The ORION

Medical Journal

Vol-19, September-December 2004

Multi Discipline Vol-19 : 193-224, 01 September 2004, International ISSN 1606-9722

Relentless Voyage to Continued Medical Education Program

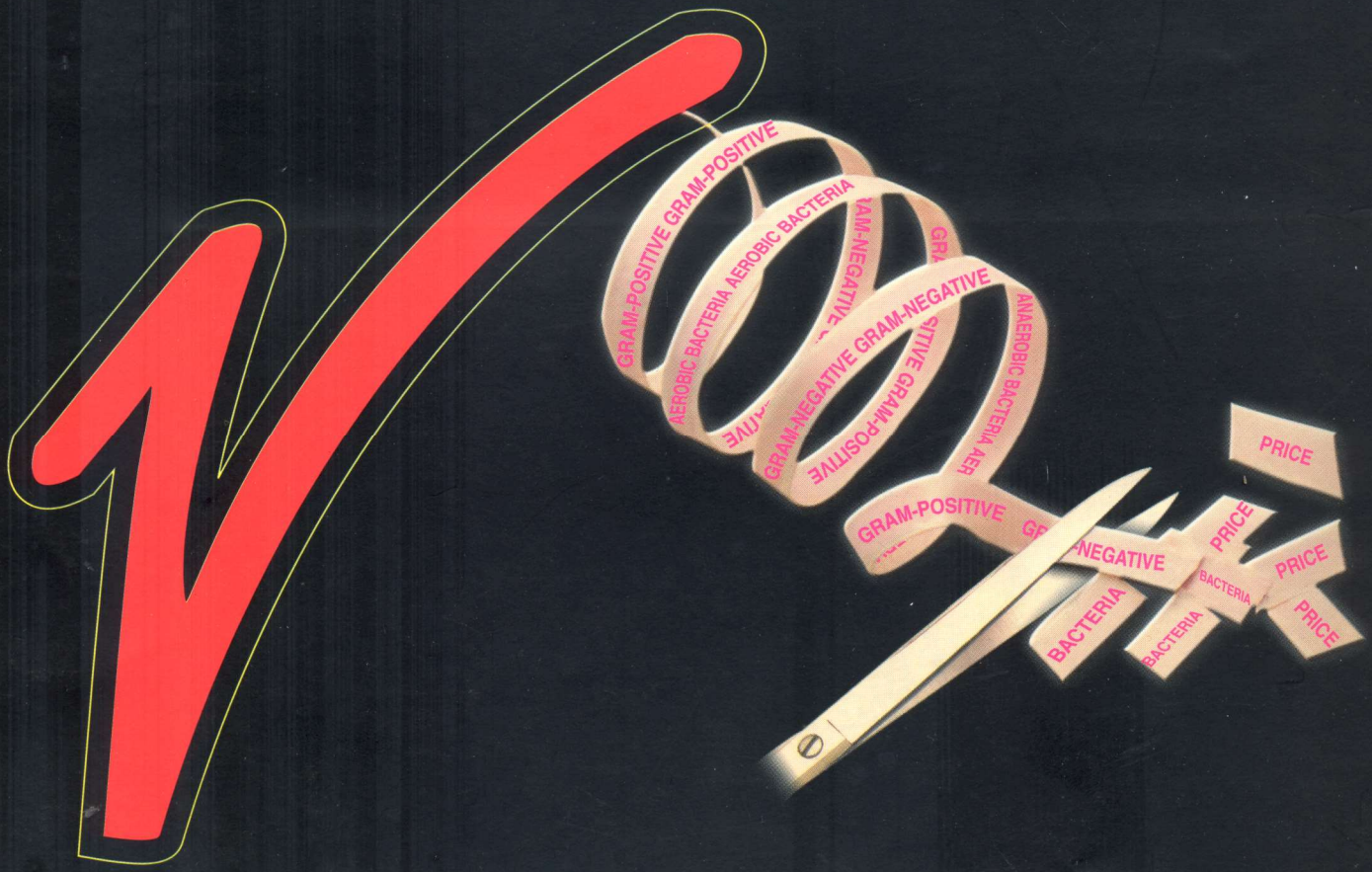
Ceftriaxone Sodium

Vertex

Safe & Save

250 mg, 500 mg & 1 gm IV & IM

At amazingly economic prices



At amazingly economic prices

Strength		Price/Vial
250 mg	IV & IM	Tk. 90/-
500 mg	IV & IM	Tk. 125/-
1 gm	IV & IM	Tk. 195/-

ORION
ORION
LABORATORIES LTD.
In Search of Excellence

Printed by : Fair Printing Press
7160680, 7169896

Procap

Omeprazole

Total protection

from

Ulcerative Complications

ORION

ORION
LABORATORIES LTD.

In Search of Excellence

Founded September 1998 • Published quarterly • Volume 19 • Wednesday 01 Sep. 2004

The ORION Medical Journal

Editor's Choice

The ORION, 5 years, relentless voice

Peerless dominion of The ORION is commemorating five years vigorous endeavor of its publication with a specialty, 'Relentless Voice towards CME'. This enormous achievement is possible because of the continuous support of the esteemed readers, the arduous efforts of the valued authors, and the endless contribution of the respective members of the Advisory and Review Boards. The ORION salutes all its well-wishers to achieve such recognition. This superlative enthuses The ORION for successive progression to be arrayed into broad medical spectrum.

Therefore, the editorial (P-194) of this issue points out Malaria, which is an important tropical health condition receiving attention and having regular updated policy by Bangladesh Government and guided by WHO. This issue is also congregated with valuable topics like "Management of male infertility" (P-195-198) discussing about the various causes of male infertility and its recent management.

A review article on "Hyperlipidemia as a risk factor for ischemic stroke" (P-199-201) nicely sketches the definition, investigation, diagnosis and management of Hyperlipidaemia.

Another original article on "Parents' attitude towards a child with surgically correctable congenital anomaly" (P-202-204) cites a hospital prospective study regarding various congenital anomalies of the children and the reactions of the parents' in treating such cases.

The review article on " Recent advances in treatment of preterm labour" (P-205-206) is focused on conservative treatment of preterm labour. Other article on "Rectal cancer" (P-207-210) gives modern information for diagnosis and treatment of the disease. Article on "Hepatotoxicity in tuberculosis treatment" (P-211-212) flushes the adverse effects of anti-tubercular therapy.

Another review article on "Role of cardiologist for the treatment of eye diseases" (P-213-214) reveals the important role of cardiologists in treating eye diseases.

An original article on "Reconstruction of diaphyseal tibial bone loss: G. A. Ilizarov technique" (P-215-217) describes the management of segmental defects within the diaphysis of long bones by applying G.A. Ilizarov technique.

The case report on "Acute myocardial infarction with normal coronary arteries in a young heroin user" (P-218-219) nicely documents a very interesting cardiac observation and successful management of the case.

A scientific letter on "Superstitions: The women are behind" (P-220) briefly describes some common gynecological miss-perceptions in Bangladesh along with their scientific solutions.

The opinion and suggestion of the valued 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.

DR. MOHAMMAD ZAKIRUL KARIM
Chief Editor, The ORION
and Manager,
Medical Services Department, ORION Laboratories Ltd.

Travel related malaria in Bangladesh: An unaddressed health issue

Faiz M A[1]

The ORION 2004 ; 19 : 194

Malaria is an important tropical health condition receiving attention and having regular updated policy by Bangladesh Government supported and guided by expert agencies like the World Health Organization. Existing malaria control and treatment policy was adopted sometime before waiting renewal following acquisition of newer information and data. Malaria is an important cause of mortality, and morbidity due to infection in South Asia. The present malaria case definitions adopted in Bangladesh include: uncomplicated malaria, treatment failure malaria and severe malaria. The definitions are applicable only in malaria endemic areas of Bangladesh which are 13 eastern bordering districts of the country. Majority (>90%) of the cases of malaria including deadly falciparum malaria are from five naturally bountiful districts of the country: Chittagong, Cox'sbazar, Rangamati, Khagrachori, and Banderban. Following signing of peace treaty a massive development work is ongoing in the three Hill districts. Having limited tourist area in the country people are being attracted in the malaria prone areas of the country for sight seeing, study tour and honey moon. Performing job in this area by non immune people include the various regimental people like police, BDR, armed forces. The present national malaria guidelines do not address the issue of internal travel related malaria in Bangladesh, although worldwide international travel related malaria cause 25,000 cases (10,000 reported) with 150 deaths.

An 18-year-old HSC examinee a resident from Dhaka presented to Dhaka Medical College Hospital in the month of December 2003, a season of dengue with 6 days' fever, gum bleeding and jaundice. Duty house officer could dig out the recent travel and stay to one of the three Hill districts. While waiting for a blood film report for malarial parasite the doctor observed rapid deterioration of the condition: impaired consciousness, development of hypoglycaemia, and convulsion. Although parenteral quinine was started, his condition further deteriorated requiring mechanical ventilation and artificial support for 19 days. The patient had positive falciparum infection and many of the severe manifestations of malaria from which he recovered in next couple of months with significant sequelae.

A newly married couple, resident of Dhaka was staying in a tea estate in Sylhet. Young wife was pregnant developed fever diagnosed as flue like illness subsequently diagnosed as falciparum malaria, developed malarial acute renal failure and shifted to Dhaka. Before starting renal replacement therapy she died unfortunately. The news attracted lots of press attention at that time. Over a short period of nine months in one adult medical unit in Dhaka Medical College Hospital at least 11 patients of falciparum malaria was admitted with history of travel or short stay in malaria prone area of Bangladesh. Three such patients of severe malaria died in hospital. In most of the cases diagnosis was delayed due lack of suspicion before admission. History of travel or stay in malaria endemic area could provide clue to early diagnosis. Dhaka being a non malaria endemic area, expertise in detecting malaria parasite is not widely available and a central malaria reference laboratory need to be activated for the purpose. The malaria diagnosis now a days became relatively easy and simple by detecting malaria specific soluble antigen using Rapid Diagnostic Test (dipstick). The test detects soluble antigen of malarial parasite within minutes and has a very high sensitivity and specificity in a clinically suspected case. Unfortunately the name'Rapid Diagnostic Test' became a misnomer in Dhaka as report is not available for patient management even in hours. The test report should be make available in shortest possible time within minutes even over mobile phone. Outcome of treatment of malaria particularly severe malaria depends upon early administration of potent parenteral antimalarial drug, once report is available the effective treatment can be provided.

The national antimalarial policy suggests chloroquine as the first line drug for treatment of uncomplicated malaria. Enough evidence of high degree failure of chloroquine from various areas of Bangladesh are available for justification not to use chloroquine in falciparum malaria in Bangladesh. Changed guidelines to address the issue has been planned. The recent recommendation and trend by the WHO is to promote combination antimalarials in uncomplicated falciparum malaria in such chloroquine resistant areas. Artemisinin-lumefantrine combination has been registered and available in Bangladesh. Two recent studies from two distinct malaria emdemic areas found high degree of efficacy of the drug with reassuring safety profile. In future the returning tourists and travelers from high risk malaria endemic areas could be diagnosed by RDT and can be effectively treated with artemisinin lumefantrine to avert development of severe malaria. Once severe malaria develops the available parenteral quinine with support of multiple system could safe life. In case of unusual contraindication of quinine alternative drug like artesunate or artemether should be made available. The recent development in the management of moderately severe malaria by using per rectal formulation of artesunate will be of much help in resource limited areas particularly in remote rural areas.

The key to early diagnosis of malaria in the capital is not to forget the travel history in any suspected case of malaria. Confirmation of diagnosis could be made by either blood film or RDT. For uncomplicated malaria artemisinin-lumefantrine should be the drug of choice. In diagnosed severe falciparum malaria in patient treatment with parenteral quinine with supportive treatment could safe life. "Awareness about malaria and various measures that travelers can take to avoid infective mosquito bites are more important then ever".

1. **Professor M A Faiz,** FCPS, FRCP, PhD
Professor of Medicine,
Dhaka Medical College, Dhaka

References

1. Zaidi A K M, Awasthi S and de Silva H J (2004). Burden of Infectious diseases in South Asia. Br Med J 328:811- 815.
2. W H O (2003). Assessment of the safety of artemisinin compounds in pregnancy.
3. W H O (2001). Antimalarial drug combination therapy. Report of a WHO technical consultation.
4. Faiz, Rahman E, Hussain M A, Rahman M R, Yunus E B , Samad R et al (2001). A randomized control trial comparing artemether and quinine in the treatment of cerebral malaria in Bangladesh. Indian J Malariology, 38:9-18
5. Wellems T E (2003). Two worlds of malaria. N Engl J Med 346; 1496-98

Management of male infertility

Salam MA[1]

The ORION 2004 ; 19 : 195-198

Male infertility is a common cause of sub fertility for which sperm disorders are the single most common cause. Genetic abnormalities, for example, micro deletions associated with the Y chromosome, defects in the androgen receptor gene and cystic fibrosis have gained recent prominence and it is envisaged that many of the 60% of men for which no cause is found may have a genetic basis for their sub fertility. Although an abnormal semen analysis is commonly the first indicator of a male factor problem, further tests are usually required. Empirical treatment with hormones, varicocelectomy and immunological treatment have been proven to be disappointing whilst the treatment of infection and obstruction do not always translate into significantly higher fertility rates. Ejaculatory disorders and impotence can be effectively treated today whilst donor insemination can be offered to men with untreatable infertility. The advent of assisted reproduction and micromanipulation has greatly improved prospects for fertility of men with very poor semen quality. However, the genetic implications of these procedures have to be quickly addressed so that fertility is maximized without risk to the progeny[1].

Sub fertility affects about 15% of all married couples. In about one third of these cases, a male factor is the primary problem and in another third, problems in both the male and female contribute to sub fertility. As a single cause of sub fertility, sperm disorders are the most frequent. With a few rare exceptions, it was traditionally regarded that male infertility was a condition which was very difficult to treat. This was mainly because the problem is not an entity but reflects a variety of different pathological conditions and effective treatment strategies were not available.

Even today, recognizable causes are present in only about 40% of men with infertility. The other 60% have normal gonadotrophin and testosterone levels and the pathophysiology remains to be elucidated although, new studies on the deletions or mutations in a number of genes may explain a substantial proportion of this group[2]. This would explain why until recently, the therapy remained mostly empiric and unsuccessful. However, advances in the field of micromanipulation techniques have revolutionized the management of the male factor in assisted reproduction and has now given hope to many men who would otherwise be unable to father a child. The optimism for this has been tempered by the genetic implications of men with very low and abnormal sperm counts, as will be seen later.

Sub fertility affects about 15% of all married couples. In about one third of these cases, a male factor is the primary problem and in another third, problems in both the male and female contribute to sub fertility. As a single cause of sub fertility, sperm disorders are the most frequent. With a few rare exceptions, it was traditionally regarded that male infertility was a condition which was very difficult to treat. This was mainly because the problem is not an entity but reflects a variety of different pathological conditions and effective treatment strategies were not available.

1. Prof. MA Salam, MBBS, FCPS
Professor, Department of Urology, BSMMU

Absent testicular tissue

This is a rare cause of male sub fertility. As the chance for natural fertility is nil, it is important that appropriate counselling be given early so that all the options could be explored with the couple. It is also important to exclude genetic and/or chromosomal disorders in such men.

Genetic causes of male infertility

Genetic factors including chromosomal abnormalities that can impair sperm production and function are numerous but rare. A high index of suspicion is necessary when taking a history and examining these men. Genetic defects are associated with a variety of clinical presentations ranging from gonadotrophin-releasing hormone deficiency to spermatogenic failure and obstructive azoospermia. Recent discoveries have now firmly focused the attention on genetic disorders as an important component in the etiology of male infertility. Testosterone is paramount in spermatogenesis in all mammals and acts via the androgen receptor (AR) which is encoded by the AR gene on the X-chromosome. Since most males with infertility have normal androgen levels, attention is now focused on the AR apparatus as a cause of defective spermatogenesis. Defective androgen binding has been detected in 12% - 15% of infertile males and mutations of the ligand-binding domain of the AR can lead to defective spermatogenesis in otherwise normal males. Other defects in the AR gene have now been shown to be associated with various conditions from androgen insensitivity syndromes to Prostatic cancer and spinal bulbar muscular atrophy. Another important genetic factor identified is the azoospermic factor (AZF) gene on the long arm of the Y chromosome. Studies on azoospermic and severely oligospermic men have shown that 12% - 18% of these men have deletions in a consistent specific portion in the AZF gene. Clinical testing for defects in the AR gene and the AZF gene is now available and it is envisaged that more men with severe oligospermia or azoospermia will undergo such studies in the future.

Other causes

Patients with thalassemia major (which is prevalent in South East Asia) develop infertility resulting from iron deposition in the pituitary gland and testis. Men with an undescended testis usually have impaired spermatogenesis that also affects the normal testis. The same is true of men with testicular cancer where there is severe impairment of spermatogenesis in 25% of cases. Hypogonadotrophic hypogonadism may be congenital as in Kallman's syndrome or acquired as in pituitary adenomas (e.g. prolactinoma), craniopharyngioma and other brain tumors. There are many drugs which have deleterious side effects on sperm production and function. Examples include sulphalazine (for inflammatory bowel disease), anabolic steroids and anticancer drugs (e.g. cyclophosphamide, procarbazine, cisplatin). The roles of environmental toxins have also become prominent in recent years. Some spermatotoxic compounds identified include pesticides (e.g. DBCP, chlordecone, carbaryl, ethylenedibromide), glycol ethers (used in paints, printing inks and adhesives) and metals (lead, cadmium and mercury). Other toxins have been shown to have estrogenic properties and have been implicated in the

gradual decrease in sperm counts in men this century. Finally, the influence of alcohol, smoking, recreational drugs and nutrition on fertility potential of the male should not be neglected. Varicoceles are present in 10% - 15% of men in the general population. Although it has been strongly implicated in spermatogenic failure, the management of this problem has become a contentious issue in recent years.

Impaired sperm transport

Approximately 5% of men with infertility have identifiable anti-sperm antibodies. The role of sperm antibodies remains highly controversial. Although it is possible that the presence of antibodies on sperm has better prognostic value than those in serum or in seminal plasma, it is likely that infertility will occur when antibodies bind to a relevant sperm antigen involved in a specific fertility function. This may explain the variation in functional defects seen in immunological infertility. Sexually transmitted diseases are an important cause of epididymitis and can lead to blockage of the ductal systems. Congenital absence of some part of the ductal system is a rare condition and may have genetic implications (e.g. congenital absence of the vas deferens and cystic fibrosis). An ejaculation and retrograde ejaculation may occur in diabetics, after retroperitoneal lymph node dissection, spinal cord injury and bladder neck surgery. Sexual dysfunction and impotence may also masquerade as infertility.

Management

History and physical examination

A thorough history may reveal an etiology even though in the majority of cases, a negative history is more common. Some important points to note include a history of hernia surgery in childhood, trauma and torsion (possible damage to the vas or testis). A past history of genitourinary infections like orchitis (eg. mumps, syphilis, tuberculosis) or epididymitis (eg. gonorrhoea, chlamydia, tuberculosis) may indicate a more serious effect on fertility. Chronic infection of the prostate and seminal vesicles are characterized by painful ejaculation, haematospermia and pain in the perineum. A delayed onset of puberty may indicate a gonadotrophin deficiency whilst a history of recurrent chest infection and bronchiectasis may be associated with epididymal obstruction (Young's syndrome), absent sperm motility (immotile cilia syndrome), and agenesis of the vas (cystic fibrosis). Testicular and sexual dysfunction may be caused by many chronic disorders such as renal failure, liver disease, malignancy and diabetes. Environmental and occupational exposure to toxins as well as a good drug history should be sought for. Some cases of infertility may have its seed in sexual dysfunction and it is imperative to establish that normal vaginal intercourse with intravaginal ejaculation occurs with regularity. A general physical examination should be carried out and should include the height, weight, body habitus and secondary sexual development. Abnormalities in these basic parameters alone may be a clue to some of the rarer genetic causes of male subfertility (eg. obesity, lack of secondary sexual characteristics, hypotonia, tall/short stature). If androgen deficiency (eg. eunuchoid, lack of facial and pubic hair, small testes, decreased libido) is suspected, look for gynaecomsatia, cryptorchidism, hypospadias, anosmia and visual field defects. Testicular volume measurement with a Prader orchidometer may give the key finding in differentiating between azoospermia due to testicular failure (small volume) and duct obstruction (normal volume). The normal adult testicular volume for Asian men is between 12 mL and 35 mL. Testicular size also indicates the degree of testicular development in hypogonadotrophic patients and of testicular atrophy in those with various forms of primary testicular pathologies. An irregular contour, induration or abnormal consistency of the testis suggests previous orchitis, surgery or malignancy. An enlarged and tense caput epididymis may be palpable in cases of obstructive azoospermia. Irregularity and induration of the epididymis and vas suggest previous infection. The presence of a varicocele should be documented and graded (grade 1 - detected on doppler on Valsalva manoeuvre, grade 2 - palpable, grade 3 - visible). A chronic prostatic infection may reveal an irregular consistency and tenderness on rectal examination.

Investigations

Semen analysis

This remains the most important basic investigation of the male factor. However, conventional parameters of semen analysis such as sperm density, percentage of motile sperm, quality of sperm movements and sperm morphology are subjective and do not give an accurate assessment of the fertility potential of an individual. Also, as sperm counts can be quite variable in the same person, it is standard practice to do 2 to 3 analyses. The extent to which standard parameters of semen analysis implicate a male factor is debatable and the conventional view that any sperm concentration under 20 x 106 sperm/mL indicated male infertility has been challenged. The majority of men who are investigated for male factor subfertility have oligoasthenoteratozoospermia of unknown cause. In view of the severe limitations of a conventional semen analysis, new tests of sperm function have been introduced but they also have limited practical applications. Among these tests include those on strict morphology evaluations, acrosomal assessment and sperm-zona binding. The presence of sperm antibodies can be detected by the mixed antiglobulin reaction test. The predictive value of this for fertilisation is variable and it has been shown that the nature of the antigen against which the seminal antisperm antibody is directed may be as important as the antibody concentration in affecting sperm function. Cervical hostility towards semen is further assessed by the sperm-cervical mucus penetration (Kremer) test. The link between white cell count (pyospermia), infection and male infertility is still being debated. Accessory gland function can be assessed by measurement of seminal fructose to assess the seminal vesicles and acid phosphatase or citrate to assess the prostate gland. In the presence of infection, the concentrations are lower although a normal value does not exclude it. If infection is strongly suspected, then the semen could be cultured for pathogenic organisms like gonococcus and chlamydia.

Hormonal profiles

The measurement of serum follicle-stimulating hormone (FSH) is a useful test to distinguish patients with azoospermia due to obstruction (normal FSH) from those with testicular damage (high FSH). In about one third of men with severe oligozoospermia or azoospermia from testicular damage, luteinising hormone (LH) levels are high whilst testosterone levels are low. The measurement of FSH, LH and testosterone levels are also useful in diagnosing men with hypogonadotrophic hypogonadism (low levels for all 3 hormones) as this condition is treatable. Testosterone and LH measurements are also indicated if there is a clinical suspicion of androgen deficiency and steroid secreting lesions such as congenital adrenal hyperplasia or hormone secreting adrenal/testicular tumours. High serum prolactin levels may cause decreased libido (and sexual dysfunction) and may also indicate pituitary disease causing secondary testicular failure.

Chromosomal and genetic studies

Men with azoospermia (or very severe oligospermia), high FSH and small testes (2 mL - 6 mL) should undergo these studies. The most common chromosomal abnormality in such cases is Klinefelter's syndrome (47 XXY) which accounts for up to 20% in some series. Screening for cystic fibrosis is required in patients with congenital absence of the vas deferens. Partial androgen insensitivity syndrome should be excluded in men with a history of cryptorchidism or orchidopexy. Molecular techniques are now available to look for deleted DNA sequences in the DAZ or RBM regions on the Y chromosome as well as checking for mutations of the androgen receptor gene. Micro-deletions of the Y chromosome are also found in up to 15% of men with idiopathic oligoasthenoteratozoospermia or azoospermia.

Testicular biopsy

The usefulness of this procedure, which had declined significantly in the last decade for various reasons, has had a recent resurgence. The decline was mainly due to the use of hormonal measurements to differentiate between obstruction and testicular failure as well as the increasing success of micromanipulation techniques. If the clinical diagnosis is uncertain or if testicular malignancy has to be excluded (eg. in men with a history of cryptorchidism), this procedure would be a useful adjunct to the other standard investigations. Testicular biopsy is now done routinely to check for spermatogenesis in non-obstructive azoospermia to determine whether it would be worthwhile to offer ICSI. It may also be done for men who undergo exploration of the vas to check for blockage. An added advantage of a testicular biopsy is the detection of carcinoma-in-situ in testicular cancers.

Miscellaneous

Testicular ultrasound facilitates the detection of hydroceles and other abnormalities of the scrotum. Color doppler ultrasound and venography can be used to detect varicoceles but are of limited usefulness as the efficacy of varicocele treatment is still unproven. If retrograde ejaculation is suspected, then a post-ejaculatory specimen of urine should be obtained to confirm the presence of semen.

Treatment

In the majority, the treatment is more empirical and even if semen variables have improved after treatment, it does not correlate with increased conception rates. With major advances in micromanipulation techniques, there is at last a reasonable chance of fertility for these men and assisted reproductive techniques is now an important treatment modality for such men.

Treatments of no proven benefit

It is now certain that hormonal therapy has no beneficial effect on the infertile male except for the rare case of Kallman's syndrome or pituitary deficiency. Hence, use of anti-oestrogens (clomiphene citrate and tamoxifen) to stimulate Leydig cells in idiopathic oligozoospermia, low dose androgen therapy, bromocriptine and vitamin E are largely ineffective. Similarly, the use of growth hormone in the treatment of male infertility has been disappointing. The management of varicoceles is also a contentious issue. Several large, well controlled studies have shown that varicocelectomy has no beneficial effect on sperm count although the procedure is still commonly performed in some centres. The role of anti-sperm antibodies is also controversial. Immunological treatment of such men (eg. with steroids has been largely ineffective compared to assisted reproduction. Intrauterine insemination (IUI), involving the deposition of prepared spermatozoa directly into the uterine cavity for men with oligozoospermia, also did not significantly improve the conception rates. If IUI is offered, it is usually done with ovarian hyperstimulation to couples who are normospermic and for a short duration only (eg. 3 cycles). More recently, the use of tubal perfusion (i.e. "flooding" the fallopian tubes with a sperm suspension) has also been tried; its efficacy is still to be determined.

Untreatable infertility

This include men with primary and acquired testicular failure (eg. Klinefelter's syndrome, undescended testes, idiopathic primary seminiferous tubule failure, trauma and exposure to cytotoxic drugs/radiation causing atrophy). They should be carefully counselled about the lack of effective therapy for themselves. Those with features of androgen deficiency should be given androgen replacement therapy. Couples in this situation may accept either donor insemination (DI) or consider adoption as a solution. Donor insemination produces pregnancy rates of 10% - 15% per month and by 6 months, approximately 50% of women are pregnant. If not pregnant by 6 months, it may be more efficient to convert to in vitro fertilisation (IVF) with donor sperm. With this method of management, there is an 80% chance of having a child within 2 years.

Infection

Men with genital tract infection should be treated with broad spectrum antibiotics such as erythromycin, doxycycline and metronidazole. However, permanent damage to the ducts and accessory glands may have already occurred and fertility may not be improved significantly.

Gonadotrophin deficiency

Although a rare condition, such men will respond successfully to treatment with human FSH and LH or human chorionic gonadotrophin (hCG) or by pulsatile GnRH therapy. As spermatogenesis takes 70 days, the treatment cycle is naturally long but results indicate that up to 50% of such men will father a child even with reduced sperm counts.

Obstructive lesions

Patients with obstructive azoospermia should be offered epididymo-vasostomy with microsurgical techniques. Patients going for vasectomy reversal should also be offered epididymo-vasostomy as opposed to re-anastomosis of the vas. This is because the pressure increase after vasectomy leads to secondary epididymal obstruction which is the cause of failure of otherwise successful vasovasostomies.

Disorders of ejaculation

Men with impotence and erectile failure should be assessed to see if any treatable conditions (eg. diabetes) are present. Otherwise, they are usually managed by a combination of sexual counselling, pharmacologic therapy (eg. prostaglandin E1) and mechanical aids (eg. vacuum pumps). Some cases of retrograde ejaculation may be treated successfully with sympathomimetic drugs. If this does not correct the problem, assisted reproductive techniques with spermatozoa isolated from the urine after previous adjustment of the urinary pH and osmolarity should be offered to the couple. More recently, vibration and electroejaculation have been introduced for treatment of retrograde ejaculation or anejaculation, mostly in tetraplegic and paraplegic patients. In this procedure, an electrical current is passed via a rectal electrode to stimulate contractions of the pelvic muscles and accessory glands, resulting in erection and ejaculation.

In vitro fertilisation (IVF)

When no specific aetiological factors are found in subfertile men, it is common practice to resort to IVF as a therapeutic option. Usually, IVF is offered to couples with low sperm counts as the procedure theoretically allows the fewer number of available sperm a greater opportunity for direct contact with the ovum. The overall clinical pregnancy rates with male factor subfertility with IVF is between 17% to 27% with delivery rates comparable with IVF performed for other types of infertility.

Micromanipulation techniques and ICSI

The field of micromanipulation to assist conception came onto the clinical scene in 1988 and has since revolutionised the management of male infertility. The advent of intracytoplasmic sperm injection (ICSI) has allowed men with 100% abnormal sperm morphology and severely compromised sperm motility to father children. Presently, when the total number of motile spermatozoa in the ejaculate is less than 5 x 106 per mL (severe oligoasthenozoospermia) or if the total motile sperm count after sperm preparation is less than 1.5 x 106 motile sperm or when progressive motility after sperm preparation is poor or when abnormal forms are high, success rates with IVF is poor. Hence, ICSI is more suitable and the results are good with fertilisation rates above 60% and clinical pregnancy rates above 30% being reported.

The success of the micromanipulation techniques is dependent on a few important factors. Firstly, the quality of the oocytes retrieved should be good. Hence, a stimulation regime that results in a higher recovery of mature oocytes may result in a higher pregnancy rate. The age of the woman is another crucial factor with a lower success rate in older women. The other negative influence on the success of ICSI is when the sperm is completely immotile, which is probably a reflection of total necrozoospermia. Finally, the technique must be faultless. ICSI has also been demonstrated to be the treatment of choice for patients with male immunological infertility.

The use of testicular sperm for ICSI in obstructive azoospermia has also resulted in viable pregnancies and in azoospermia due to testicular failure, ICSI has a successful implantation rate of 18%. ICSI has also been extended for use in cases where there is need for a high fertilisation rate eg. natural cycles and immature oocytes which have matured in vitro. Couples who have failed IVF as well as men with spermatogenic failure due to external causes (eg. drugs, chemotherapy, radiotherapy) have also benefited from this technique.

Although ICSI has revolutionised the management of severe male factor infertility, the genetic implications of the procedure have only recently come into prominence. There have been reports of increased incidence of sex chromosome abnormalities after ICSI. At least 3 types of nuclear DNA mutations have some relation to spermatogenesis. It has been shown that severe oligospermia has been linked to deletions present on the long arm at the azoospermia factor (AZF) region of the Y chromosome. Mutations in the androgen receptor (AR) gene on the X chromosome have also been shown to cause sperm defects. The treatment of one such patient with androgen therapy has resulted in a successful pregnancy. Mutations in mitochondrial DNA have also been reported in sperm with reduced motility. It has been recommended that screening for defects in the Y chromosome and the androgen receptor gene be done routinely for patients undergoing ICSI. Cystic fibrosis should also be excluded in patients with bilateral congenital absence of the vas deferens.

Conclusion

It has become clear that the application of assisted reproductive technology to male infertility represents a major advance in the last decade. With further advances in molecular biology in understanding the molecular basis of male infertility, more improvements and refinements in treating such men should become available. At the same time, we should not ignore the ethical considerations that come with such new treatment strategies so that the fertility prospects of such men can be realised with minimal risks to their progeny.

References

1. Emil A. Tanagho, Jack W. McAninch; Smith's General Urology; 15th edn. McGraw Hill 2000.
2. Walsh, Retik, Vaughan & Wein; Campbell's urology; 8th edn; W.B. Saunders Company,2002.
3. Siroky, Edelstein & Krane; Manual of urology; 2nd edn. Lippincott Williams & Wilkins, 1999.
4 Gillen Water JY, Grayhack JT; Adult and Pediatric urology; Mosby2003.
5. MA Salam, Principles and practice of Urology, a comprehensive text, Brown Walker, Florida, USA 2003 and MAS publication, Dhaka for Local edition

Hyperlipidemia as a risk factor for ischaemic stroke

Khan MRK[1]

The ORION 2004 ; 19 : 199-201

Introduction

Stroke is the third commonest cause of death after ischaemic-heart disease and cancer in developed countries and is responsible for a large proportion of physical disability[1]. WHO defined stroke as rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting more than 24 hrs, or leading to death with no apparent cause other than that of vascular origin[2].

The main types of stroke and their relative occurrences are: Ischaemic stroke - 85% & Haemorrhagic stroke -15% The ischaemic stroke is the resultant effect of the occlusion of the cerebral blood vessels by thrombus or embolus, non-atheromatous diseases of the vessel wall, e.g. collagen diseases and vasculitis, diseases of the blood e.g. coagulopathies and haemoglobinopathies, decreased cerebral perfusion due to shock of any cause and cardiac dysrhythmias which leads to infarction of brain. Haemorrhagic stroke results from rupture of blood vessels as rupture of Charcoat-Bowchard aneurysm in hypertension, congenital aneurysm or artereriovenous mal- formation (AVM)[3]. Stroke and ischaemic heart disease share important risk factors such as age, hypertension, diabetes and cigarette smoking[4]. Although serum cholesterol is a strong and consistent risk factors for coronary heart disease, its importance in stroke remains controversial as serum cholesterol concentration is strongly related to death from ischaemic stroke but not from intracerebral or subarachnoid haemorrhage rather men in the lowest category of serum cholesterol (4.14 mmol/L=160 mg/dl) had higher death rates from both intracerebral and subarachnoid heamorrhage than other men[5]. The higher the LDL level or, LDL cholesterol level, the higher the coronary heart disease risk and HDL cholesterol is inversely related[6-7].

Rossner et al in a study emphasized that the importance of a low HDL concentration as an important independent risk factor for ischaemic stroke in the young adult[8]. Based on six years of follow up evaluations of the Framingham, Mass, men and women aged 49 to 82 years, it was found that a low density lipoprotein (LDL) cholesterol concentration with a statistically significant excess of stroke in women and of deaths from non-coronary heart diseases in both sexes[7]. Iso et al in a study concluded that there is an inverse relationship between the serum cholesterol level and the risk of death from haemorrhagic stroke in middle aged American men, but that its public health impacts is overwhelmed by the positive association of higher cholesterol level with death from non-haemorrhagic stroke and total cardiovascular disease[9]. Quizibash et al in a study of TIA and ischaemic stroke concluded that fibrinogen and lipids are important risk factors for ischaemic stroke. The pattern of changes mirrors that found in ischaemic heart disease[10]. Linderstrom et al in a study found total cholesterol as positively associated with ischaemic stroke but only for levels > 8 mmol/L, corresponding to the upper 5% of the distribution in the study population. For lower plasma cholesterol values the relative risk remained nearly constant. Plasma triglyceride concentration was significantly associated with a risk of ischaemic events. There was a negative log linear association between HDL cholesterol and ischaemic stroke. There was no indication that the effects of plasma lipids were different in women and men[11]. Tell et al in a review of more than 20 publications a relation was sought between plasma lipid and lipoprotein concentrations and cerebrovascular atheroscleros leads to the general conclusion that such a relation exists and that is stronger in older than in younger individuals[12].

There is no doubt that increasing levels of total plasma cholesterol and LDL-cholesterol and to, a lesser extent, decreasing levels of HDL - cholesterol, are strong risk factors for coronary heart disease[13-14]. The relationship between cholesterol or, lipid fractions and stroke is less clear-cut but there is almost certainly some association[15]. There is a study which show hyperlipidaemia as risk factor for Ischemic stroke[16] and presence of hypercholesterolaemia in higher and higher middle class Bangladeshi population[17].

Atherosclerosis

Atherosclerosis global in distribution, the principal cause of the heart attack, stroke and gangrene of the extremities is responsible for 50% of all mortality in the USA, Europe and Japan[18]. Atherosclerosis is a disease primarily of the elastic arteries (e.g. aorta, carotid, and iliac arteries) and large and medium sized muscular arteries (e.g. coronary and popliteal arteries) although any artery may be affected, which is a progressive disease that starts in childhood[19]. The basic lesion-The atheroma, or fibrofatty plaque-consists of a raised focal plaque within the intima, having a core of lipid (mainly cholesterol and cholesterol esters) and a covering fibrous cap. Atheromas are sparsely distributed at first, but as the disease advances, they become more and more numerous, sometimes covering the entire circumference of severely affected arteries. As the plaque increase in size, they progressively encroach on the lumen of the artery as well as the subjacent media. Consequently, in small arteries, thrombus are occlusive compromising blood flow to distal organs, and causing ischaemic injury, but in large arteries they are destructive weakening the affected vessel wall, causing aneurysm or rupture or favouring thrombosis. Moreover, extensive atheromas are friable often yields emboli of their grumous contents into the distal circulation (atheroemboli). Epidemiological studies indicate that there are several risk factors of atherosclerosis e.g. age, sex, diet, hypertension, diabetes mellitus, hypercholesterolaemia, cigarette smoking, obesity, physical inactivity, type A personality and high carbohydrate intake[19]. Among the risk factors, hypercholesterolaemia and hypertriglyceridemia are important. The biologically important lipids are the fatty acids and their derivatives, the neutral fats (triglycerides), the phospholipids and related compounds and the sterols (cholesterol and its derivatives). The lipids are hydrophobic substances and cannot circulate in the plasma in free form. The free fatty acids are bounded to albumin whereas, cholesterol, phospholipids, triglycerides are transported

1. **Dr Md Rezaul Karim Khan,** MBBS, FCPS (Med), MD (Neurology)
Associate Professor, Dept. of Neurology, BSMMU

in the form of lipoprotien complexes. There are six families of lipoprotein, e.g. chylomicrons, chylolmicron remnants, very low density lipoprotein (VLDL), intermediate density lipoprotein (IDL), low density lipoprotein (LDL) and high density lipoprotein (HDL)[20].

A Subject of great interest is the role of the cholesterol in the aetiology and course of atherosclerosis. It is characterized by infiltration of cholesterol and appearance of foam cells in the intima and growth factors that produces proliferative lesions. The normal range for plasma cholesterol is said to be 120 - 200 mg/dl, but it is now clear that there is a tight, positive corelation between the death rate from ischaemic heart disease and plasma cholesterol levels above 180 mg/dl. Furthermore, it is now clear that lowering plasma cholesterol by diet and drugs slows and may even reverse the progression of atherosclerotic lesions and the complications they cause[21]. Plasma cholesterol levels are elevated by diet rich in cholesterol and saturated fats, such as egg yolk, animal fats, and butter.

Hyperlipidaemia

Hyperlipidaemia is a major public health issue in the developed world. It is increasingly being recognized as a health problem in developing countries including Bangladesh. Hyperlipidaemia is such a disorder which require life-long monitoring, dietary manipulation, often drug therapy. Effective strategies for assessment and lipid control are being established[22]. The term hyperlipidaemia refers to conditions with raised levels of plasma cholesterol, triglyceride and low HDL. Hyperlipidaemia may be primary due to a number of inherited conditions or secondary. The cause may vary but the result is often an increased risk of cardiovascular disease. Lipid metabolism can be influenced by both genetic and environment factors and in majority of cases of hyperlipidaemia reflect interplay between the two.

A definition of the condition

The desirable upper limit for total plasma cholesterol varies in different countries. A WHO report and a multidisciplinary workshop have considered population means of 5.2 and 4.7 mmol/L respectively. The incentive of seeking a lipid lowering regimen of increased effectiveness is the acceptance by many investigators that desirable cholesterol levels are considerably lower than those traditionally assumed. It has been observed in our population that the serum cholesterol level in higher and higher middle social classes are within the range when intervention to reduce is essential[17]. A practical approach to treating those at increased risk of cardiovascular disease for people who have a plasma cholesterol level more than 6.7 mmol/L or fasting triglyceride greater than 2 mmol/L.

Plan of investigation

Hyperlipidaemia is often classified by the clinical signs as corneal arcus, xanthelesma, tendon xanthomata, indicating raised LDL with or without raised VLDL Tg, family history, total cholesterol and TG levels, observation of stored plasma for opalescence. Visual inspection of the stored serum involves subjective judgement but it is highly informative. Clear serum most often indicated a normal lipid pattern or hypercholesterolemia(IIa). Uniform lactescence indicates the presence of endogenous hypertriglyceridemia (Type IV/IIB). A creamy layer at the meniscus, with lactescent subnatant indicates endogenous hypertriglyceridemia with chylomicra (Type V/III), A lactescent or creamy later floating at the meniscus with a clear subnatant, Chylomicronaemia (Type V).

Table 1 : Classification of hyperlipidaemia
The Fredrickson/WHO classification of hyperlipoproteinaemia[23]

Type	Lipoprotein increased	Lipids increased
I	Chylomicrons	Triglycerides
IIa	LDL	Cholesterol
IIb	LDL and VLDL	Cholesterol and triglycerides
III	beta-VLDL (= IDL + chylomicron remnants)	Cholesterol and triglycerides
IV	VLDL	Triglycerides
V	Chylomicrons and VLDL	Cholesterol and triglycerides

Secondary hyperlipidaemia

Some of the common causes are diabetes mellitus, alcohol excess, nephrotic syndrome, hypothyroidism, renal failure, obesity. Correction of the underlying causes normalize lipid levels.

Plan for diagnosis

Hyperlipidaemia is usually asymptomatic but it may be revealed through a history of premature vascular disease in patients or their families. Physical signs Corneal arcus, xanthelesma, tendon xanthoma, planar xanthomas usually indicate raised LDL with or without VLDL TG. Eruptive xanthomas : Marked increased in VLDL TG Chylo (Type IV/V), yellowish discoloration of palmar creases and tubo-eruptive xanthoma on knees or elbow: Type III hyperlipidaemia.

Screening

Screening for hyperlipidaemia should begin no later than age 35 for men and age 45 for women. Individuals with additional risk factors should be screened earlier. If total cholesterol is less than 5.2 mmol/L no further analysis unless there is patient with coronary heart disease or bad family history. If the value is more than that and other abnormalities are suspected, then a fasting sample for cholesterol, triglyceride and HDL cholesterol may be done.

Goals for therapy

The strategy for treatment depend on desirable level lipids. A guideline has been forwarded by National Cholesterol Education Programme (1997) and American Diabetic Association (1998).

Table-2: Desired levels of cholesterol

Total Cholesterol	<5.2 mmol/L (200 mg/dl)
LDL	<2.6 mmol/L (100mg/dl) if there is IHD
	<3.35 mmol/L (130mg/dl) for all
HDL	male > 0.9 mmol/L (35 mg/dl) female 1.1 mmol/L (45 mg/dl)
TG	<1.7 mmol/L (150 mg/dl) desirable >2.3 mmo/L (200mg/dl) acceptable

Management

Overall assessment plan

Step 1	Define the lipid abnormality
Step 2	Assess other atherosclerotic risk factors.
Step 3	Investigate and treat secondary causes of hyperlipidaemia
Step 4	Family screening
Step 5	Repeat blood lipid levels
Step 6	Establish goals for therapy

Initial diet therapy-low in saturated fats and energy with high in vegetables and fibres should continue for at least 12 weeks when lipid values are repeated. Drug therapy is indicated when total cholesterol level is 6.5 mmol/L or more after the diet therapy (at least 12 weeks). Drug therapy is life long. There are four classes of lipid altering agents in wide use: bile acid binding agents (resins), niacin, fibrates and HMG CoA reductase inhibitors[24,25]. In conclusion, hyperlipidemia is a major risk factor for coronary artery disease and ischaemic stroke as well. So awareness should be created among the general population regarding its dietary control, physical exercise and if needed drug therapy to reduce the morbidity and mortality from atherosclerotic vascular disease.

References

1. Allen CMC, Lueck CJ. Diseases of the nervous system. In: Haslette C, Chilvers ER, Hunter JAA, Boon NA, editors.Davidson's principles and practice of medicine. Churchill living stone 1999; 923- 1024.
2. Hatano S. Experience from a multicentre stroke register - a preliminary report Bull world Health Organ 1976; 54: 541 - 53.
3. Lindsay KW, Bone I, Call cutter R. Neurology 3rd ed. Churchill livingstone 1976; 236-92.
4. Dyken ML, wolf PA, Barnett H, Berganj, Hasswk, Kanel W B et al. Risk factors in stroke. A statement for physicians by subcommittee on risk factors for stroke of the stroke council. Stroke 1984; 15:1105-11.
5. Marmot MG, Poulter NR. Primary prevention of stroke. Lancet 1992; 339:344-47.
6. Miller NE. Forde OH, Thelle DS, Mjos OD. High density lipoprotein and coronary heart disease: A prospective case- control study. Lancet 1977; 1:965-7.
7. Gordon T. Kannel WB, Castelli WP, Dawber TR. Lipoproteins, Cardiovascular disease and death: The Framingham study. Arch Intern Med 1981; 141:1128-31.
8. Rossner S, Kjellin KG, Mettinger KL . Normal serum cholesterol but low HDL cholesterol concentration in young patients with ischaemic cerebrovascular disease. Lancet 1978; 1: 577-79.
9. Iso H, Jacobs Jr. DR, Wentworth D, Neaton JD, Cohen JD. Serum cholesterol . levels and six years mortality from stroke in 350,977 men screened for the multiple risk factor intervention trial. N Engl J Med. 1989; 320:904-10
10. Quizibash N, Jones L, Warlow C, Mann J. Fibrinogen and lipid concentrations as risk factors of transient ischaemic attacks and minor ischaemic stroke. BMJ 1991; 303: 605-9.
11. Lindenstrom E, Boysen G, Nyboe J. Influence of total cholesterol, High density lipoprotein cholesterol and triglycerides on risk of cerebrovascular disease: Copenhagen city heart study. BMJ 1994; 309: 11-5.
12. Tell GS, Philos Dr, Crouse JR, Furberg CD. Relation between blood lipids, lipoprotein and Cerebrovascular disease - a review. Stroke 1988; 19:423-30.
13. Martin MJ, Hulley SB, Browner WS , Kuller LH, Wentworth D. Serum cholesterol, Blood pressure and mortality: Implications from a cohort of 31662 men. Lancet 1986; 2: 933-6.
14. Pocock SJ, Sharper AG, Phillips AN. Concentrations of High density lipoprotein cholesterol triglyceride and total cholesterol in ischaemic heart disease . BMJ 1989; 298: 998-1002.
15. Quizibash N, Duffy SW, Warlow C, Mann J. Lipids are risk factors for ischaemic stroke: Over view and review. Cerebrovasc Dis 1992; 2: 127-36.
16. Khan MRK. Relationship between blood lipids, lipoproteins and ischaemic stroke. MD (Neurology thesis), Dhaka University, 2000.
17. Chowdhury S, Huda AMS. Study on serum cholesterol level in apparently healthy persons of different socio-economic groups in Dhaka. Bangladesh Medical Journal 1979; 7: 65- 73.
18. Ross R. The Pathogenesis of atherosclerosis: a perspective for the 1990's. Nature 1993; 362 :801 - 9.
19. Schoen FJ. Blood vessels. In: Cotran RS, Kumar V, Robbins SL, Schoen FJ. editor.Robbins Pathologic basis of disease. WB saunders company, 1994; 467 -16.
20. Ganong WF. Review of Medical Physiology. 19th ed. Prentice - Hall International, Inc 1999: 286-97.
21. Peto R, Yusuf S, Collins R . Cholesterol level trials in their epidemiological context.Circulation 1985 ; 72 (Suppl. 111) : 451-70.
22. Man J, Ball M. Hyperlipidaemia. Medicine International 1985; 6: 580- 84.
23. Durrington PN. Lipid and lipoprotein disorders . In: Weatheral DL, Ledingham JGG, Warrel DA editors. Oxford University press. UK, 1996: 1399-14
24. Expert panel on cholesterol education program of National heart, Lung and Blood Institute, Bethesda. Cholesterol - adult treatment panel report. Arch Intern Med. 1988; 148: 36-69.
25. Chowdhury S. Hyperlipidaema. Continuing medical education lecture notes, BCPS 1999: 143-8.

Publisher's Note

Contents of articles published in this journal are those of authors and do not neccessarily reflect those of its editors or of Orion Laboratories Ltd.

PUBLISHED BY
Chief Editor
The ORION
Orion Laboratories Ltd.
153-154 Tejgaon I/A, Dhaka-1208
PABX : 9888494, 9888176
Fax : 880-2-8826374, E-mail : orionmsd@dhaka.net
Web: www.orion-group.net/journals

Information for Authors

The valued authors should follow the manuscript guideline (Information for Authors) for submitting the article in "The ORION" An abridged version of Information for Authors was printed in the volume 12 and 13.
For further information please contact
Executive Editor : The ORION
E-mail : orionmsd@dhaka.net
Web: www.orion-group.net/journals (Vol. 12/13)

Parents' attitude towards a child with surgically correctable congenital anomaly

Islam MK[1]

The ORION 2004 ; 19 : 202-204

Abstract

A hospital prospective study was conducted in the department of paediatric surgery at Sylhet MAG Osmani medical college hospital (SOMCH), Sylhet, Bangladesh from July 2000 to June 2001. Parents of 150 children (150 father & 150 mother) were interviewed about their attitude towards their children with surgically correctable congenital anomalies. The male-female ratio of the patients was 2.6:1. The study revealed that most of the parents (48.66% mother & 38.67% father) had no educational background. 96% parents thought that the anomaly has simply God gifted. 32.66% parents had no idea about the nature of abnormality but the rest had a variable orientation about it. The anomalies were mostly single and involved almost all systems of the body and only 4% had multiple defects. 73.33% patients knew that treatment is available at Sylhet MAG Osmani medical college hospital. From the study it was found that 88% children with congenital anomalies had no social problems related to their deformity. The rest 12% had various social problems with their parents, relatives and friends. On the other hand, 40% of mother was very depressed and 43.33% fathers were moderately depressed for their deformed children. But the parents, whose babies had minor abnormality, were not depressed at all. Regarding the parental expectation, it was found that most of them (55.33%) expected that children must be cured and the rest 44.33% expected that the child may be cured. We did not encounter any parent who thought that it was impossible to cure his child. Among the 150 patients, 95.33% survived and were discharged in good condition and only 4.67% died. On the other hand, 63.33% mother and 72% father were fully satisfied after seeing the outcome of treatment.

Key words

Parents' attitude, Congenital anomaly.

Introduction

Correction of various congenital abnormalities in a child is a challenge for a paediatric surgeon. The parents play a vital role in this whole process of management. As the government has no direct responsibility for these disabled children, the parents have to take the initiative to bring the child to the hospitals. It involves both money and time of the parents. So, the attitude of the parents towards these unfortunate children is very important and hence it is essential to make them normal by surgery as well as for their future adjustment in the society. If the parents have the normal affection, sympathy and courage they bring their children to the hospitals without delay. Level of education also plays a positive role in this situation. On the other hand, if the parents become frustrated, helpless or if they do not have sufficient knowledge, their initiative becomes minimum.

Materials and methods

It was a prospective study conducted in the department of paediatric surgery of Sylhet MAG Osmani medical college hospital from July 2000 to June 2001, a period of 1 year. The patients with different surgically correctable congenital anomalies were interviewed through a questionnaire. The children were admitted through both the surgical outdoor clinic and emergency departments. These formed only a part of total admission in the ward. The children, who had both the parents available for interview during admission, were enrolled in the study. Thus a total number of 150 mother and 150 father were interviewed separately.

The children were mostly referred by various specialists of the area including paediatric surgeons (n-46). The rest were referred either by local GP (n-42) or by others like Quacks, Homeopaths etc (n-36). Some of them also came directly (n-26) to SOMCH. The diagnosis was confimed by clinical examinations and various investigations. The patients with anomalies of almost all the systems of body were including in the study. The history of treatment before coming to SOMCH was obtained. Some had treatment from Local GP and Specialists (n-50), Quacks, homeopaths (n-24) and Local hospitals (n-37). Others who needed staged operations, were treated at SOMCH (n-12). Lastly, a few of them did not receive any treatment outside (n-27).

Among the 150 patients, 72.67% were male and 27.33% female. The male-female ratio was 2.6:1. To Know the educational background of the parents, they were divided according to their level of education. The level ranged from 'no education' up to, Graduation'. The antenatal history of the mother of the effected child was taken in details. According to the age of the mother during current pregnancy, the women were categorized into 5 groups. It was between 15 to 20 years; 21 to 25 years ; 26 to 30 years; 31 to 35 years and>35 years. The number of present pregnancy was also noted. The immunization against Tetanus during pregnancy was monitored. They were classified into 'Fully immunized (n-79),'partially immunized' (n-43) and 'Not immunized' (n-28). Only 5 mothers had various complications during pregnancy like pre-eclamptic toxaemia with convulsion, fever, weakness and accidental injury.

The parents' feeling about the congenital anomaly of their child was assessed meticulously by their opinion, mood and gesture and they were classified into 3 groups ('very depressed', 'moderately depressed' and 'not depressed'). It should be mentioned here that no standard psychological test was applied here to measure the level of depression. Definite questions were asked to them about the probable cause, social, problems, their knowledge related to the anomaly, its treatment and result of treatment etc. Finally the expectations of the parents from the treatment and their satisfaction level were assessed.

Results

From the study, it was revealed that 144 (96%) parents felt indifferent or helpless as they thought the anomaly was 'God gifted'. On the other hand, only 06 (4%) thought that the fault lies in mother or in father. Most of the parents in the study had no educational background. 48.66% mothers and 38.67% father were found to be illiterate. On the other hand, only 6.67% mothers and 10% father was graduate

1. **Prof. Dr. Md. Kabirul Islam,** MBBS, MS (Paed. Surgery), FICS (Paed. Surgery), Head of the Dept. of Paediatric Surgery Dhaka Medical College, Dhaka.

Table-1: Level of education of the parents.

	Level	Mother	Father
1.	No Education	73 (48.66%)	58(38.67%)
2.	Primary (incomplete)	21 (14.00%)	22(14.67%)
3.	Secondary (incomplete	09 (06.00%)	10(06.67%)
4.	S.S.C	27 (18.00%)	20 (13.33%)
5.	Madrasa	00(00.00%)	08(05.33%)
6.	H.S.C	10(06.67%)	17(11.33%)
7.	Graduate	10(06.67%)	15(10.00%)
	Total	**150(100.00%)**	**150(100.00%)**

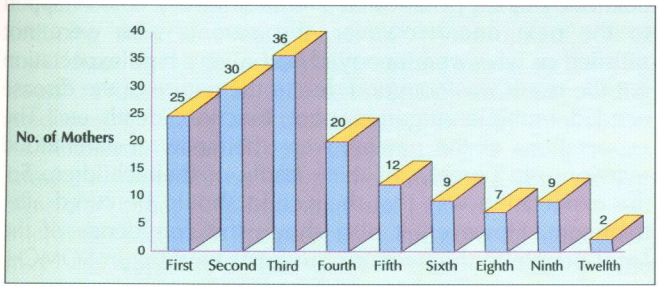


Figure-1 : Number of current pregnancy

shows the number of the current pregnancies which shows most were the child of 3rd pregnancy (in-36, 24%). 67.34% of parents had variable knowledge about the nature of congenital anomaly as most of them (44%) heard about such anomaly, 12.67% have seen it in the locality. On the other hand, 32.66% parents had never seen or heard of such anomalies.

Table-2: Previous knowledge of the parents about the congenital anomaly of their child.

	Knowledge	Parents	Percentage
1.	Seen in the family	32	10.67
2.	Seen in the locality	38	12.67
3.	Heard of it	132	44.00
4.	Never seen or Heard	98	32.66
	Total	**300**	**100.00**

Congenital inguinal hernia, Hydrocele, Cleft lip etc. were the commonest anomalies. On the other hand, Anorectal Malformations (ARM), Hirschsprung's disease, Omphalocele etc. were the forms which were not seen previously by the parents. However, most of the anomalies of the study were ARM (24.00%) and only 4% had multiple anomalies.

Table-3: Disease profile of the patients.

	Systems involved	Parents	Percentage
1.	Genito-Urinary system	35	23.34
2.	Gastrointestinal system	20	13.33
3.	Ano Rectum	36	24.00
4.	Head & Neck	20	13.33
5.	Abdominal wall	33	22.00
6.	Multiple anomalies	06	04.00
	Total	**150**	**100.00**

73.33% parents knew that treatment was available at SOMCH and the rest 26.67% were not sure about it.

Surprisingly, most of the children (88%) did not have any social problem due to their anomaly. They were well accepted by the parents and did not have any problem in going to school or playing with other children. Only 2% children, mostly with ARM were not accepted by the parents and 8% were not accepted by the society. It included Ambiguous genitalia, Ectopia vesicae etc. Majority of the parents of such children were depressed to different extent. Among them, mothers (40.00%) were mostly very depressed and fathers (43.33%) were 'moderately depressed'.

Table-4: Social problems of the patients.

	Problems	Number	Percentage
1.	Not accepted/Abused by family	03	02.22
2.	Not accepted by society	12	08.00
3.	Sympathetic to parents	03	02.00
4.	No problem	132	88.00
	Total	**150**	**100.00**

Table-5: Parents feeling and satisfaction

		Father (%)	Mother(%)
1.	**Parents' feeling:**		
a)	Very Depressed	56 (37.33%)	60 (40.00%
b)	Moderately Depressed	65 (43.33%)	56 (37.33%
c)	Not Depressed	29 (19.34%)	34 (22.67%)
	Total	**150 (100.00%)**	**150 (100.00%)**
2.	**Parents' satisfaction:**		
a)	Fully Satisfied	108 (72.00%)	95 (63.33%)
b)	Partially Satisfied	28 (18.67%)	37 (24.67%)
c)	Not Satisfied	10 (06.67%)	12 (08.00%)
d)	Annoyed	04 (02.66%)	06 (04.00%)
	Total	**150 (100.00%)**	**150 (100.00%)**

The depression ocurred incase of anomalies which needed surgery like in Hirschsprung's disease, ARM or which has guarded prognosis like Omphalocele, Ectopia vesicae etc. On the other hand, parents with simpler anomailes like Hernia, Hydrocele, Cleft lip etc. were not depressed at all (22.67% mother, 19.34% father).

Regarding the expectation of the parents from treatment, they reacted strangely. Only 55.33% expected that their child must be cured whatever is the problem. And none of them expected that the disease is impossible to cure.

Table-6: Expectation of the parents from treatment.

	Expectations	Number	Percentage
1.	Must be cured	166	55.33
2.	May be cured	134	44.67
3.	Impossible to be cured	00	00.00
4.	Not sure	00	00.00
	Total	**300**	**100.00**

They were so confident that there was none who was not sure about the outcome. One child had Oesophageal atresia with ARM and the general condition was very poor due to low birth weight. But the parents' expectation was very high and they believed that their child must survive.

However, among the 150 children, 95.33% survived and were discharged from the hospital. Of them 30 children needed further surgery and were adviced to come after a definite interval. Only 4.67% died. All of them had either very bad form of anomalies which were not fit for survival or they came very late with features of septicaemia. However, most of the parents of the study, both mother (63.33%) and father (72.00%) were fully satisfied after the treatment in SOMCH. But some of them were not satisfied or even annoyed (Table-5). The parents of the children who died or needed multiple surgeries were in these groups.

Discussion

Paediatric surgery' is relatively new as an individual branch of surgery in Bangladesh. The first pediatric surgery unit was founded in 1979 at Dhaka Shishu (children) Hospital. From that time, the paediatric surgeons had started to manage the congenital anomalies in regular fashion. But the starting was very slow. In average, only 43 major operations were performed per 1983[1]. Sylhet MAG Osmani medical college hospital is a tertiary level general hospital at sylhet, a division of Bangladesh situated at the North-Eastern part. The population of this 12,596 sq. Km. area is about 7.8 million. Most of the children with various surgically correctable congenital anomailes attend the paediatric surgery department of SOMCH which has been founded in 1995.

Parents play a crucial role in the life of a child suffering from congenital anomaly since their guidance contribute to the degree to which child learns to cope with his or her disability.Our study reflects the attitude and feeling for the parents to their children with various degree of surgically correctable congenital anomalies. It ranged from simple anomalies like congenital inguinal hernia, hydrocele to much complicated ARM, Hirschsprung's disease, Oesophageal atresia etc. In the English literature, only few articles could be found which is related to our study[2,3,4,5]. However, some authors have described the attitude or the knowledge of the parents about their child with a particular single congenital anomaly[6,7,8,9,10]. But our study contains a variety of anomalies involving almost all parts of the body. Here, a particular anomaly was not highlighted rather the various effects, especially the social factors were discussed.

Most of the congenital malformation has a causative factor. An intelligent mother can guess some of the causes like trauma, illness or use of drugs during pregnancy which might effect her conception. In our study, 96% parents thought that the defect was God gifted and they were not able to find any possible cause. It is due to lack of Knowledge and to some extent due to their faith on God. This was also reflected by the educational background of the parents which shows that most of them were illiterate. It was also seen that only about 32% parents had no knowledge about the anomaly of their children. It agrees with study of Beeri and his colleageues[6] who found 36% parental diagnosis of congenital heart disease of their children were incorrect. The ignorance of their child's problem did not correlate with its severity or complexity but rather with parental background. There observation was, less educated the parent, the more likely was the problem perceived incorrectly.

The study revealed that most of the children were from a multipara mother and maximum of them were the result of 3rd pregnancy. 88% of the children of our study did not have any social problem due to their anomalies. But in a study, Bode and his colleagues found that in 23% cases the parents neglected the child who had a major congenital defect[11]. The other form of problems were starvation, locking up or eviction. The reasons for our findings might be due to that the children had anomalies with minor function disturbance. On the other hand , hypospadias, hernia, hydrocele etc. occupied a good portion of our study. These anomalies could be easily hidden by the clothing. On the other hand, patients with overt defects like cleft lip/palate, ARM etc. had definite problems.

The level of mental depression in the parents was almost similar in both the mother and father. Most of them were depressed to a certain level. But the mothers were depressed mainly due to the disease process. They had also a fear that they might be blammed for giving birth to a defective child. The fathers' depression was mostly related to money. They were worried about the cost of treatment, loss of their daily income and also for the future expenditures to rear up the child. On the other hand, in Bode's study[11] the reasons for the parents' depression were financial constraints, hopelessness and shame associated with grotesque lesions, broken family and maternal pregnancy. The pattern of the parent's depression is also reflected when we look at the level of satisfaction of the parents. After operation when the children become normal, most of the fathers were fully satisfied realizing that no more money will be needed for further treatment. But the mothers were still fearful for the next baby as they think that similar anomaly could happen to the next one. However, the parents who were not satisfied or who were annoyed had a very high expectation but the result was not good due to the nature of the disease needed multiple surgeries, poor function, death etc. The expectations of the parents were their natural parenthood reaction. No parent can think badly of their children. So, the expectation was that their child should be cured after treatment. However, it also shows the confidence of the local people to the pediatric surgeons working in SOMCH.

Conclusion

It could be said that most of the parents of our study think that the congenital anomaly were God gifted and they were depressed for the incidence. Majority of the children with such abnormality were however, accepted by the society. The study also showed that the parents were aware that paediatric surgical service to correct the abnormality of their children is present at SOMCH. The expectation of the parents from the treatment was very high and at the same time the service could satisfy most of them.

References

1. Bagwell CE, Shadling B. Pediatric surgery in Bangladesh. J Ped Surg 1986;21(9):789-91.
2. Johns n. Family reactions to the birth of a child with a congenital abnormality. Med J Aust 1971;1(5):277-82.
3. Koop C E. The handicapped child and his family. Linacre Q 1981;48(1):23-32.
4. Koop CE. The family with a handicapped newborn. Hum Life Rev 1981;7(1):116-23.
5. Russel PM. The handicapped child and his family. Nursing 1981;1(23):1007-8.
6. Beeri M, Haramati Z, Rein JJ, Nir A. Parental knowledge and views of pediatric congenital heart disease. Isr Med Assoc J 2001;3(3):194-7.
7. Tyl J, Dytrych Z, Helclova H, Schuller V, Matejcek Z, Berankova A. Psychological and social stress in children with cleft lip and palate. Cesk Pediatr 1990,45(9):532-6.
8. McAndrew I. Children with a handicap and their families. Child care Health Dev 1976;2(4):213-8.
9. Darling RB. Parents, physicians and Spina bifida. Hasting's Cent Rep 1977;7(4):10-4.
10. Aspinall CL. Dealing with the prenatal diagnosis of clefting: a parent perspective. Cleft Palate Craniofac J 2002;39(2):183-7.
11. Bode co, Odelola MA, Odiachi RO. Abuse and neglect in the surgically ill child. West Afr J Med 2001;20(2):86-91.

WE MOURN

With a profound sense of grief, we announce the sad demise of Professor Dr. M. A. Quaderi, MBBS, MRCP (London), FRCP (London), MRCP (Glasg), FRCP (Glasg), FCPS (BD); First Vice Chancellor of Bangabandhu Sheikh Mujib Medical University and the honorable member of the Advisory Board of "The ORION" medical journal on Wednesday, 28 July, 2004 at 11:45pm. We express our sincere condolences and sympathy to each and every members of his family, every attendant during his hospital stayed time, all colleagues, and every fellows. May Almighty keep him in eternal peace.

Recent advances in treatment of preterm labour

Nasreen SZA[1]

The ORION 2004 ; 19 : 205-206

Preterm labour (PTL) is the major cause of perinatal mortality and morbidity. 13 million PTL occurs worldwide in each year. Though PTL means birth before 37 completed weeks but babies born 34 weeks experience most complications. Prevention and treatment of PTL is the important means of reducing adverse events for child[1]. Aetiology of PTL is multifactorial but infection is possible cause up to 40% cases[2]. Preventions of PTL are very difficult but finding predisposing factors and treatment accordingly may reduce its incidence. Avoidance of smoking, heavy work, mental stress are important non-drugs measurement early warnings signs of PTL may help in timings and route of delivery which improves outcome[3]. Pre-pregnancy measure to reduce PTL may be applicable for genital tract anomalies like metroplasty for septated uterus cerclage or cervical incompetence (at 12-14 weeks gestations). But evidence of randomical trial showed that one woman in 30 cases will benefit from cervical suture. If infection is suspected from previous PTL it seems reasonable to take HVS electively at 29-24 weeks gestations[4].

Outpatients home monitoring of uterine contraction are not feasible. Sonographic evaluation of precosious cervical ripening from 24 weeks gestation has varying support for many years. But biochemical markers of PTL by estimating fetal fibronectin are another promising method[5]. Treatment needs to be systematic and methodical. Usually it involves assurance, hydration, antibiotic, tocolytics and steroids. Assurance is the key of treatment. It reduces mental stress. These patients should be admitted or referred into hospital where all the neonatal backup services are available. Hydration by parental fluid reduces uterine contraction for a while. Timed delivery in a appropriate set up bring the success[6].

Tocolytic

Still there is no clear evidence that these drugs improves outcomes following PTL and so it is reasonable not to use them randomly. However, tocolytics drugs should be considered for few days while completion of course of conteco costeroid or in utero transfer of the fetus to a tertiary centre. A wide variety of agents have been advocated to suppress uterine contraction, these are β-agonist like salbutamol, terbutalin, calcium channel blockers (nifidipine), indomethacin prostaglandin synthetase inhibitor,magsulphate. Nitric oxide donar and oxytocin receptor antagonist 'atosiban', meta analysis of studies showed that tocolytics reduces the Preterm birth occuring up to seven days after treatment[7]. Ritodren is no longer being used as its severe adverse effect. β-agonists are associated with palpitation ,rarely pulmonary oedema. Indomethacin may increase the risk of premature closure of ductus arteriosus, renal, cerebral vasculits and nercotizing colitis[8]. Nifedipine use seems reduces the resin of neonatal respiratory distress syndrome and jaundice. Atosiben has comparatively less adverse effect[11]. Therefore, among tocolytes, Atosifin is preferably. Data of systematic review provide insufficient evidence of any maintenance therapy will prevent PTL[9].

1. **Dr. Sk. Zinnat Ara Nasreen,** MBBS, MRCOG, FCPS
Associate Professor and Head Dept. of Obst.& Gynae
Z H Sikder Women's Medical College & Hospital, Dhaka.

Antibiotics

Spontaneous PTL is associated with infection and there is good evidence that antibiotics used in women with PROM can delay delivery and reduces feto maternal infections morbidity. In absence of infection, antibiotics has little to do. Preview meta analysis found that antibiotics increased the chance of prolong the pregnancy by 7days[10]. However majority of women will deliver in this time regardless of antibiotics therapy and only 15% of women likely to get benefit from antibiotics. The earlier gestation and having the abnormal genital flora are most likely to benefits from antibiotics. For prophylactic, combination parental oral antibiotics may be necessary on the other hand for therapeutic use intervention antibiotics are most likely to be of greatest benefit. Finally antibiotics should be used only for those women with evidence of infection. Since only in these women are antibiotics likely to be of benefit.

Corticosteroid

The benefits of single course of corticosteroids between 28-34 weeks of gestation on respiratory maturation without serious side effect[11]. Others have done research that consolidated the work[12]. The timing of therapy in PTL is critical. The best neonatal respiratory results comes after a complete course of two doses of betamathasone 12mg at 24hr apart or 4 doses of dexamathason 6mg 4 hrs apart. Delivery 3-7 days after this completed course is ideal. Before 24 weeks and after 34 weeks there is little value of steroid. However caution should be used in women who present with membranes reputed for over 24hrs,here the risks of infection are much higher.

For diabetic mother fine-tuning of diabetics control with insulin is necessary[13]. Multiple pregnancy needs special consideration. Tuberculosis is common in Bangladesh, it itself might mitigate against the use of anti-nettle steroid. Balance against the risk of a flare of TB and RDS is needed. No doubt steroid reduces RDS, intra-ventricular hemorrhage, narcotizing colitis in babies born for PTH, though it can not halt the process of PTL. Long tune side effect of single dose seen minimal. The same cannot be said for repeated doses where a body of observational data is developing which shows no increase protection but detriment to fetal grooms and development. Finally proper timing and appropiate route of delivery of preterm baby in good neonatal backup series bring the desired success.

References

1. Villar J,Ezcura E J, Gurtner et al. Pre-term delivery syndrome: the unmet need.In: Kierse MJNC. (ed) New perspectives for the effective treatment of pre term labour- an international consensus. Research and clinical forums 1994; 16;9-38.
2. Lamont R F, Fisk N M. The role of infection in the pathogenesis of preterm labour.Prog Obstet Gynaecol 11993;10;135-158.
3. Lettieri L, Vintzileos A M, Rodis JF et al.Does idiopathic preterm labor resulting in preterm birth exist? Am J Obst. and Gynecol 1993; 168;1480-1485.

4. Chan A, Scott J, McCaul K; Pregnancy outcome in south Austrlia 1995.Annual outcome of the pregnancy outcome unit,Epidemiology Branch, South Australian health commission.1995.
5. MCR/RCOG Working party on cervical cerclage(1993) Final report on the multicentric randomized trial cervical cerclerge. British journal of oobstetrics and gynaecology 100,516-523.
6. Gibbs RS, Romero R, Hillier SL et al. (1992) A review of premature birth and subclinical infection. American journal of obst. And gyneacology;166; 1515-1528.
7. Lockwood CJ, Senyei AE, Dische MR (1991) Fetal fibronectin in cervical and vaginal secretions as a predictor of preterm delivery. New england journal of Medicine 325; 669-674.
8. Tsokos N, Newnman J, Langford SA (1988) Intravenous tocolytic therapy for long distance aeromedical transport of women in preterm labour in western australia. Asia/Oceania Journal of obst and gynaecology.14;21-22.
9. Eronen M, Pesonen E, Kurki T et al. The effects of indomethacin and beta-sympathomimatic agent on the fetal dactus arteriosus during treatment of premature labor; a randomised double blind study.Am J Obstet Gynecol 1991;164;141-6.
10. Worldwise atosiban versus beta agonist study group. Effective and safety of ythe oxytocin antagonist atosiban versus beta-adrenergic agonist in the treatment of preterm labour. BJOG 2001;108;133-42.
11. Crowther CA, Moore V. Magnesium for preventing preterm labour. Cochrane Database Syst Rev 2001;(1).
12. Magawan BA, Bain M, Juszczak E, McInney K et al. Neonatal motalities amongst Scottissh preterm singleton births (1985-1994). Br J Obstet Gynaecol 1998;105;1005-1010.
13. Yoon BH Romera R, Yang SH et al. Interleukin concentration in umbilical cord plasma are elevated in neonates with matter lesion associated with periventricular leucomalacia. Am J Obstet and Gynaecol 1996; 174;1433-1440.

Rectal cancer : A review

Uddin MM[1]

The ORION 2004 ; 19 : 207-210

Introduction

Rectal cancer is one of the major health problem of the Westernized World. It is the 3rd most diagnosed malignancy accounting for 10% to 15% of newly diagnosed cancers in Europe and United States[1,2,3,4]. It is a dynamically changing diseases entity[5,6]. It's incidence varies from place to place and occurs most frequently in the population with the highest standard of living excepting Japan[7]. North America, Australia, New Zealand, North & West Europe have a very high incidence of the disease[8]. In USA, it's incidence rate increased from mid 1970 through 1992, decreased from 1992 to 1995 and stabilized from 1996 to 2000[9]. But there is no Central Cancer Registry in our country. Both Population Based & Hospital Based Cancer Registry are yet to develop. So, it is difficult to define the exact picture of rectal cancer prevailing among the population of our country. Only the Oncology Department of different Medical College Hospitals & Institutes have just started to maintain the registry of cancer patient attending the department. But the standard of documentation is not up to the mark. Again all the Oncology Departments are not provided with radiotherapy machines. So the figures vary from centre to centre mainly due to the biasness of radiotherapy. For that reason, colorectal cancer accounted for 2.06% of all the cancers among the patients attending the Department of Radiotherapy, Dhaka Medical College Hospital whereas it accounted for 7.36% among those attending the Department of Radiotherapy of Sher-E Bangla Medical College Hospital[10,11,12].

Epidemiology

Gender

There is no conclusive evidence of sex predominance. Both sexes can be equally affected[8]. But in majority of the cases male predominance slightly over female[13].

Age

Rectal cancer is the disease of elderly people and the peak incidence is in the 7th decade of life[14]. Less than 20% cases are diagnosed in persons under 50 years of age. It is rare in adolescents and young adults[15-16]. Only a few cases have been reported in children[17]. But this scenario is just reverse in our country due the reasons yet to be find out. In a study done by the author as a principal investigator over 102 rectal cancer patients from 1994 to 2002 titled "Rectal Cancer-Experience with 102 cases" (accepted for publication in The Journal of Teachers Association of Sir Salimullah Medical College, also presented as a Scientific Paper in the Conference of Asian Clinical Oncological Society in Seoul, Korea, 2003) patients aged between 10 and 92 years. Mean age at diagnosis was only 43.38 years, 52.94% aged within 40 years. Three patients were of pediatric age group.

Race

The incidence of colorectal cancer has increased by 30% in blacks since 1973 and is now higher than in whites[18].

1. **Dr. Md. Mokhles Uddin,** MBBS, FCPS
Associate Professor, Radiotherapy Department
Sir Salimullah Medical College.

Etiology

Not definitely known, but the following factors are found to be associated with this cancer:

Environment

Asians, Africans and South Americans have low incidence of colorectal cancer. But when they migrate to North America, they suffer more from this type of cancer. Environment has been blamed for this higher incidence[18].

Diet

Diet rich in fat and cholesterol have been linked to an increased risk of colorectal cancer. Dietary fat causes endogenous production of secondary bile acids, neutral steroids and increases bacterial degradation of these acids & steroids , thereby promoting carcinogenesis. Historically, diet rich in cereal fiber, bran, yellow or green vegetables are said to have a protective effect[18].

Genetic factor

There are groups that have a very high incidence of colorectal cancer. These groups include those with hereditary conditions such as; familial polyposis, hereditary nonpolyposis, Lynch Syndrome of variant I & II, ulcerative colitis[19] . Together they account for 10% to 15% of colorectal cancers. More common conditions with an increased risk are ; personal history of colorectal cancer, previous operation -even cholecystectomy, first degree family history, previous history of ovarian, endometrial and breast cancer[20,21]. These high risk groups account for 23% of all colorectal cancer.

Signs & symptoms

Patients with rectal cancer may present with change in bowel movements; rectal fullness, urgency, tenesmus, bleeding per rectum. Pelvic pain indicates advanced stage of the disease and is due to local extension of the tumor to the pelvic nerve. Symptoms due to metastatic spread depends upon the sites of deposit.

Screening and Diagnosis

Fecal occult blood test: It is inexpensive, but have been associated with many false positive and false negative results. About 50% of the colorectal cancer go undetected , they are not bleeding at the time of the test[18].

Digital rectal examination

Simple to perform and can detect lesions up to 7 centimeters from the anal verge.

Sigmoidoscopy

Flexible proctosigmoidoscopy is safe and more comfortable than examination with a rigid proctoscope. Colonoscopy is for exclusion of associated colonic growth.

Barium enemas

Here again the problem of 2% to 61% false negative findings due to poor preparation and difficulties in detecting smaller lesions.

Biopsy

Biopsy of the detectable lesion is essential for confirmation of diagnosis. It is safe and easy to take the biopsy endoscopically.

Investigations for staging and treatment

- Chest X-ray to confirm/exclude any metastatic deposits.
- CT-Scan/MRI of abdomen and pelvis.

- Trans rectal ultrasonography.
- Complete blood count including platelet count.
- Liver and renal function tests
- Urine analysis
- CEA

Cellular classification

Adenocarcinoma: Constitutes 90% to 95% of rectal cancer[22]. They may present with multiple degrees of differentiation and variable amount of mucin. Mucinous variant is characterized by huge amount of extracellular mucin in the tumor with the tendency to spread within the peritoneum. It is commonly seen in younger patients having less favourable prognosis. Signet ring cell type, an uncommon variant contains large quantities of intracellular mucin causing the displacement of cytoplasm and nucleus. They involve the submucosa making difficulties in diagnosis with conventional imaging techniques.

Other variants

Are scirrhous type, squamous cell carcinoma, adenosquamous carcinoma, undifferentiated carcinoma, neuroendocrine and carcinoid tumors. Sarcoma accounts for 0.1% to 0.3% of all rectal cancers and melanomas are rare.

Stage information

Treatment decisions should be made with reference to the TNM classification rather than older Duke's or the Modified Astler- Coller (MAC) classification schema[23].

TNM definitions

Primary tumor (T)

- TX: Primary tumor can not be assessed
- T0: No evidence of primary tumor
- Tis: Carcinoma in situ: intraepithelial or invasion of the lamina propria. It includes cancer cells confined within the glandular basement membrane or lamina propria (intramucosal) with no extension through the muscularis mucosae in to submucosa.
- T1: Tumor invades submucosa.
- T2: Tumor invades muscularis propria.
- T3: Tumor invades through the muscularis propria in to the subserosa or in to nonperitonealized pericolic or perirectal tissues.
- T4: Tumor directly invades other organs or structures, and/perforate the visceral peritoneum.

Regional lymph nodes (N)

- NX: Regional lymph nodes can not be assessed.
- N0: No regional lymph node metastasis
- N1: Metastasis in 1 to 3 regional lymph nodes.
- N2: Metastasis in 4 or more regional lymph nodes.

Distant metastasis (M)

- MX: Distant metastasis can not be assessed.
- M0: No distant metastasis
- M1: Distant metastasis.

Stage 0

- Tis, N0, M0

Stage I

- T1,N0,M0. • T2, N0, M0.

Stage II

- T3, N0, M0 • T4, N0,M0

Stage III

- Any T, N1. M0 • Any T, N2, M0

Stage IV

- Any T, Any N, M1.

Treatment option overview

Colorectal cancer is a highly treatable and often curable disease when diagnosed and treated early. Marked advances have been noticed in the management of this disease in the Western Society[8]. Here death rates have been declining for both whites and blacks[24]. Followings are the treatment options:

Surgery

The most effective option of rectal cancer is surgical resection of the primary and regional lymph nodes for localized disease[18]. The technique of rectal excision has impact upon the rate of local recurrence. Meticulous surgical resection with at least 2 centimeters distal surgical margin including node bearing mesorectum has reduced the rate of local recurrence.The major limitations of the surgery are; presence of sphincter in the lower end of rectum which controls defecation and the inability to obtain a radical margins because of the presence of bony pelvis. However, the surgical procedures are :

Resection anastomosis

This is the preferred method of surgery. Here resection of the primary with adequate free margin including resection mesorectum and anastomosis(colorectal or coloanal anastomosis) are done. But the growth should be at least 6-7 cms above the anal verge. Here anal sphincter is preserved and colostomy is avoided - thus providing with a better quality of life.

Abdominoperineal resection (APR)

When the growth is within 6 cms from anal margin or the growth is bulky one, resection anastomosis can not be done. APR is the appropriate surgical option in this situation. The patient will have to bear the burden of permanent colostomy. Care is given to preserve the autonomic nerve, thus minimizing the bladder and sexual function morbidity.

Local excision

Trans anal local excision is only recommended in T1 well to moderately differentiated rectal cancer with out histologically proven lympho vascular involvement, provided that a full thickness negative margin may be achieved. Pre opreative trans rectal ultrasonogram is helpful in defining lesions that can be resected satiofactorily by local excision.

Aggressive surgery

Partial or total pelvic exenteration in uncommon situation, where bladder, uterus, vagina or prostate are invaded.

Palliative surgery

Surgical resection/ anastomosis or bypass of obstructing lesions in selected cases or resection for palliation are done in selected advanced cases. Surgical resection of isolated metastases in lung, liver and ovaries can be done for palliation.

Adjuvant therapy

Approximately 75% of the patients with rectal cancer present at a stage when all the gross tumor can be surgically resected[18]. Nevertheless, despite the high resectability rate, almost half of all the patients will die from metastatic disease, primarily because of the residual disease that is not apparent at the time of surgery[25]. These individuals are the candidate for local or systemic adjuvant therapy. Usually the patients of real Stage-I with wide surgical resection do not need adjuvant therapy. Mainly the patients of Stage-II & III become benefited from adjuvant therapy.

Radiotherapy

Mainly used as adjuvant therapy in Stage -II & III rectal cancer to reduce the locoregional recurrence. Here the

primary and the regional nodal areas are irradiated. Usually 50 to 55 Gys are given by conventional fractions. In most trials, adjuvant radiotherapy alone have shown to decrease the local recurrence but without definite effect on survival [26,27]. Radiotherapy is used in selected advanced cases for palliation of local symptoms. Pain is decreased in 80% of the irradiated patients, control of bleeding in 70% cases. But obstruction is difficult to be relieved by radiation[18]. Endocavitary brachytherapy with or without external beam radiation can give results equivalent to surgery in selected patients of Stage-I with tumors less than three centimeters, well differentiated, without deep ulceration[28,29,30,31].

Chemoradiation

Means radiotherapy along with simultaneous chemotherapy. These combined modalities are the best post operative adjuvant therapy. They result in local failure rates lower than with either radiation therapy or chemotherapy alone[32].

Neo-adjuvant therapy

Therapy given before surgery, specially in advanced (T3 & T4) rectal cancer. These cases are difficult to be managed by surgery. Pre operative neo-adjuvant therapy(radiotherapy with or with- out chemotherapy) regresses the tumor, thus making them operable[33,34,35,36]. Sphincter can be preserved by neo-adjuvant therapy in selected cases when the tumor located near to the anal sphincter.

Chemotherapy

Main treatment for advanced and recurrent rectal cancer is palliation with 5-Flurouracil based chemotherapy[37,38]. Chemotherapy is also given along with radiation as adjuvant in Stage-II& III and neoadjuvant to surgery in locally advanced cases. Response has been improved but with a variable effect on survival when modulated by leucovorin or methotrexate[39,40]. Randomized clinical trials show that alpha interferon appears to add toxic effects but no clinical benefit to 5Flurouracil therapy. Continuous infusion of 5-Flurouracil have resulted in increased response rates in some studies, with a modest benefit in median survival. Oral regimens using pro drugs of 5-Flurouracil pharmacologically stimulate continuous infusion and under clinical evaluation. Irinotecan is now standard therapy for patients with Stage-IV disease who do not respond to or progress on 5-FU[41,42,43]. Oxaliplatin alone or combined with 5-FU and leucovorin has shown promising activity in previously treated and untreated patients and in patients with 5-FU refractory disease [44,45,46].

Follow up

Following completion of treatment, periodic evaluation is an integral part of rectal cancer management. It helps in identification and management of any recurrent disease. In our country majority of the patients present in advanced stage of the disease, so curative therapy can not be given. We have also limitation in expert manpower and machinaries for diagnosis & treatment of rectal cancer. Co-ordinated treatment approach, regular follow up provision and proper documentation system are to be developed. In conclusion we want to say that though rectal cancer is highly treatable and often curable when diagnosed and treated early, yet it is highly expensive in Bangladeshi perspective. So measures to be taken for prevention and early detection. People should be encouraged in taking sufficient vegetables, fruits and abstained from smoking, alcohol intake. Chemoprevention to be aimed for blocking the actions of carcinogens on the cells before the appearance of cancer. The most well studied agents in prevention of colorectal cancer includes; antioxidants, vitamin-C, vitamin-E, calcium, nonsteroidal anti-inflammatory drugs[18].

References

1. Chu KC, Tarone RE, Chow WH: Temporal patients in colorectal cancer incidence, survival and mortality from 1950 through 1990. J. Natl. Cancer Inst. 86:997-1007, 1994.
2. Parkin DM, Pisani P, Ferlay J: Global Cancer Statistics. CA Cancer. J. Clin. 49:33-64, 1999.
3. Landis SH, Murray T, Bolden S. Cancer Statistics199. CA Cancer J. Clin. 49: 8-31, 1999.
4. Midgley R, Kerr D: Colorectal Cancer. Lancer 353:391-399, 1999.
5. Zeigler RG, Devessa SS, Frumeni JF, Hellman S, Rosenberg SA: Epidemiology Pattern of Colorectal Cancer. Devita VT, Hellman S, Rosenberg SA: Important Advances in Oncology. Philadelphia, JB Lippincott: 209, 1986.
6. Cohen AM, Minsky BD, Shirlsky RL: Colorectal Cancer. Devita VT Jr, Hellman S, Rosenberg SA: Cancer- Principles & Practice of Oncology. 5th edition. Lippincott Raven Publishers: 1144-1197, 1997.
7. Annual Global Data on Mortality: Mortality by Cause, Sex & Age. World Health Statistics Reports. 22: 462, 1969.
8. Water house J, Carree P, Muir C: Cancer incidence in five countries. IARC Scientific Publications; Lyon, IARC:15,1976.
9. Hannah K, Weir, Miachael J, Thun MD, Benjamin F, Hansky, Lynn AG, Ries MS, Holly L, Howe, Phyllip A etal: Annual Reports to the Nation on the Status of Cancer, 1975-2000. Journal of National Cancer Institute, Vol-95, No-17:1276-1299, Sept. 2003.
10. Akhtar PS, Uddin MM, Sarma SK: Patterns of Malignant Neoplasm- A Three Years Study. BMJ. Vol-27, No-2:29-32,1994.
11. Sarma SK, Akhtar PS, Alam AMMS, Ansary HR & Uddin MM: Distribution Pattern of 3399 New Cancer Patients- A One Year Study,. Khulna BMJ:15-18, June 1992.
12. Uddin MM, Baki MO, Rahman SMA: Patterns of Malignant Neoplasms Among the Patients Attending the Department of Radiotherapy, Sher-E Bangla Medical College & Hospital. TAS Journal, Vol-9, No-23&34:29-32, July-Oct, 1998.
13. American Cancer Society: Cancer Facts & Figures-1997. Atlanta. American Cancer Society, 1997.
14. Uddin MM, Baki MO, Faruk GM, Zinnah ZI, Islam A, Manik ZH, Akhtar PS, Ali Y: Intestinal Neoplasms - A Study of 53 Cases. Ban. Can. Reports. Vol-23, N0-1,2: 16-23,1998.
15. Pissioties CA, Gulesserian HP and Condon RE: Colorectal Cancer in the 1st 25 years of life. J. Surg. Oncol. 6:87-91, 1974.
16. Pissioties CA, Gulesserian HP and Condon RE: Colorectal Cancer in the 1st 25 years of life. J. Surg. Oncol. 6:87-91, 1974.
17. Cain AS and Longio LA: Colorectal carcinoma in children. J. Pediatric Surg,5: 527-532, 1970.
18. Ellenhorn JDI, Coia LR, Alberts SR, Hoff PM: Colorectal and anal cancer. Pazdur R, Coia LR, Hoskins WJ, Wagman LD: Cancer Management: A Multidisciplinary Approach. 6th edition Prr Mel villeny:305-331, 2002.
19. Thorson AG, Knezetic JA< Lynch HT: A century of progress in hereditary non polyposis colorectal cancer(Lynch Syndrome). Dis Colon Rectum 42(1):1-9, 1999.
20. Ransohoff DF, Lang CA: Screening for colorectal cancer.N.Engl. J. Med.325(1): 37-41, 1991.
21. Fuchs CS, Giovunnucci EL, Colditz Ga et at: A prospective study of family history and the risk of colorectal cancer. N. Engl. J. Med. 331(25): 1669-74, 1994.
22. Hermanek P: Evolution and Pathology of Rectal Cancer. World J. Surg. 6:502, 1982
23. Colon and rectum. In American Joint Committee on Cancer: AJC Cancer Staging Manual. 5th edition. Philadelphia, Pa: Lippincott-Raven Publishers:83-90, 1997.
24. Lipkin M, Reddy B, Newmark H, Lampredth SA: Dietary Factors in Human Colorectal Cancer. Ann. Rev. Nutr. Newyork , USA;19: 545-86,1999.
25. Hearld RJ, Ryall RD: Recurrence after total mesorectal excission for rectal cancer. Lancet 1(8496): 1479-82, 1986
26. Martin EW, Mintony P, Carey LC: CEA directed second- look surgery in the asymptomatic patients after primary resection of colorectal carcinoma. An. Surg. 202(3): 310-7,1985.
27. Kachnic LA, Willet CG: Radiation therapy in the management of rectal cancer. Curr. Oin. Oncol. 13(4): 300-6,2001.
28. Siscy B, Graney MJ, HinsonEJ: Endocavitary irradiation for adenocarcinoma of the rectum. CA Cancer J.Clin 34(6): 333-9, 1984.
29. Konder IJ, Gilley MT< Shemesh EL et al: Radiation therapy as definitive treatment for selected invesive rectal cancer. Surgery 114(4): 850-6; discussion856-7, 1993.
30. Maingon P, Guerif S, Darsouni R et at: Conservative management of rectal adenocarcinoma by radiothertapy. Int J. Radiat Oncol Bios Phys 40(5): 1077-85,1998.

31. Aumock A, Birnbaum EH, Fleshman JW et al: Treatment of rectal adenocarcinoma with endocavitary and external beam radiotherapy:results for 199 patients with localized tumors. Int J Radiant Oncol Bios Phys 51(2): 363-70,2001.
32. Kollmorgen CF, Meagher AP, Wolff BG:The long term effect of adjuvant post operative chemoradiotherapy for rectal carcinoma on bowel dysfunction. Ann. Surg.220(5): 576-82, 1994.
33. Mohiuddin M, Mark G, Bannon J: High dose pre-operative radiation and full thickness local excission- a new option for selected T-3 distal rectal cancers. J. Radiat. Oncol. Biol. Phys.30(4): 845-9, 1994.
34. Mohiuddin M, Regine WF, Marks GJ: High dose pre-operative radiotherapy and the challenge of sphincter preservation surgery of cancer of distal 2 cms. Of rectum . Int. J. Radiat Oncol. Bios. Phys. 40(3): 569-74, 1998.
35. Valentine G, Cocco C, Cellini N: Pre-operative chemoradiation for extraperitoneal T-3 rectal cancer : acute toxicity, tumor response and sphincter preservation. Int. J. Radiat. Oncol. Bios. Phys. 40(5): 1067-75, 1998.
36. Scheele J, Stangl R, Altendorf-Hofman A: Hepatic metastasis from colorectal carcinoma: impact of surgical resection on natural history. Br. J. Surg. 77(11): 1241-6, 1990.
37. Schmoll HJ, Buchele T, Grothey A: When do stand with 5-Flurouracil? Semin. Oncol. 26(6): 589-605, 1999.
38. Grothey A, Scmoll HJ: New chemotherapy approaches in colorectal cancer. Curr. Opin. Oncol. 13(4): 275-86, 2001.
39. Buroker TR, O'Colonel MJ, Weand HS: Randomized comparison of two schedules of 5-Flurouracil and leucovorin in the treatment of advanced colorectal cancer. J. Clin. Oncol. 12(1): 14-20, 1994.
40. Poon MA, O' Colonel MJ, Weand HS: Biochemical modulation of flurouracil with leucovorin: confirmatory evidence of improved therapeutic efficacy in advanced colorectal cancer. J. Clin. Oncol. 9(11): 1967-72, 1991.
41. Rothenberg ML, Eckardt JR, Kuhn JG et al: Phase-II trial of Irinotecan in patients with progressive or rapidly recurrent colorectal cancer. J Clin Oncol 14(4):1128-35, 1996.
42. Conti JA, Kemeny NE, Salz LB et al: Irinotecan is an active agent in untreated patients with metastatic colorectal cancer.J Clin Oncol 14(3): 709-15, 1996.
43. Rougier P, Van Cutsem E, Bajetta E et al : Radndomized trial of irinotecan versus flurouracil by continuous infusion after flurouracil failure in patients with metastatic cancer. Lancet 352(9138):1413-8, 1998.
44. De Gramont A, Vignoud J, Tournigand C et al: Oxaliplatin with high dose leucovorin and 5-Flurouracil 48 hours continuous infusion in pretreated metastatic colorectal cancer. Eur J Cancer 33(2): 214-9, 1997.
45. Bleiberg H, de Gramont A: Oxliplatin plus 5-Flurouracil: clinical experience with advanced colorectal cancer. Semin Oncol 25(2 suppl5) :32-9, 1998.
46. Cvitkovic E, Bekradda M: Oxaliplatin: A new therapeutic option in colorectal cancer. Semin Oncol26(6): 647-62, 1999.

Hepatotoxicity in tuberculosis treatment : A review

Musa AKM[1]

The ORION 2004 ; 19 : 211-212

Introduction

Tuberculosis is a chronic bacterial infection caused by Mycobacterium tuberculosis. Tuberculosis is among the top ten causes of global mortality and affects low income communities. The incidence of tuberculosis varies from 9 cases per 1,00,000 population per year in the USA to 110-165 cases per 100,000 population in the developing countries of Asia and Africa. Currently more than one third of the worlds population is infected with M. tuberculosis & 8 million new cases and approximately 2 million deaths are expected each year. Effective antitubercular therapy is an important step in the prevention of tuberculosis. Yet all are potentially hepatotoxic. At least 1-2% of patient develop hepatitis, which causes difficulty in management may lead to discontinuation of therapy leading to defaulter; Defaults lead not only to treatment failure but also the emergence and transmission of drug resistant organism.This article review the potential hepatotoxic effect of tuberculosis chemotherapy in patients with or without pre-existing liver disease[2].

Fig 1 : Mycobacterium tuberculosis fluorescent staining with auramine

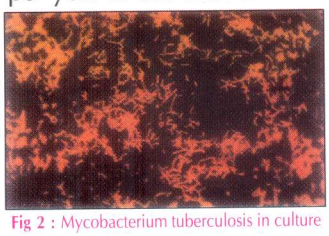


Fig 2 : Mycobacterium tuberculosis in culture

Classification of drugs[3]

A. Hepatotoxic	B. Non-hepatotoxic
Isoniazid	Ethambutol
Rifampicin	Streptomycin
Pyrazinamide	Kenamycin, Amikacin
Ethionamide	Cycloserine
Para-aminosalicylic acid	Fluoroquinolones

Isoniazid (INH)

INH is one of the main drug in tubercular chemotherapy (bactericidal), first introduced in 1950s. Reports in the late 1960s suggested that INH causes hepatitis. The largest and most comprehensive study of INH hepatitis was conducted by US public health services during 1971-1972. 14,000 persons receiving INH preventive therapy was monitored for development of hepatitis. Summary of this study shows that-

(i) Overall rate of probable INH hepatitis were 1% but was clearly age related with no cases among those under 20 years and highest rate of 2-3% among those over 50 years.

(ii) Hepatitis was 4 times higher among those consuming alcohol daily than those who do not drink.

(iii) Rates are lower among blacks and higher among whites.

(iv) Increased hepatotoxicity among women who are pregnant in 3rd trimester and immediate post partum period with co-administration of acetaminophen[3,4,5,6,7,8,9,10,11,12].

In a recent study, the relative risk of hepatotoxic side effects from Isoniazid was elevated more than 11 fold in the presence of active hepatitis (HBeAg+ve). The proinflammatory environment induced by actively replicating Hepatitis B may increases the idiosyncratic toxicity of isoniazid[13].

Sub clinical liver injury as indicated by elevated ALT occur in 12-18% of those receiving INH. While most elevated hepatic enzymes will normalize during continued use of INH, a few patient progress to overt disease, with hepatic necrosis. Progression is associated with symptoms like anorexia, vomiting, abdominal discomfort, weakness and fatigue. These symptoms should be closely monitored and prompt discontinuation is warranted. If jaundice develops there is 10% mortality[9].

Rifampicin

Introduced as a first line antituberculosis drug in 1960 and became the most vital component of short course chemotherapy in 1970s. Because it acts through P-450 enzymatic pathway its drug interaction are an important consideration in planning maintenance therapy.

- Transient elevation of ALT occur in about 1-4% of patient.
- Liver dysfunction associated with Rifampicin is of either hypersensitivity or cholestatic type.
- In the presence of liver disease it may be necessary to reduce the dosage of Rifampicin and monitor serum concentration to avoid hyperbilirubinemia. In the presence of cholestatic jaundice further dose reduction is required[2,3,7,8,11].

Pyrazinamide (PZA)

Pyrazinamide is a derivative of nicotinamide and is included in first line drug because of its particular ability to kill persisters that is mycobacteria that are semi dormant often within cells. PZA is potentially hepatotoxic drug but it is a dose related phenomenon with doses of 40-50 mg/kg/day 15% develop drug induced hepatitis where as 2-3% of patient develop hepatitis with doses of 20-30 mg/kg/day. Clearly the use of Isoniazid, Rifampicin and Pyrazinamide may pose serious problem in patient who have tuberculosis and pre-existing liver disease or in whom hepatic dysfunction develops either clinically or chemically after initiation of tuberculosis treatment. Patients with underlying liver disease are subject to a higher incidence of drug related idiosyncratic or hepatotoxic reactions. It is important therefore to identify high risk patient (table II) who may require closer survillance. for symptoms of clinical and biochemical hepatitis[2,3,13,14].

Table I. High risk patients for hepatotoxic reaction to anti tuberculosis drugs[2]

- Persons more than 35 years of age.
- Persons from areas where hepatitis is endemic.
- Postpartum African-American and Hispanic women.

1. **Dr. A.K. M Musa,** FCPS (Medicine) DTCD, MCPS
Assistant Professor, Dept. of Medicine, BIRDEM.

- Persons with
  - Alcohol induced liver disease on a history of substance abuse.
  - A history of malnutrition or Kwashiorkor
  - AIDS or HIV infection.
  - Active or chronic viral hepatitis.
  - A history of chronic use of enzyme inducing agent or medication causing drug interaction. Drug induced hepatitis in a recent study in Singapore revealed that the incidence of TB drug induced hepatitis was 5.3% age more than 60 year, abnormal baseline transaminase/bilirubin levels and female sex were risk factor associated with development of TB drug induced hepatitis. The median time of drug induced hepatitis was 38 days[14].

Treatment of patients with liver disorder

The patients with the following condition can receive short course chemotherapy regimens provided that there is no clinical evidence of chronic liver disease, hepatitis virus carriage, past history of acute hepatitis, excessive alcohol consumption.

Established chronic liver disease

Isoniazid plus Rifampicin plus 1 or 2 non hepatotoxic drugs such as Streptomycin and Ethambutol can be used for a total treatment duration of eight months. An alternative regimen is Streptomycin plus Isoniazid plus Ethambutol in the initial phase followed by INH and Ehambutol in the continuation phase with a total treatment duration of 12 months. Patients with liver disease should not receive PZA. Therefore the recommended regimen are the following- 2SHRE/6HR or 2SHE/10HE [3,15,17]

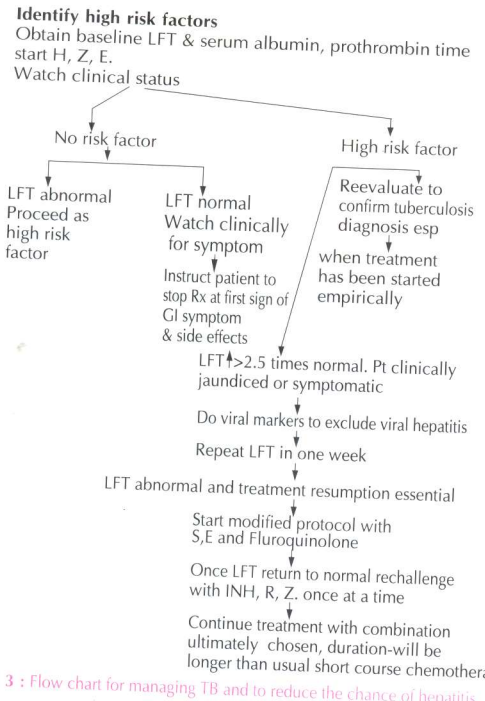


Fig. 3 : Flow chart for managing TB and to reduce the chance of hepatitis

Treatment of TB during acute hepatitis (Acute viral hepatitis)

It is rare eventually that patient has TB and also at the same time acute hepatitis unrelated to TB or anti TB treatment. Clinical judgement is necessary. In some cases it is possible to defer TB treatment until acute hepatitis has resolved. In other case when it is necessary to treat TB during acute hepatitis the combination of Streptomycin and Ethambutol upto maximum duration of 3 months is safest until the hepatitis has resolved. The patient can receive a continuation phase of six month with Isoniazid and Rifampicin[3,15,17]. Treatment of drug induced hepatitis during antitubercular therapy has been described in flow chart.

Monitoring of antitubercular chemotherapy

- It is always recommended that antitubercular drugs should be started after confirmation of diagnosis.
- Those who have established CLD should be closely monitored.
- Those whose age is more than 50 years should be closely monitored.
- Base line LFT. e.g. SGPT & S. bilirubin should be done if it is raised HBsAg & Anti HCV should be sent.
- Every patient receiving antiTB should be clinically seen by consultant physician at least once in a month.
  Patients should be carefully educated about the sign and symptom of drug induced hepatitis (dark urine, loss of appetite, vomiting, abdominal discomfort) should be instructed to discontinue treatment promptly and see their health care providers.
- Pt should be counselled to avoid alcohol completely.
- Pregnant women should be closely monitored. Ask to avoid analgesic like paracetamol in third trimester.
- PZA should be avoided in patients with abnormal baseline findings on LFT.
- Try to find out offending drug by doing following investigation:
  S. bilirubin, SGPT, SGOT, Alkaline phosphatase, Serum uric acid, CBC, ESR

Disproportionate increase in bilirubin level in relation to liver enzymes levels may be due to the use of Rifampicin, where as abnomal findings on LFT and hyperuricemia with or without arthritis may led the clinician to incriminate Pyrazinamide. During reintroduction of drugs-offending agents should be introduced lastly with close monitoring.

Conclusion

Side effect of most commonly and first line antitubercular drug range for minor gastrointestinal symptom to severe hepatotoxicity, if unrecognised they can lead to increase morbidity and mortality as well as higher healthcare cost. Erratic treatment protocols should be avoided. Recognition of the problem and planning and implementation of modified treatment protocols when needed may play a dominant role in treating and controlling tuberculosis and may prevent morbidity and mortality sometimes associated with tuberculosis treatment.

References

1. Sinder DE Jr. Roper WL; The new tuberculosis; N. Engl. J. Med. 1992; ; 703-5.
2. Ali J. Hepatotoxic effects of tuberculosis therapy: Post grad Med. J volume 99/No 5/May 1996. 217-236.
3. Lutwich LI Tuberculosis- a clinical Handbook ; chapman and Hall Medical; 1998.
4. Kopanoff DE. Snider DE (1978) Isoniazid related hepatitis. A US public health service co-operative surveillance study. American Rev. Resp disease. - 117, 991-1002.
5. Mitchel I, Weuden J. Fitts, et al; Antituberculosis therapy and acute - Liver failure. Lancet 1995; 345 (3948) 555-6.
6. Parthasarathy R; Sarma Gr; Hepatic toxicity in South Indian Patients during treatment of tuberculosis with short course regimen containing Isoniazid, Rifampicin-and pyrazinamide ; Tubercle; 1986; 67(2) 99-108;
7. Sirgh J. Arora A. et al: Antituberculosis treatment induced hepatotoxicity, role of predictive factors. Post grad Med. J. 1995 71(836); 359-62.
8. Steele MA; Buk RF; Toxic hepatitis with isoniazid and rifampicin; a meta analysis chest 1991 99(2) 465-71.
9. Sherlocks; Diseases of the liver and biliary system Blackwell scientific Publication 8th Editon 283-94.
10. Mae Nalley; Peter R-GI Liver Secrets 158-65.
11. Parsons, PE; Pulmonary Respiratory therapy Secrets 191-198.
12. CROFTON J- HORNE N; MILLER F; Clinical tuberculosis.
13. Peter AP; voigt M; Severe Isoniazid Hepatoxicity more likely in the presence of active Hepatitis B. Am. J. gastroenterology 2002, 97; 1198-1203.
14. TB focus Novartis Teleman MD. Chee CB; Hepato toxicity of tubercular chemotheraphy. Vol 1, No.3, Sept. 2002, Page-3.
15. WHO; 1997. Standard treatment Regimen of tuberculosis; guidelines for national programmes. second Edition 1997. 25-31 (WHO/TB/97-220).
16. Clinical tubmlosis; Davis PDO chapman & Hall fist Edition 1994.
17. Seaton A, Seaton D; Crofton & Douglas"s Respiratory Disease 5th Edition-Black well science 558.
18. Raviglion Mc, O, Brien R-Tuberculosis in Harisons principals of internal medicine, 15th Edition 1024-26.

Role of cardiologist for the treatment of eye diseases

Haque M M[1], Alam N[2]

The ORION 2004 ; 19 : 213-214

Introduction

Eye disease is not always a single entity. It may be multifactorial and multidimensional. Many systemic and cardiac problems such as Hypertension, Ischaemic heart disease, Bronchial Asthma, DM etc may be associated with eye diseases. Cardiologist play a vital role in the management of cardiac and other systemic diseases, preparing the patients for safe and sound eye surgery. Post-operative management also includes cardiologist's role to continue the previous treatment by adjusting the effective drugs with doses.

Opinion regarding specific diseases

Hypertension

Persistent rise of blood pressure more than 140/90 mmHg irrespective of age, sex and mental status is usually defined as hypertension. Many risk factors contribute to hypertension among which smoking, dyslipidaemia, Diabetes Mellitus, age older than 60 years, sex (men and post menopausal women), family history etc. are very important[1]. Adequate control of hypertension is always important as there is a great risk of target organ damage (TOD). Commonest TOD are in heart - LVH, angina/MI, heart failure; in brain - stroke, TIA; in kidney - nephropathy, renal failure; in eye - retinopathy; in peripheral vessels - peripheral occlusive vascular disease (POVD) etc. Adequate control of hypertension can be achieved by life style modifications include to keep body weight normal, to limit alcohol intake, to increase physical activity, to reduce sodium intake & to increase potassium intake, to stop smoking etc. Drug therapy is also multidimensional starting from simple low dose thiazides or beta-blockers, up to calcium channel blockers, ACE-inhibitors (ACEI), Angiotensin receptor blockers, vasodilators etc. Safe and sound eye surgery can not be done in hypertensive patients due to risk of exclusive bleeding, sudden increase in BP leading to CVD, arrythmias, heart failure etc.

Coronary Heart Disease

Coronary heart disease (CHD) is usually results from partial or complete occlusion of any coronary artery by atheromatous plaque, thrombus or vasospasm with or without chest pain. Angina pectoris is a discomfort in the chest and adjacent areas due to a transient inadequate blood supply to the heart. Angina is of various types: stable, unstable, prinzmetal's etc. Ischaemia without any symptoms is called silent ischaemia; which is only diagnosed by incidental ECG- where changes are ST-segment elevation or depression. Important causes of silent ischaemia are - DM, leprosy, neuropathy, myopathy etc. Myocardial infarction may be defined as myocardial necrosis secondary to an acute interruption of the coronary blood flow. According to duration myocardial infarction is usually three types: acute, recent & old. Each has got different ECG and enzyme changes[2]. In silent myocardial infarction, patients has got no chest pain. He or she may not attend any doctor. For this reason fatal cardiac problems may be ignored by an expert Physician or Cardiologist while one incidental ECG is sufficient enough to draw a correct diagnosis. In acute myocardial infarction all types of surgical intervention is strictly contraindicated due to risk of fatal arrhythmias like VT, VF, cardiac arrest, heart failure etc till patient becomes haemodynamically stable. In recent MI eye surgery is contraindicated, except life threatening any ocular condition like traumas, where surgery may be done with caution under strict cardiac supervision. In old MI, eye surgery can be done with caution.

Other Cardiac Problems

There are many other cardiac problem among which heart failure (CCF, LVF), cardiomyopathies (DCM, HCM, RCM), Pericardial diseases (acute pericarditis, pericardial effusion) etc. In heart failure any sorts of surgical procedure is contraindicated, but after control of heart failure eye surgery can be done under L/A with caution. Ocular surgery in cardiomyopathy can be done with caution unless there is any evidence of HF or fatal arrhythmias[3]. In pericardial disease, ocular surgery should be avoided in acute inflammatory condition and pericardial temponade; but in minimal asymptomatic pericardial effusion ocular surgery can be done under L/A with caution. In pulmonary embolism any sorts of surgical procedure is strictly contraindicated.

Cardiac arrythmias

There are many cardiac problems which cardiologists have to manage before, during and after eye surgery under L/A or G/A. Commonest cardiac arrythmias are extrasystoles (PAC & PVC), Atrial fibrillation, ventricular tachycardia and fibrillation, conduction defects like right and left bundle branch blocks; first, second degree & complete heart blocks etc[4]. Eye surgery should be done very carefully when patients have any sorts of cardiac arrythmias. Atrial extra systoles are usually benign, not always associated with organic diseases. But premature ventricular contractions are usually associated with IHD, MI, HTN etc. Use of some sympathomymetic and adrenergic drugs like adrenaline, dopamine, dobutamine, atropine, isoprenaline etc should be used with caution as these agents may aggravate extrasystoles together with increase in heart rate. In Atrial fibrillation operation can be done with mild caution from cardiological point of view in asymptomatic patients. But when AF is associated with other systemic and cardiac diseases like thyrotoxicosis, cardiomyopathy, in those cases surgery should be done after control of AF with non-selective ß-blockers and cardiac glycosides (digitalis). Heart blocks are of various types. Eye surgery can be done with mild caution in 10HB, 20HB, RBBB etc. LBBB is usually associated with IHD, MI, HTN. So in these conditions eye surgery should be done under strict cardiac monitoring and pulse oxymetry except acute MI where it is contraindicated. Another important point is that eye surgery can not be done in CHB, VT, VF as these conditions may lead to cardiac arrest within seconds to minute. Patients with PPM implanted for the management of CHB and other symptomatic second degree, bifascicular and trifascicular blocks should undergo eye surgery with some precautions: 1) To avoid electrocautery, 2) To avoid adrenaline, atropine. 3) To avoid adrenaline, atropine. In

1. **Dr. Mirza Manzurul Haque,** MBBS, D.Card, FRSH (London)
Cardiologist & Physician, Consultant, Islamia Eye Hospital

2. **Dr. Nazmul Alam,** MBBS, D.Card, M.Phil
Junior Consultant, Cardiology, Islamia Eye Hospital

cardiac conduction defects ß-blockers such as atenolol, metoprolol, timolol, carvedilol should be avoided due to decrease in heart rate, cardiac conductivity and contractility[5].

Some Medical Problems

There are some important medical problems which cardiologists have to look after during management of eye patients. Those are DM, electrolyte imbalance, lung diseases etc.

Diabetes mellitus

Diabetic patients are particularly prone to CHD. But there is also a diabetic form of cardiomyopathy. DM is commonly associated with HTN. DM is managed with diet control, exercise, oral Hypo-glycaemic agent and insulin. Eye surgery cannot be done without proper control of DM as there is a risk of delayed wound healing, development of retinopathy and corneal hazziness, optic neuritis, occasionally hypoglycaemic shock which is life threatening, risk of excessive bleeding and HF with stroke when DM is associated with HTN & cardiomyopathy. Electrolyte imbalance is a fatal complication of diabetes.

Lung diseases

Eye surgery can not be done in acute bronchial asthma, acute pulmonary embolism, pulmonary hypertension, acute pneumonia, open TB, advanced malignancy etc[6]. Eye surgery can be done with caution under strict cardiac monitoring in chronic bronchial asthma which is under control with bronchodilator therapy; in COPD after one to two weeks treatment; in chronic old PT treated or under anti Koch's therapy. In acute respiratory problems patient will be restless, dyspneic, cyanosed, will be unable to lying flat, associated with hypoxaemia. So smooth eye surgery is impossible at this critical condition.

Hyperlipidaemias

Raised serum lipid profile above normal with or without any clinical presentation. Commonest complications are: in heart- IHD, MI, HTN; in kidney - renal artery stenosis; in peripheral vessels - peripheral occlusive vascular diseases; in brain -cerebral ischaemia, infarction, TIA; in eye - central and peripheral retinal arteries and veins occlusion etc. Cardiologists should look after and to manage all dyslipidaemic conditions in eye patients.

Conclusion

Many congenital and valvular diseases are not always associated with chest pain, SOB, Palpitation. Those may be asymptomatic for many years but can easily be diagnosed incidentally by ECG and other cardiovascular modalities. Long standing cardiac diseases usually produce HF and fatal arrythmias, ultimately leading to death. From cardiological point of view all patients requiring surgery under L/A or G/A should undergo thorough clinical examination, cardiovascular evaluation & ECG examination as a routine investigation irrespective of age and sex.

References

1. Julian D.G., Cowoan J.C, Melerachan J.M (eds) (1998). Cardiology New york, WB Saunders. 322-23
2. Opie. L. (1994) The Heart, London Grune & Stratton.122
3. Olsen E. (1993). Cardiomyopathies, Berlin: Springer - Verlag. 98-99
4. Tierney L.M. Mcphee S.J. Papadakis M.A (eds) (2004). Current Medical Diagnosis & Treatment. New York lange Medical Books/McGraw-Hill. 358-60
5. Hall R.J. C & Julian DG (1989) Diseases of cardiac valves. Edinburgh: Churchill Livingstone. 144
6. Rich S. Braunwald E., Grossman W. (1997), Pulmonary Hypertension In Braunwald E. (Ed.) Heart Diseases. 5th edn. Philadelphia: Saunders. 211-13

Reconstruction of diaphyseal tibial bone loss : G.A.Ilizarov technique

Bari MM[1], Rizvi KAA[2]

The ORION 2004 ; 19 : 215-217

Abstract

The management of segmental defects within the diaphysis of long bones is one of the most challenging problems that the surgeon confronts in his practice. The procedures traditionally used to bridge bone gaps include autogenous bone grafting[1], posterolateral bone grafting[2], transplantation of allograft bone[3] & fibular protibia procedures[4]. All the above traditional methods of management of bone defects sometimes require multiple surgical interventions. The treatment period is long & weight bearing may not be possible while the functional results are often less than satisfactory. Recent studies showed that the G.A. Ilizarov Technique is a more popular than vascularised bone grafts especially for big bone defects[5].

The Ilizarov Technique

The Ilizarov circular external fixator was designed in early 1950s. It is a modular device allowing controlled mechanical forces (compression & distraction) to be applied at a pathological bone site. The system uses thin wires that are placed in different planes & are secured to modular rings under tension. These thin wires act as a small spring within a more rigid system of rings & concerning rods. In this way the system provides stability against angular, rotational & translational displacements, while it is relatively flexible in axial direction, allowing controlled axial loads to be applied at the zone of osteogenesis[7]. Mecoy, Chao & Kashman[8] have compared the mechanical properties of four difirent external devices. They demonstrated that the Ilizarov external fixator had the lowest overall stiffiness but high resistance to bending & rotation strains. It provides a dynamic osteosynthesis system, which prevents (bending, translational & rotational) harmful forces & alows only the useful (axial) forces to act at the osteogenesis site. This probably stimulates bone regeneration. In addition, Ilizarov apparatus allows multiplanar & multidirectional correction of deformities[9]. G.A. Ilizarov using his apparatus, developed new methods for salvage & reconstruction of a variety of a serious congenital & acquired orthopaedic probems such as clubfoot, radial clubhand, hand & leg length discrepancies, infected & non-infected non-unions, mal-unions, segmental bone defects, chronic osteomyelities & joint contractures.

Biology of osteogenesis by Ilizarov technique

The Ilizarov methods basically consist of application of mechanical forces to induce new bone formation. This can be accomplished by two separate biological processes distraction osteogenesis & osteogenesis by changing the mechanical environment at a pathological bony site. Distraction osteogenesis is the method of lengthening a long bone without grafting. After a diaphyseal corticotomy, the early mesenchymal ingrowth (early callus), is elongated by gradual, progressive distraction using a dynamic external fixator[9]. Corticotomy is a low energy osteotomy in which only the cortex is being cut. In this way the endosteum within the medullary canal, along with the medullary vessels are preserved. Gradual distraction of the corticotomy site organises the early callus into a cylinder of parallel fibers of collagen. The fibers are generally oriented longitudinally parallel to the tensile force, joining the distracted corticotomy surfaces & filling the gap created by distraction. Gradually as the distraction proceeds these fibers begin to ossify. As long as distraction is continuing a central region (the interzone), consisting histologically of undifferentiated cells, does not undergo ossification, allowing for the lengthening to continue. Ossification is carried out from both corticotomy surfaces towards the central interzone & extends through the entire cross section of the newly formed tissue. When the desire lengthening is obtained the distraction is stopped & the interzone ossifies. Later, under the compression forces, applied by muscle contraction & weight loading the newly formed cylinder of solid bone remodels into cortex & medullary canal. The remodelling process may require years to produce mature, lamellar cortical bone, Osteogenesis may be achieved by changing the mechanical enviroment to stimulate a pathologic bony interface (e.g. non-union) & restore bony continuity. By this technique variations of compressions & distraction forces across a non-union or a pseudoarthrotic site are applied to induce osteogenesis.

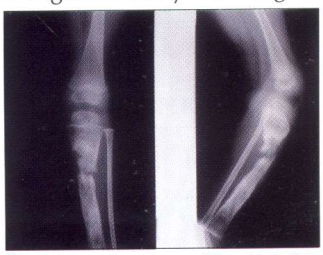


Fig.1: Chronic osteomyelitis of left tibia

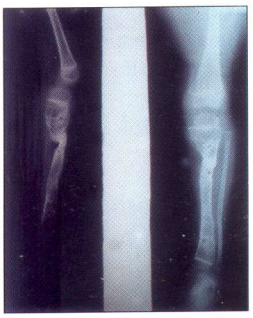


Fig.2: Final status; ILIZAROV apparatus is removed

The sequence of compression distraction depends on the rigidity & compression of the pathologic bony interface. There are many critical factors related to osteogenesis. The local blood supply & the integrity of the periosteum are of great importance. Ilizarov emphasized the importance of careful corticotomy to prevent damage to the periosteum & the importance of careful corticotomy to prevent damage to the periosteum & to the medullary vessels. Recent experimental as well as clinical studies however, have demonstrated that dissection of the nutrient vessels during the corticotomy, plays no significant role because the local vascularity is rapidly restored. The integrity of the periosteum is the most important factor for new bone formation.

Another factor promoting the bone formation is the stable fixation of the bone fragments, so that the forces applied at the osteogenic zone are controlled both in their magnitude & their orientation. Another critical mechanical factor is the rate & the rhythm of distraction. Ilizarov found experimentally, that distraction at a rate of 0,25mm every 6 hours (1mm/day) is ideal. Distraction at a faster rate causes local ischaemia & subsequently retardation of osteogenesis of poor quality of the newly formed bone[9,10,11,12]. (Distraction at a slower rate will cause premature

1. **Dr. Md. Mofakhkharul Bari,** PhD (Ortho)-Tashkent
M.D; M.S (Ortho & trauma)-Kiev, Ilizarov Fellow
Associate Professor, NITOR
2. **Prof. Kh. Abdul Awal Rizvi,** MS (Ortho), Visiting Fellow (Edin)
Professor of Orthopedics & Traumatology, NITOR

consolidation of the corticotomy[11]. It seems that the ideal place for the corticotomy is at the metaphyseal region. Metaphyseal corticotomy must be preferred whenever possible. Weight bearing is considered to be essential both for bone regeneration & consolidation. We used the above biological processes of distraction in our practice.

Materials

For the last 14 years (1990-2003) in different hospitals 56 cases of tibial diaphyseal defects were operatted on by the Ilizarov method. Male predominated with an average age of 35 years.

Table-1

Male (69.57%)	42
Female (30.43%)	14

The age of the patients ranged between 02-58 years (average 35). The main aetiology was open fractures as presented on

Table-2

Aetiology	
Open fractures	28 cases
Complications of surgically treated fractures	7 cases
Osteomyelitis	16 cases
Congenital pseudoarthrosis	5 cases
Total	56 cases

Twenty patients had active infections with drainage & twelve were previously infected. The majority of the patients had undergone several previous operations including compression plating, external fixation, bone grafting & plastic operations. Many patients had shortening & angular or rotational deformity, The average duration of the bone defects was 10 months. After resection of the infected & necrotic bone the intercalate defect was 4.8 cm in averge range 3.5-8.5 cm).

Methods

A proximal corticotomy & gradual transportation of a bony fragment towards the fragment opposite to the segmental defect (the target zone) was performed. Using the Ilizarov device the bone fragments, proximal to the intercalate defect, were fixed in good alignment. A bone fragment of adequate length was then created after the corticotomy. 7 to 10 days after corticotomy, the bony fragment was gradually transported axially across the defect. The transportation was achieved by the use of olive wires & inclined rods, or by transporting central ring connected to the bone fragment with two or more wires. As the bone segment was transported, a new gap was created behind it, while the length of the original gap was gradually reduced & finally when the leading edge of the transported bone reached the bone surface opposite the segmental defect, it was closed. The new gap, created behind the transported bone, was regenerated by distraction osteogenesis. At the target zone variations of compression-distraction forces were applied to induce osteogenesis. When the local circumstances allowed, two bone fragments, one proximally & one distally to the defect, were transported towards the centre. By this bifocal transportation the filling of the gap was accelerated.

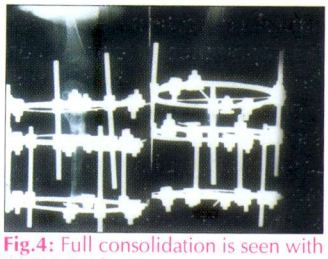


Fig.4: Full consolidation is seen with ILIZAROV fixator

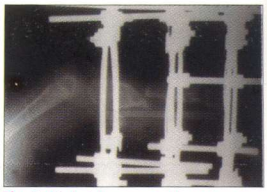


Fig.3: Debridement and corticotomy done in the tibia. ILIZAROV fixator is seen.

Results

Regeneration of the distraction gap was achieved in all 56 patients. Union at the target zone was achieved in 55 patients out of 56 cases & union was not related to the length of the bony defect. In one patients there was a failure of union at the target zone. This was due to incomplete removal of the eburnated & atrophic bones. Healing of the infection occured in all patients without a second operation. Residual varus deformity remained in two patients with 10 & 12 degrees deformity respectively.

Complications

Pain at the site of the wires a frequent problem during transportation of the intercalate segment. The most common complication was pin track infection & it was treated by local care & in 2 cases it was neccessary to replace the wires. There was no incidence of pin track osteomyelitis. Oedema of the leg & foot was always present during bone transportation. Joint stiffness of the knee & ankle occured very often during bone transportation, but after the removal of the fixator the rehabilitation of these joints resulted to the full recovery of joint motion. There was no incidence of neurovascular complications. Psycological intolerence was seen in one young patient. He required moral support until the end of the treatment.

Discussion

Ilizarov method for the treatment of pseudoarthrosis & segmental bone defects has many advantages[10,13]. But several technical problems may arise if the details of the technique are not followed precisely. Very important thing is to excise all the infected & necrotic tissues. The inexperienced surgeons usually fail to carry out a sufficient radical debridement. With the experimental & clinical experience, it is evident that regeneration of bone at the site of distraction can be obtained safely. It was evident in our cases that wide debridement accelerated healing & helped to control infection. For successful bone transportation, it is also important to maintain the bone ends in good & stable position. In order to provide firm stability & avoid axial deviation during distraction, the assembly of fixator in our cases usually required one or two rings proximally, 1 in the intercalate segment & 1 or 2 distally. Another important factor is to achieve good contact of the bones, when the transported fragment contacts the bone surface at the target zone (opposite the segmental defect). A partial contact in 1 of our cases was the cause of non-union. The importance of controlling precisely the movements of the transporting bone fragment has been emphasised by many authors [5,6,11,12,13].

Conclusion

The Ilizarov techniques for the treatment of segmental defects of diaphyseal long bones are effective & offer many advantages. One of the greater advantages of this technique is that it allows for the simultaneous treatment of bone loss, infection, non-union, deformity & problems of the soft tissues at the same time. In our all cases complications were not severe & did not affect the results.

References

1. Green SA, Dlabal TA (1983) : The open graft for septic non-union.
2. Reckling FW, waters CH (1980) : Treatment of non-unions of fractures of the tibial diaphysis by posterolateral cortical cancellous bone grafting J. Bone Joint Surg Am : 62 : 936.
3. Mankin Hj; Dopplet s. Tonford W. (1983) clinical experience with allograft implantation. The first ten years. Clin. Orthop 174 : 69.
4. May LW, Jupiter JB weiland Aj (1989). Current concept Review.
5. Alonso J; Regazzoni P. (1990) : The use of Ilizarov concept with the AO/Asif tibular fixator in the treatment of segment defects. Orthop clin of North America 21 (4) 655.
6. Ilizarov GA. (1975) : Basic old transosseous & distraction ostesynthesis. Orthop Travmatol Proez 10 : 7-15.
7. Kenright J. Richardson JB Goodship AE et. al. (1986) : effect of controlled axial micromotion on healing tibia fractures. Lancet 2 : 851
8. Mccoy MT, Chao eys, Kasman RA (1983). comparison of mechanical performance in 4 types of external fixators clin orthop 180 : 23
9. Paley, D (1990). Problems obstacles, & complications of limb lengthening by the Ilizarov technique clin. Orthop 250:81.
10. Paley D, Catagni MA, Argnani et al (1987) Ilizarov tretment of non-unions with bone loss. Clin. Orthop 223:213.
11. Goly & Khovsky V, Frankel V, (1993). Operative manual of Ilizarov techniques. Ed. Mosby.
12. Kalnberg B.K. compression-distraction apparatus & system & system of stability. Riga 1981.
13. Ga Ilizarov. Transsseous osteosythesis, theoritical & clinical aspects of the regeneration & growth of tissues, Springer (1992).

Acute myocardial infarction with normal coronary arteries in a young heroin user: A case report

Chakraborty B[1], Perveen S[2], Mollah M H[3]

The ORION 2004 ; 19 : 218-219

Summary

Substance abuse with cocaine or heroin are associated with multiple cardiovascular complications including acute myocardial infarction (AMI), left ventricular hypertrophy, fatal arrhythmias, sudden cardiac death and cardiomyopathy. We describe a case of AMI with normal coronary arteries in a 23-year old young man who collapsed within few minutes of sniffing heroin. He was documented to have ventricular tachycardia (VT) during admission which was converted to sinus rhythm after cardioversion. Subsequently he was found to have an acute anterior myocardial infarction with significant left ventricular dysfunction. Coronary angiography conducted later on was found to be normal.

Key words

AMI with normal coronary arteries, case report

Introduction

Cocaine-associated AMI is a well reported entity[1-3]. Heroin abuse and AMI has already been reported[4]. AMI with normal coronary arteries is a syndrome resulting from numerous conditions but the exact cause in a majority of the patients remains unknown. This type of myocardial infarction have been documented in pregnancy and among cigarette smokers and cocaine users[5-7]. Here the authors report a case of AMI in a young healthy male patient with history of substance abuse and his three year follow-up. This paper also discusses the possible pathological mechanisms underlying the pathogenesis of AMI with normal coronary arteries secondary to heroin abuse and current ideas on the management of cocaine or heroin induced AMI.

Case report

A 23 year old young man developed sudden onset of marked palpitation following few minutes of sniffing heroin. He also developed severe chest pain along with profuse sweating and within short time he collapsed. He was immediately brought to a coronary care unit. Electrocardiogram (ECG) revealed broad complex tachycardia suggestive of VT. As he was haemodynamically unstable VT was converted to sinus rhythm with cardioversion. ECG taken after cardioversion showed wide spread ST segment elevation in anterior leads with reciprocal ST depression in inferior leads. The diagnosis of AMI was made on ECG changes and cardiac enzyme profile. He was thrombolysed and his further hospital stay was uneventful. Echocardiogram was done one week after the acute event. Echo-Doppler study revealed dilated left ventricle with fairly good LV systolic function. Overall Left ventricular ejection fraction (LVEF) was 50%. Regional wall motion abnormalities were consistent with previous Septal and Apical myocardial infarction. Coronary angiogram conducted few weeks later was found to be normal. After counseling the patient quitted drug addiction and remains asymptomatic from cardiac point of view at three year follow-up.

Discussion

AMI is the most commonly reported cardiac consequences of cocaine misuse, usually occuring in men who are young, fit and healthy and who have minimal, if any, risk factors for coronary artery disease[5]. The mechanism by which cocaine induces AMI is largely not understood. Though cocaine induced AMI and arrhythmia are common heroin induced AMI is rare. But heroin induced AMI and cardiac decompensation have been reported in recent past[3,6].AMI

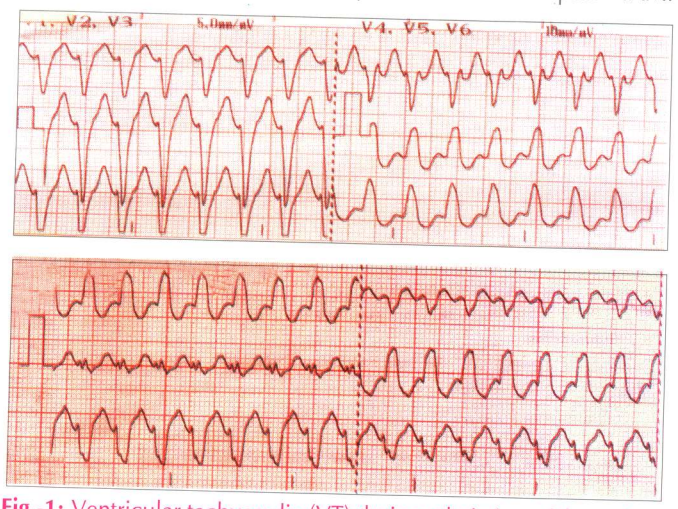


Fig.-1: Ventricular tachycardia (VT) during admission of the patient

occuring in young people with angiographically normal coronary arteries is well described but the pathophysiology of the condition remains unclear. The possible mechanisms causing AMI with normal coronary arteries are hypercoagulable states, coronary embolism, an imbalance between oxygen demand and supply, intense sympathetic stimulation, non-atherosclerotic coronary diseases, coronary trauma, coronary vasospasm, coronary thrombosis and endothelial dysfunction[7].It primarily affects younger individuals, and the clinical presentation is similar to that of AMI with coronary atherosclerosis. AMI with normal coronary arteries primarily affects younger persons and is distinctly rare in patients older than 50 years[8]. Our patient was young and his coronary angiogram did not show any significant coronary artery disease. Possibly he developed AMI complicated by VT due to severe coronary vasospasm. In AMI with normal coronary arteries, complications such as malignant arrhythmias, heart failure and hypotension are generally less common and prognosis is usually good[7]. But our patient developed VT and was admitted in the hospital in collapsed state.

AMI in patients with history of cocaine or heroin abuse are some times associated with significant coronary artery disease[9,10]. In one series 90 patients with cocaine use presenting with AMI underwent coronary angiography. Significant disease (>50%

1. **Dr. Baren Chakraborty** FCPS (Med), FACA(USA), FCCP(USA), FRCP(I), FRCP (Edin)
Professor of Cardiology, Bangladesh Medical College

2. **Dr. (Major) Shaila Perveen** FCPS (Med)
Classified Specialist in Medicine,
Combined Military Hospital , Dhaka.

3. **Dr. Mujibul Haque Mollah** MRCP
Associate Professor and Head, Department of Nephrology,
Bangladesh Medical College

stenosis) was present in 45 (50%) patients[9].AMI related to heroin use with significant coronary artery disease was previously reported in the medical literature. A young woman developed AMI due to an acute thrombosis of the left anterior descending artery induced by intravenous heroin use has been documented[4]. So substance abusers may have AMI with significant coronary artery disease. The patient reported here was treated for AMI according to the standard guidelines. He was treated with thrombolysis, antiplatelet therapy, heparin, vasodilators and calcium channel blocker. At three year follow-up our patient was doing well. He quitted drugs and is now asymptomatic from cardiac point of view. Recurrent infarction, post infarction angina, heart failure and sudden cardiac death are rare in this condition. Long term survival mainly depends on the residual left ventricular function. The reported case was documented to have reasonably good left ventricular systolic function at one year follow-up and we expect good long term survival is this particular case.

Conclusion

AMI can occur in young persons with normal coronary arteries and the diagnosis should be considered in young patients presenting with severe chest pain, particularly those abusing cocaine or heroin, so that reperfusion therapy can be initiated promptly. Thrombolytics, aspirin, nitrates and beta blockers should be instituted as a standard therapy for AMI. Once normal coronary arteries are identified on subsequent coronary angiography, beta-blockers should be replaced by calcium channel blockers as coronary vasospasm appears to play a major role in the pathophysiology of this condition.

References

1. Frishman WH, Del Vecchio A, Sanal S et al. Cardiovascular manifestations of substance abuse part 1:cocaine. Heart Dis 2003;5(3): 187-201.
2. Kloner RA, Rezkalla SH. Cocaine and the Heart. N Engl J Med 2003;348(6):487-8.
3. Weber JE, Shofer FS, Larkin GL et al. Validation of a brief observation period for patients with cocaine-associated chest pain. N Engl J Med 2003;348(6):510-7.
4. Sztajzel J, Karpuz H, Rutishauser W. Heroin abuse and myocardial infarction. Int J Cardiol 1994;47(2):180-2.
5. Vasica G, Tennant CC. Cocaine use and cardiovascular complications. Med J Aust 2002;177(5):260-2.
6. Chowdhury AN, Das J. Myocardial decompensation in heroin addicts. J Assoc Physicians India 1993;41(3):180.
7. Tun A, Khan IA. Myocardial infarction with normal coronary arteries:the pathologic and clinical perspectives. Angiology 2001;52(5):299-304.
8. Tun A, Khan IA. Acute myocardial infarction with angiographically normal coronary arteries. Heart Lung 2000;29(5):348-50.
9. Kontos MC, Jesse RL, Tatun JL et al. Coronary angiographic findings in patients with cocaine associated chest pain. J Emerg Med 2003;24(1):9-13.
10. Benzaquen BS, Cohen V, Eisenberg MJ. Effects of cocaine on the coronary arteries. Am Heart J 2001;142(3):402-10.

Superstitions: The women are behind

Hussain M A[1]

The ORION 2004 ; 19 : 220

To The Editor

I would like to share some experiences about some superstitions that the women of our society facing and we, the doctor's community specially the gynecologists society of Bangladesh, have noble responsibility to give clear understandings regarding the matter. The women of our country are far behind the women of the developed countries in many respects. Education can bring this difference to a minimum. Many women of our society particularly the elderly women are behind different superstitions. There is no proper education about the structure & reproductive organs of the women. This is the reason for believing in such superstitions and thereby suffering out of them. As soon as a girl reach her puberty, there occurs cyclical changes in the inner lining of her womb.

These changes occur so that a baby in its earlier life can settle inside the womb. If there is no pregnancy then the whole inner lining breaks & it comes out mixing with blood. This is the menstruation. Menstruation doesn't mean the passage of bad blood. We don't have bad blood in our body. So believing that menstruation means passage of bad blood is a superstition. Normal menstrual blood should not clot. So if clot or lump passes during period, it means that woman is loosing more blood & needs treatment.

Vaginal discharge is the commonest gynecological symptom. Women can have vaginal discharge normally. There can be discharge immediately before and immediately after a period. Infact, menstruation initially start as a discharge, then there is bleeding and then again there is discharge which ends within a few days. Women may get a discharge for 2-3 days in the middle of their cycle in between their period. This is because of hormonal changes that occur at the time of ovulation. Women may get discharge following sexual excitement. There is a rich belief that with discharge, women lose energy. No one loses energy with discharge. This is a great superstition. About discharge, one should be concerned only when there is itching of the private part, there is bleeding with discharge. Postmenopausal women should not have any significant discharge. She should see a doctor if there is any discharge.

This is a belief that if a pregnant woman takes more food, she is likely to have a caesarean section. A woman doesn't need to increase the amount of her food intake during pregnancy too much. But she needs to take nutritious foods esp. egg, milk, meat, fish, vegetables during pregnancy. This nutritious food in right amount will keep the baby growing properly in her womb, even without increasing the maternal weight to a great extent. The fact is that too much food do not increase the size of the baby but on the other hand too small amount of food will hamper growth of the baby and leads different complication. So every woman should take adequate and nutritious food during pregnancy in order to help her baby growing. Adequate food intake during pregnancy does not increase risk of caesarean section. It is the responsibility of the doctors of our country to spread this knowledge to our patients so that they do not suffer unnecessarily by believing this superstition.

1. **Prof. M. Anwar Hussain,** MBBS (DMC), FRCOG (London), FICS
Department of Obstetrics & Gynaecology, BSMMU

Launching of New Products

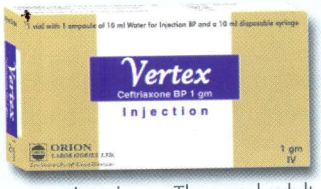
Orion Laboratories Limited has recently introduced the following two products in the market

Vertex

Ceftriaxone Sodium

Safe & Save

Vertex (ceftriaxone) is a 3rd generation broad-spectrum parenteral cephalosporin antibiotic. It has potent bactericidal activity against a wide range of Gram-positive and especially Gram-negative organisms. The spectrum of activity includes both aerobic and some anaerobic species.The specialty of Vertex is its amazingly economic price. The usual adult daily dose is 1- 2 gm once daily (or twice daily in equally divided doses) for 4 - 14 days depending on the type and severity of infections.



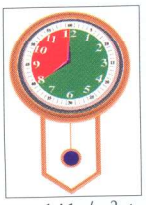
Ceftriaxone Sodium Vertex	Strength	Price/Vial
	250 mg IV & IM	Tk. 90/-
	500 mg IV & IM	Tk. 125/-
	1 gm IV & IM	Tk. 195/-

Telsan

Telmisartan INN 40 mg

Ensures truly 24- hour antihypertensive coverage

Telsan (Telmisartan) is FDA approved angiotensin II receptor (type AT_1) antagonist. This drug provides completely 24 hours antihypertensive activity including the last 4 - 6 hours crucial periods because of its longer half-life, slowly dissociates with AT_1 receptor & good tissue penetration. Telsan provides quicker control of blood pressure than other ARBs due to its quicker onset of action. It also reduces cerebral and cardiovascular events such as stroke and myocardial infarction that occur in the early morning. Moreover, Telsan reduces hypertrophy and arterial stiffness in diabetic patients and also reduces LVMI from 141g/m^2 to 125g/m^2. It is indicated for the treatment of hypertension and heart failure. Telsan is available as 40 mg tablet. The usual dosage of Telsan is one tablet once daily. MRP of Tab. Telsan is TK.10.00/ tab.



MSD NEWS

MSD personnel of ORION Laboratories Limited spent a prompt schedule in organizing seminars / Clinical meetings and Internee Doctors Reception Program in various venues all over the country as a part of their Continued Medical Education (CME) Program.

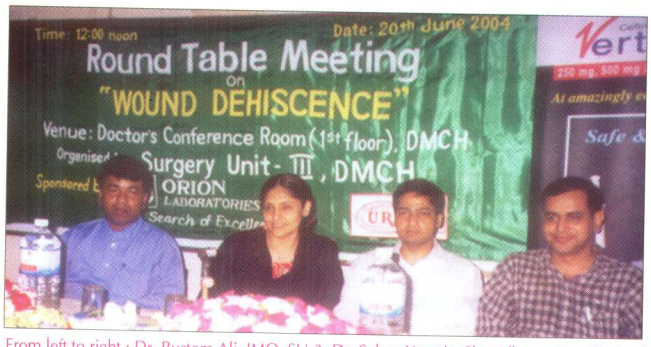
Scientific seminar

Ankylosing spondylitis: A management update

Orion Laboratories Ltd. sponsored a scientific seminar on "Ankylosing spondylitis: A management update" at Milon Hall, BSMMU on 25th April 2004. Prof. M A Tahir, Pro Vice Chancellor, BSMMU chaired the session. Dr. Suzon Al Hasan, Asst. Prof. of Physical Medicine, RMCH & Dr. Ismail Patwary, Assoc. Prof. of Medicine, SOMCH discussed on the topic respectively.

Round Table Meeting

"Wound Dehiscence"



From left to right : Dr. Rustom Ali, IMO, SU-3; Dr. Salma Yesmin Chowdhury, Asstt. Prof. of Surgery, U-3; Dr. Bakhtiar Uddin Jewel, A/R, SU-3; Dr. Hasan Imam, HMO, SU-3.

Orion Laboratories Limited arranged a RTM on "Wound Dehiscence" on 20th June 2004 at Clinical Conference Room of DMCH. Dr. Md. Feroze Quader, Associate Professor, Dept. of Surgery, DMCH, chaired the occasion. Dr. Salma Yesmin Chowdhury, Assistant Professor, Dept of Surgery, DMCH was present as Chief guest. Dr. Hasan Imam, HMO, Surgery Unit-3, DMCH discussed on the topic.

"Chronic Pancreatitis"

Another RTM on "Chronic Pancreatitis" held on 22nd June 2004 at Clinical Conference Room of DMCH. Dr. AKM Fazlul Hoque, Associate Professor, Dept. of Surgery, DMCH, chaired the occasion. Professor Syed Mahabubul Alam, Dept of Surgery, DMCH was present as Special guest. Dr. Md. Mostafizur Rahman, IMO, Surgery Unit-5, DMCH discussed on the topic.

"Management of Pelvic Fracture"

From left to right : Dr. N.K. Alam, Consultant Casualty Surgery U-1; Dr. M.A. Momen, Consultant Casualty Surgery U-2; Mr. Abu Taher, RSM, OLL, Dhaka.

RTM on "Management of Pelvic Fracture" held on 24th June 2004 at Cardiology Conference Room of DMCH. Dr. M. A. Momen, Consultant, Casualty Surgery dept, DMCH, chaired the occasion. Dr. N. K. Alam, Consultant, Casualty Surgery dept, DMCH was present as Chief guest. Dr. AKM Fazlur Rahman, IMO, Casualty Surgery Unit-1, DMCH discussed on the topic.

Venue: Dhanshiri Restaurant, Gulshan, Dhaka.

Orion Laboratories Limited arranged a RTM on "Management of Otitis Media" on 10th June 2004 at Dhanshiri Restaurant, Gulshan, Dhaka. Dr. Abdus Samad, Consultant, SAHIC, Dhaka, chaired the occasion. Dr. Latiful Haque Mahmood, MO, SAHIC, Dhaka discussed on the topic.

Venue: Sharopkathi Health Complex,Sharupkathi.

RTM on "Hypertension" on 25th July 2004 at Sharopkathi Health Complex, Sharupkathi. Dr. Liakot Ali Khan, THA, chaired the session and Dr. Alamgir Hossain, RMO discussed on the topic.

Venue: Thana Health Complex,Mohadebpur.

RTM on "Vertex" on 19th July 2004 at Thana Health Complex, Mohadebpur. Dr. S. M. Boslul Hossain, THA & FPO, chaired the session and also discussed on the topic.

Venue: Thana Health Complex,Nojipur.

RTM on "Vertex" on 18th July 2004 at Thana Health Complex, Nojipur. Dr. Abdus Satter, THA & FPO, chaired the session and also discussed on the topic.

Venue: Hospital Conference Room, Sylhet MAG Osmani Medical College& Hospital, Sylhet.

RTM on "Ovarian Tumour" on 21st July 2004 at Hospital Conference Room, SOMCH, Sylhet. Dr. Lubli, C/A, Gynae. Unit-2, SOMCH, Sylhet, chaired the occasion and also discussed on the topic.

Venue: Hospital Conference Room, Sylhet MAG Osmani Medical College& Hospital, Sylhet.

RTM on "Eclampsia" on 15th July 2004 at Hospital Conference Room, SOMCH, Sylhet. Dr. Jibon, C/A, Gynae. Unit-3, SOMCH, Sylhet, chaired the occasion and also discussed on the topic.

Venue: Hospital Conference Room, Sylhet MAG Osmani Medical College& Hospital, Sylhet.

RTM on "Management of Meningitis" on 27th July 2004 at Hospital Teaching Corner, SOMCH, Sylhet. Dr. Jahangir, C/A, Medicine Unit-3, SOMCH, Sylhet, chaired the occasion and Dr. Imran, C/A, Medicine Unit-3 discussed on the topic.

Internee Doctors Reception Program and Scientific Seminar

From left to right : Dr. G.M. Raihanul Islam, Dr. Mofakharul Islam, Brig. Gen. Abul Kalam Azad, Proff. Fazlur Rahman, Dr. Wasim Hussain, Dr. Monoarul Islam, Dr. Md. Zakirul Karim, Mr. Salahuddin

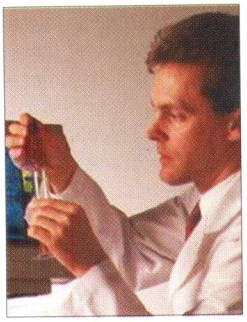
Venue: Auditorium of Rajshahi Medical College, Rajshahi

Orion Laboratories Limited congratulate the Intern Doctors of Rajshahi Medical College and arranged a grand gala reception program and Scientific Seminar on "Renal Transplantation" at 8:00 pm on 14th July, 2004 at Auditorium of Rajshahi Medical College, Rajshahi. Dr. Md. Mofakharul Islam, G.S, BMA, Rajshahi, welcomed the participants. Dr. Md. Wasim Hussain, President, BMA, Rajshahi, chaired the session. Prof. Md. Fazlur Rahman, Principal, RMC and Brig. Gen. Md. Abul Kalam Azad, Director, RMCH was present as chief guest and special guest respectively. Dr. AKM Monoarul Islam, Asst. Prof. of Nephrology, RMCH and Scientific Secretary, BMA, Rajshahi was present as Keynote speaker of the session.

Medi News

Zinc - Contributing to Better Health

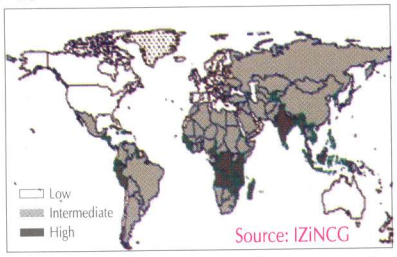
During the first half of the 20th century, researchers discovered that zinc is essential for the normal growth and survival of plants and animals. Despite these observations, many nutritionists doubted that zinc deficiency occurred in humans because zinc is naturally present throughout the environment and obvious clinical signs of deficiency were not apparent. Today, however, zinc deficiency is recognized as an important and widespread risk to human health. Clear evidence of human zinc deficiency began to emerge during the 1960s, when Dr Ananda Prasad first reported cases of dwarfism and delayed sexual maturity among Middle Eastern adolescents. When zinc supplements were given to these adolescents, their height, weight, bone development and sexual maturation improved significantly. Since then, many researchers working in different areas of the world have found that zinc supplementation increases growth among stunted children and reduces the prevalence of common childhood infections, such as diarrhea and pneumonia. Zinc deficiency has serious consequences for health including:



- Impairment of the immune system and as a result, increased prevalence of childhood infections, such as diarrhea and pneumonia;
- Impaired growth and development of infants, children and adolescents;
- Impaired maternal health and pregnancy outcome.

The manifestation and severity of zinc deficiency varies at different ages. In infants up to two months of age, for example, diarrhea is a prominent symptom. Early zinc deficiency leads to impairment of cognitive function, behavioral problems, mood changes, memory impairment, problems with spatial learning, and neuronal atrophy. Skin problems become more frequent, and gastrointestinal problems, anorexia and mood changes less frequent, as the child grows older. Hair loss, growth retardation, inflammation of the eyelids and conjunctiva and recurrent infections are common findings in school-aged children. Chronic non-healing leg ulcers and recurrent infections occur among the elderly.

Studies of zinc supplementation in nine lower-income countries in Latin America and the Caribbean, south and Southeast Asia, and the western Pacific, have shown that supplemental zinc led to an average 25% reduction in the prevalence of diarrhea. Further studies in Africa have also demonstrated similar reductions in the incidence or number of days with diarrhea, confirming that zinc prevents diarrheal infection across a wide range of geographical regions. Studies of lower respiratory infections conducted in India, Jamaica, Peru and Vietnam have shown a 41% reduction in the incidence of pneumonia when children received zinc supplements. Studies on malaria have shown that zinc may reduce the severity of Plasmodium falciparum infections in children. A study in India on infants born with low birth weights showed that daily zinc supplements reduced mortality by 68%.



Several options are available to fight zinc deficiency in populations at risk - zinc supplements, fortification of common foods with zinc, and modifying dietary habits. Many forms of zinc are available at low cost for use as supplements. Researchers suggest that soluble forms of zinc salts, such as zinc acetate, zinc sulphate or zinc gluconate, should be used in supplement formulation, and that supplements should be taken daily and preferably between meals. Supplemental zinc is recommended, for example, as an adjunct therapy during the treatment of diarrhea in children, whereby a high daily dosage is administered for a short period. For infants and small children, zinc supplements are often given in the form of flavored syrup. (Fig Pep) Chewable tablets have been used for school children. The optimal form of the supplement depends on the age of the target group, cultural preferences, and the need to include additional nutrients in the supplement. High-fat, micronutrient-fortified spreads may provide another option for zinc supplementation. In many situations, zinc can be included in programs already delivering daily or weekly nutrient supplements.

WHO has developed a system - named CHOICE (CHOosing Interventions that are Cost-Effective) - for identifying and reporting cost-effective health interventions consistently across different regions of the world. CHOICE options are contained in a new statistical database, one of the largest research projects ever undertaken by the World Health Organization. Zinc supplementation and fortification are shown to be very cost-effective public health interventions in all regions of the world. In relation to combined (zinc, iron and Vitamin A) interventions to reduce risks to children under five years of age, WHO observes that "Zinc fortification is, perhaps, the surprise, being more cost-effective than the other options in all regions. To the extent that the same food vehicles could be used to fortify zinc and iron, the cost-effectiveness of the combined intervention would be even more attractive, making it one of the most attractive options available of any type of intervention." Except in regions where Vitamin A is not a major risk (Europe), "the combination of zinc and Vitamin A fortification (or supplementation) with treatment of diarrhoea and pneumonia is the most cost-effective combination of preventative and curative actions." "This report provides a road map for how societies can tackle a wide range of preventable conditions that are killing millions of people prematurely and robbing tens of millions of healthy life," said WHO Director-General, Dr Gro Harlem Brundtland, when she presented the Report in 2002.

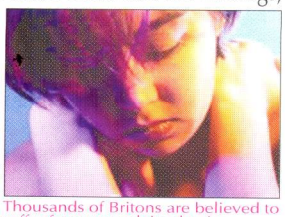
Today, zinc is known to be the most ubiquitous of all trace elements involved in human metabolism. Zinc participates in all major biochemical pathways and plays multiple roles in the perpetuation of genetic material, including transcription of DNA, translation of RNA, and ultimately cellular division. More than 300 enzymes require zinc for their catalytic function. And for millions of people around the world, a few extra milligrams of zinc each day can make the difference between illness and a healthy and productive life. *ZINC WORLD.org*

Mystery pain 'is all in the mind'

Mysterious pain, such as lower back pain, may originate in the brain rather than the body, according to a study. Scientists from University College London (UCL) and the University of Pittsburgh carried out tests on eight people. Some were hypnotised and told they were in pain.

Medi News

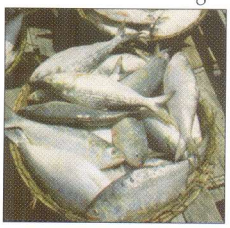
Others were subjected to physical pain. Scans showed that both experienced similar brain activity. The researchers said the findings, published in NeuroImage, suggested that pain can sometimes begin in the brain. "The fact that hypnosis was able to induce a genuine painful experience suggests that some pain really can begin in our minds," said Dr David Oakley, director of the hypnosis unit at UCL. *bbc.com/health*



Thousands of Britons are believed to suffer from unexplained pains

Eating Fish May Prevent Irregular Heartbeats

A diet rich in baked or broiled fish may protect against atrial fibrillation, a potentially dangerous cardiac condition. According to a new study, eating broiled or baked fish reduces your chances of developing this common irregular heartbeat. However, eating fried fish or fish sandwiches does not carry the same benefits. "Eating tuna or other fish that is broiled or baked is associated with a lower risk of atrial fibrillation, which is a very common heart rhythm abnormality, especially among elderly people," said study author Dr. Dariush Mozaffarian, a researcher at the Channing Laboratory at Brigham and Women's Hospital. Mozaffarian's team collected data on 4,815 men and women over 65 who participated in Cardiovascular Health Study, during 12 years of follow-up, there were 980 cases of atrial fibrillation among the study particpants. Compared with those who ate fish only once a month or less, individuals who ate fresh or canned tuna or other broiled or baked fish two to four times per week had a 28 percent lower risk of developing atrial fibrillation. *bbc.com/health*



Warning on complementary therapy

The public must not place too much faith in the ability of complementary medicines, a leading expert has warned. Edzard Ernst, the UK's only professor of complementary medicine, said most therapies were unproven. Some of the few that had been vigorously tested did work, but others did not, he told a briefing on Monday. Professor Ernst highlighted cancer websites peddling potentially dangerous therapies, and the risk of herbal medicines damaging conventional drugs. *bbc.com/health*

Complementary therapies can be dangerous

Weather is a trigger for migraine

Researchers have produced compelling evidence that weather conditions can trigger a migraine. More than half of people with headache were affected by the weather, Boston's Children's Hospital found. Some were sensitive to temperatures and humidity, while others reacted to changes in air pressure, Dr Prince's team report in the journal Headache. They said those prone to "weather" migraines could track forecasts to pre-empt and prevent an attack. *bbc.com/health*

Stormy weather was a trigger for some people's migraines

TV 'linked to short-sightedness'

Watching too much television and spending too long in front of a computer is behind rising rates of short-sightedness, say scientists. Australian researchers examined rising rates of short-sightedness in Asia. Some experts say genes are behind the rise. But the researchers found people's lifestyle was to blame, according to a report in New Scientist magazine. They said the findings may also explain rising rates of short-sightedness in other parts of the world. East Asia has much higher rates of short-sightedness or myopia than other parts of the world. In Singapore, 80% of 18-year-old men recruited to the army are short-sighted. This compares with 25% just 30 years ago, which can lead to blindness. *bbc.com/health*

Watching too much television may be to blame

Computer 'toxic dust' linked to diseases

"Toxic dust" found on computer processors and monitors contains chemicals linked to reproductive and neurological disorders, according to a new study by several environmental groups. Electronics companies began using polybrominated diphenyl (PBDEs) and other flame retardants in the 1970s, arguing that the toxins prevent fires and cannot escape from plastic casings. "This will be a great surprise to everyone who uses a computer," said Ted Smith, director of the Toxics Coalition. "The chemical industry is subjecting us all to what amounts to chemical trespass by putting these substances into use in commerce. They continue to use their chemicals in ways that are affecting humans and other species. The Agency for Toxic Substances and Disease Registry, part of the U.S. Department of Health and Human Services, and several other organizations have confirmed that PCBs damage brains of human fetuses. *cnn.com/HEALTH*

Quitting Smoking Can Add 10 Years to Life

Quit smoking: You'll live longer -- maybe 10 years or more. Quit before age 35, and you can avoid early death almost entirely. A landmark 50-year medical study from Great Britain shows that at least one-half of those who begin smoking young are eventually killed by the habit. Many of those deaths occur between ages 35 and 59. Lead researcher Richard Doll, MD, emeritus professor of medicine at the University of Oxford, who launched the study in the 1950s when he was in his 30s. His first report in 1954 confirmed the link between smoking and lung cancer. Now in his 90s, Doll has published his full report in the latest British Medical Journal. The report is based on the 34,439 doctors' annual questionnaires about their health habits, including smoking, from 1951 until 2001. Causes of death were noted for every doctor. Doctors were studied because the researchers felt doctors may be more accurate about their smoking. Among the findings: About 42% of smokers who started young could expect to die early (before age 70) from smoking-related diseases -- 10 years earlier, on average. Some lost a few decades of life, Doll notes. The tobacco-related causes of death included lung cancer; heart disease; cancers of the mouth, pharynx, and esophagus; and respiratory disorders such as emphysema. Daily cigarette smoking was highest during World War II, especially among men -- three times greater than the previous years, writes Doll. *Web Med/Health*

Deslor

Tablet & Syrup

Desloratadine

The 3rd generation antihistamine

Non-sedative
More effective

ORION
LABORATORIES LTD.
In Search of Excellence