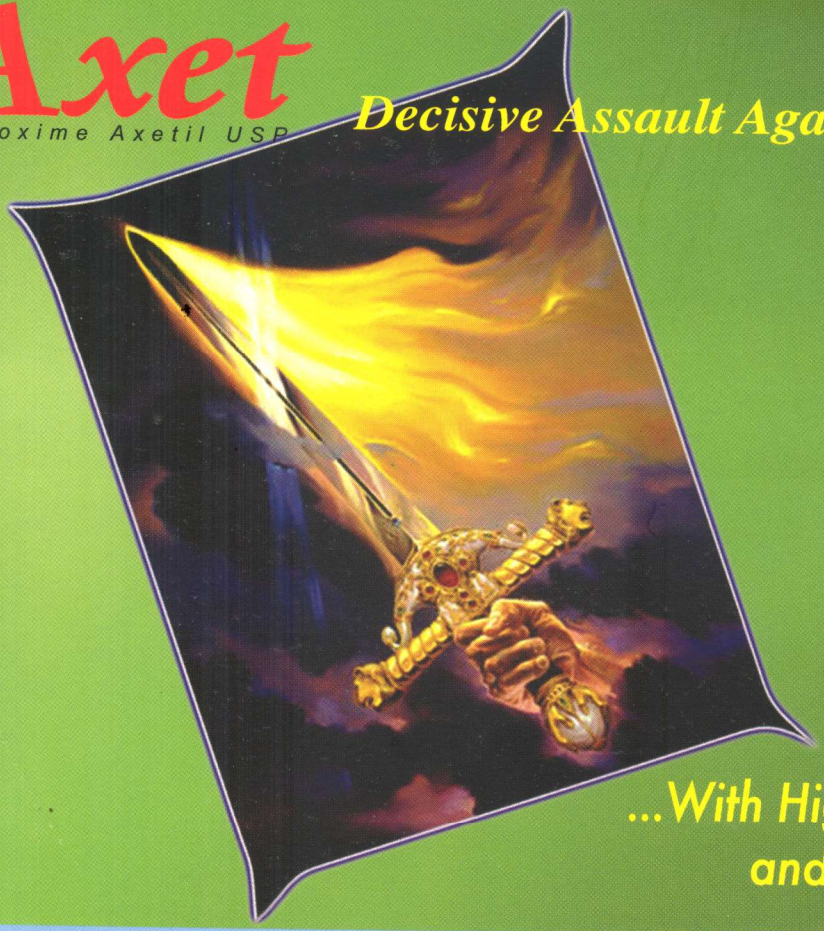

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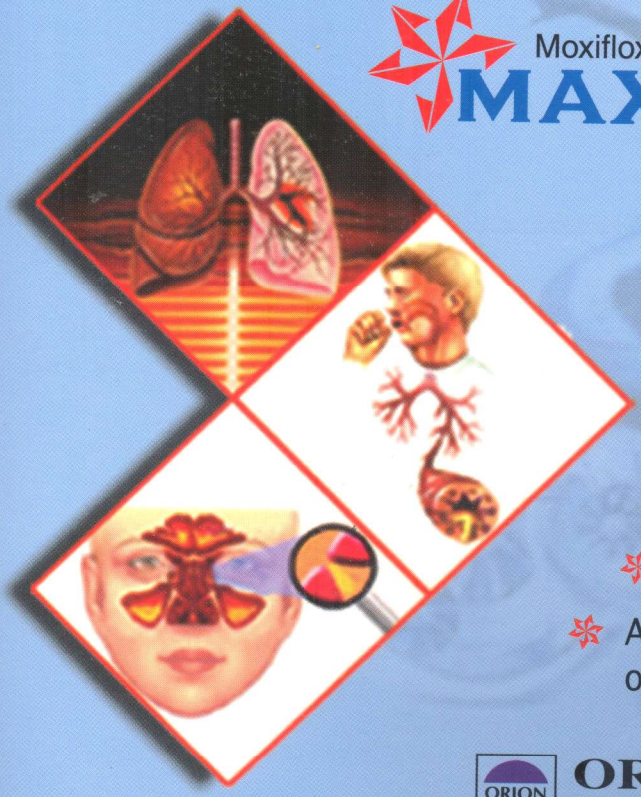

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