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"The ORION", is one of the leading Medical Journals of the country which has been published successfully for the last 10 years. "The ORION", not only meets the quantity but also satisfies the quality of the publication by peer review, reference input, text index, latest medical & scientific news and information corner on zinc. Recently "The ORION" is looking forward to having a complete HTML Indexing with all its volumes to make it more user friendly to the authors, readers, members and subscribers. This issue (Volume 32, Issue 1) comprises 03 original articles and 05 review articles.

Editorial (P-610) of the volume `An overview of infertility' states that 1 in 7 couples in industrialized countries is infertile and a large number of couples in Bangladesh are also suffering from this problem. It suggests that rational use of different drugs, surgery and newer IVF techniques can be the good solution to many of these infertile cases.

The first original article (P-612) `Effect of zinc supplementation on appetite, growth & body composition in children suffering from nonspecific etiology of feeding refusal with failure to thrive' states that oral zinc supplementation can improve the appetite associated with the weight gain in children with poor feeding without any adverse effect on body composition. The second original article (P-616) on `Effects of nutrition education on nutritional knowledge of the respondent mothers and STP of their hospitalized children' reveals the nutritional knowledge level of Bangladeshi mothers & it is seen that nutrition education reduces the rate of anemia in the children of case group, increases the mothers' knowledge about the types of food responsible for body growth & development and also increases the knowledge of testing of Iodine in salt. The last original article (P-619) `Determination of MIC and MBC of selected Azithromycin capsule commercially available in Bangladesh' finds the highest MIC and MBC volume of azithromycin capsule against *Pseudomonus* spp, *Shigella* spp. & *E. coli*. It also examines the tolerance and resistance of the drug.

The first review article (P-621) `Carotid angioplasty and stenting, an alternative to carotid endarterectomy' reviews the development of carotid artery disease treatments and evaluate the acceptance of carotid artery stenting as a better alternative. Second review article (P-623) `Managing postoperative pain' reviews the proper assessment of pain and the therapeutic measures required to manage the pain effectively. It also reveals that administration of opioid and non opioid analgesics combination is a better choice to reduce the pain. The third review article (P-629) on `Hepatorenal syndrome' recaps classification, pathogenesis, diagnostic criteria & management of Hepatorenal syndrome (HRS) in brief and it summarizes that pharmacotherapy can reverse HRS & that improvement is maintained despite withdrawal of drugs in majority of patients. Forth review article (P-633) on `Clinical problems related to anti-tubercular drug therapy' mainly highlights the global & national prevalence of tuberculosis along with its management protocol with different clinical conditions like renal insufficiency, hepato-toxicity, diabetes mellitus, pregnancy and lactation. Last review article (P-636) on `Lasers in dermatology: Four decades of progress' states the technical advancement of treating dermatological problems by laser therapy in last 4 decades. The article also shows the hope of emerging laser surgery in future.

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

DR. KAZI RAFIQUL ALAM
Chief Editor
The ORION Medical Journal

An overview of infertility

Chowdhury TA[1], Chowdhury TS[2]

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Infertility is a condition that causes considerable psychological distress to the couples. Even though the exact prevalence of infertility in Bangladesh is difficult to ascertain, it affects 10 to 15% couples in the western world[1]. There has not been any major increase in the prevalence of infertility in recent years, but there is a greater awareness of the problem and also availability of more effective treatments like in vitro fertilization even in countries like Bangladesh.

Epidemiological data indicate that conception occurs in 84% of women within 12 months and 92% by second year of ceasing contraception[1]. So infertility can be defined as inability to conceive after one or two years of regular unprotected sexual intercourse[2]. It can be broadly divided into primary infertility where couples have never conceived previously and secondary infertility where couples have had a pregnancy, although not necessary a successful one.

Either the male and female partners can be responsible for infertility in around 30% cases or both are involved in another 25 to 30% cases. In the remaining 10 to 15% case, no cause could be found out, which is known as unexplained infertility.

Semen analysis remains the most important aspect of male investigations. World Health Organization values for definition of normality are widely accepted[3]. Additional investigations are required if semen report fail to meet these criteria. Serum FSH differentiates between obstructive and non-obstructive azoospermia and has enormous prognostic value if ICSI (intracytoplasmic sperm injection) is to be considered. Serum testosterone is only indicated in suspected hypogonadism. Serum prolactin is suggested in men with coital difficulty. Semen culture is only required if there is microscopic evidence of infection.

Investigations to find out the capacity of sperm to fertilize an ovum are difficult to interpret. Even though post coital test is useful providing information about sperm function[4], systemic review of literature suggests that this test lacks validity for routine use.

Significance of antisperm antibody present in serum or semen is unclear. It mostly develops following vasectomy or infections like epididymitis or orchitis. It is of clinical importance if reversal is required.

Imaging of the male genital tract include thermography, Doppler USG or retrograde venography to diagnose varicocele. In obstructive azoospermia, vasography may be suggested in order to find out the site of obstruction. Testicular biopsy has been virtually replaced by serum FSH estimation.

About 15% azoospermic men are found to have abnormal karyotype like Klinefelter's syndrome. So karyotyping may be suggested in men with azoospermia or severe oligospermia.

During management of male infertility, men should be advised to reduce alcohol intake, stop smoking and use or recreational drugs which interfere with fertility.

There are various treatments for male infertility. Even though the WHO suggests that there is an inverse relationship between semen quality and the presence and severity of varicocele[5], at present there is no evidence that surgical treatment of clinically detectable varicocele with oligospermia improves pregnancy outcome. Hypogonadotrophic hypogonadism in men can be successfully treated with exogenous gonadotrophin or GnRH therapy. Ejaculatory problems are often treated with alpha adrenergic and anticholenergic drugs.

Acute bacterial infection of the genital tract should be treated with antibiotic even though there is no evidence that antibiotics improve male fertility. Epididymovasostomy is suggested in post vasectomy cases. Orchidopexy is suggested when ever there is testicular maldescent.

There are various empirical treatments for male infertility which has not shown to be effective. There is no evidence to recommend gonadotropin, GnRh, testosterone, anti estrogens like clomiphen or tamoxifan in treatment of male infertility. Bromocriptine is only beneficial in men with hyper prolactenemia. Antioxidants like glutathione, vitamin E and C may improve semen parameters but this mode of treatment requires further evaluation. Systemic steroid therapy does not improve immunological male infertility and it is not recommended.

Assisted reproduction has great role in male infertility. IUI (intrauterine insemination) improves the relative odds of pregnancy if semen parameters are abnormal, even though the pregnancy rates remain low (4-6%)[6]. Men with severe sperm abnormalities or non-obstructive azoospermia now can be managed by microsurgical sperm retrieval with ICSI (Intra Cytoplasmic Sperm Injection) but it puts the female under hazard of assisted reproduction.

Regarding females, investigations are done to find out if the woman is ovulating. Laboratory evidence may be obtained through measurement of serum progesterone in the luteal phase of menstrual cycle. If there is history of irregular menstruation or periods of amennorhoea, especially associated with obesity, hirsuitism or galactorrhoea, additional biochemical tests like serum FSH, LH, TSH and prolactin in early follicular phase should be done.

When the preliminary investigations suggest that the woman is ovulating and sperm production is satisfactory, pelvic assessment should be undertaken. If there is identifiable risk factors for pelvic pathology like past history of pelvic inflammatory disease, previous ectopic pregnancy or symptoms suggestive of endometriosis, either hysterosalpingography or laparoscopy with dye hydrotubation is advised. Sonohysterography, an alternate outpatient investigation may be used as well but it has yet to gain widespread popularity.

Treatment of ovulatory failure depends upon the cause. In WHO group I ovulatory dysfunction (due to hypothalamo pituitary failure), weight gain is the most effective treatment if there is significant weight loss. Use of pulsatile GnRh agonist is mainly indicated where endogenous GnRh levels are very low. In hyperprolactenemia, medical therapy including bromocriptine, cabergoline or quinigalide are most effective to reduce the prolactin level. Surgery is required when there is large macro adenoma.

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In type II ovulatory failure (mainly PCOS) treatment options include, weight loss and lifestyle modification. Insulin sensitizing agents like metformin reverse some of the metabolic effects of PCOS (Polycystic ovary syndrome) and act as pre-treatment and co-treatment agent with anti estrogens[7]. Clomifene is most widely used anti estrogen. Multiple pregnancy can occur in around 7 to 10% cases and mainly involves twins. OHSS (Ovarian hyper stimulation syndrome) is rare. A distant link with ovarian cancer has been described in women receiving more than 12 cycles of clomifene, so it should be used to the lowest effective dose and duration of use. Gonadotropins (hMG, purified FSH, recombinant FSH) are used when patient fail to ovulate with clomiphen with or without metformin. Miscarriage rate is quite high (25-30%) in gonadotropin ovulation induction[6]. Multiple pregnancy rate is 15 to 20% and rate of OHSS is 1-2%[8]. Recently aromatase inhibitors like letrozol are used in anovulatory women with PCOS who are resistant to clomifene but large randomized trials are required to investigate its effectiveness. Laparoscopic ovarian drilling is widely used now days. It results in mono follicular ovulation which means the risk of OHSS and multiple pregnancies can be avoided. It also increases ovarian sensitivity to subsequent treatment with clomifene. There has been no evidence of premature menopause for women followed up for over 10 years[6].

Egg donation is the only treatment option for type III ovulatory failure (Ovarian failure).

In case of infertility due to tubal cause, medical treatment has limited values. Chemotherapy has a definite role in cases of tuberculosis even though it will not reverse the damage present. Surgery offers the best results when carried out in properly selected cases. Salphingography with tubal catheterization or hyteroscopic tubal recanalization can be the treatment options. Compared to IVF (In vitro fertilization), tubal surgery carries no risk of OHSS and a lower risk of multiple pregnancies and miscarriage, even though ectopic pregnancy is a possible outcome with all surgical techniques. Most cases of tubal sterilization can be treated with tubal reanastomosis. IVF is the first-line treatment if there is moderate to severe tubal disease and should be discussed if pregnancy does not occur 12 to 18 months after surgery.

Endometriosis is commonly associated with infertility. Medical treatment has no role in endometriosis related infertility[9]. Surgery is often the only treatment but in cases of moderate and severe disease, assisted reproductive techniques should be considered as an alternative or after unsuccessful surgical treatment.

Effective treatment of unexplained infertility includes super ovulation and intrauterine insemination and in vitro fertilization. A Meta analysis has demonstrated statistically significant benefit following treatment with clomifene in inexplained infertility[10].

Significant developments have taken place in the field of assisted reproduction over the last 15 years. IUI (intra uterine insemination) involves timed introduction of washed motile sperm into the uterine cavity. It is a relatively less invasive procedure which is considered in cases of mild male infertility, unexplained infertility and coital or ejaculatory failure. IVF is a method of assisted reproduction when the sperm and oocytes are mixed to allow fertilization to occur in vitro. The resulting embryos are then transferred into the uterus. Success rate of IVF has risen significantly during the course or last 10 years and have reached 28.8% live birth rate/embryo transfer for women under the age of 38 years and 24.3% for all age groups[11]. Lastly the advent of ICSI (intracytoplasmic sperm injection) has revolutionized the management of couples suffering from severe male factor infertility.

There has been a vast improvement in the management of infertility in the last 20 years. The rational use of different drugs, surgery and newer IVF techniques holds the promise of a solution for many infertile couples. But for clinicians, it is also a challenge to deploy these new techniques safely and effectively. So adequate evaluation must be done before they are used in routine clinical practice.

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THREE COPIES of the manuscript should be sent in a heavy paper envelope. Manuscripts must accompany a covering letter signed by all authors. This must include (i) information on prior or duplicate publication or submission elsewhere of any part of the work as defined earlier in this document (ii) a statement of financial or other relationships that might lead to a conflict of interest (iii) a statement that the manuscript has been read and approved by all the authors, that the requirements for authorship have been met and (iv) the name, address, and telephone number of the corresponding author, who is responsible for communicating with the other authors about revisions and final approval of the proofs. The letter should give any additional information that may be helpful to the editor.

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Original Article

Effect of zinc supplementation on appetite, growth & body composition in children suffering from non-specific etiology of feeding refusal with failure to thrive

Shakur MS[1], Bano N[2], Malek MA[3], Kundu SK[4], Ahmed AU[5]

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Abstract

In order to evaluate effect of zinc supplementation on appetite, growth and body composition in children suffering from non specific etiology of poor feeding associated with failure to thrive (FTT), we conducted a double blind randomized control trial (RCT). Children between 36 to 72 months having weight for age between 60% to 89% of National Center for Health Statistics (NCHS) median and not gaining weight satisfactorily (weight gain less than 100gm in last 3 months) but developmentally normal and active child with no apparent significant acute or chronic medical or surgical disorders during last 3 months were included in the study. We initially assessed 100 such children. After fulfilling inclusion criteria, finally 40 children were allocated in RCT to receive supplementation with either oral zinc 20 mg/day mixed with multivitamin (Group A, n=20) or oral multivitamin only (Group B, n=20) for 21 days. Both the groups were comparable with respect to initial baseline characteristics including anthropometric, body composition and zinc status. Body composition was measured by using bioelectric Impedence analysis (BIA). Children assessed one month after initiation of intervention revealed significant number of children in group A developed improved appetite in comparison to group B (60% VS 15%, RR 8, 95% CI 1.75-36.48). Increase appetite was associated with significant increase in weight gain, in group A in comparison to group B (RR 9, 95% CI 1.64-49.41). Increase weight gain was associate with increased fat free body mass (FFBM) in majority of children in group A. No significant side effect were report in each group. However 50% children in group A, whose appetite increased with zinc supplement, developed reappearance of their poor appetite after completion of zinc supplement. It can be concluded from the study that oral zinc supplement can help in improving appetite associated with weight gain in children with poor feeding due to non-specific cause with FTT without any adverse effect on body composition.

Key words

Zinc, appetite, weight gain, body composition, children, Bangladesh.

Introduction

Zinc is a very essential micronutrient and has important role in child health and development. Zinc which is present in more than 100 metalloenzymes, has been among the essential micronutrients necessary for growth and prevention of infections. Zinc is essential for protein synthesis, including immunoglobulin and mediators of cell mediated immunity[1]. Zinc deficient children are vulnerable to infectious disease including pneumonia, even in anthropometrically well nourished children[2]. Children receiving supplemental zinc recovered earlier from acute and persistent diarrhoea than the control children[3,4]. Several studies have documented the effect of zinc supplementation on growth[5]. One interesting property of zinc is that it improves test equity[6]. One of the most frequent paediatric problem, mostly among children of middle and higher socioecomic class which concern parents and for which frequent paediatric consultations are sought both at hospital paediatric outpatient level and paediatric private surgery is feeding refusal with or without failure to thrive in otherwise developmentally normal, non sick and physically active children. Both parents and paediatricians not infrequently become frustrated as most of the times little can be done, to improve child's eating behavior. Zinc supplementations to such children are now practiced in Bangladesh by some health care providers on the basis of unpublished observation that it may improve appetite and weight gain to such children. However, there are concerns also among health care providers which include paediatrician in particular, whether zinc supplementation to such children adversely affects the child including adverse effect on body composition. However objective evidence of the effects of zinc supplementation on human appetite is woefully limited and to date no such published controlled study done in Indian subcontinent. We therefore undertook the study to test our hypothesis that zinc supplementation improve the appetite associated with weight gain in children suffering from nonspecific etiology of feeding refusal with failure to thrive without any significant harmful effect including adverse effect on body composition.

Subjects and methods

During a 12 months period, a double blind randomized controlled interventional study involving children between 36 months to 72 months with primary complaints by parents of poor appetite and not gaining weight more than 100 gm during last three months follow up but without any clinical evidence of significant acute or chronic medical or surgical problems currently or during last three months with developmentally normal and active children were included in the study. Severely undernourished and anthropometrically normal or over weight children were excluded from the study and weight for age between 60%-89% of NCHS were included in the study.

In all provisionally selected children blood was drawn for complete blood count and blood film study and urine were collected for routine test and culture. Routine investigation for stool was also done for ova, protozoa and cyst, for possible parasitic infestation. Children having haemoglobin more than 10 gm/dl with normochromic normocytic blood picture and no significant bacteriurea in urine culture, with no protozoa cyst and ova on routine stool examination were included in the study. Weight was measured by digital (Seca model 835, Todd scales UK) weight machine with graduation to 20 gm. Body composition was measured using BIA, which is reliable, valid, safe, noninvasive approach for rapid measurements human body composition[7]. It was performed in all two groups of children, before intervention and after the end of one month of study of children of zinc intervention group only whose weight increased significantly with improved appetite by portable bioelectric impedence analyzer (Body stat model 1500, Body stat Limited, Isle of Man, British Isles) using tetra polar electrode,

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placing two electrode in right lower limbs and two in upper right limbs. An electric impulse of 800 MA at 50 KHZ was then passed through the body of the child and reading of the resistant (electric impedence) was recorded[7]. A linear regression equation was used to calculate the total body water (TBW), FFBM or lean mass using age specific formulas and age specific constants of body density[8,9]. Fat mass (FM), percentage of fat mass and percentage of body solid were then calculated simply from percentage of FFBM and percentage of TBW respectively. Zinc was estimated by flame atromic absorption spectrophotometry. Serum and hair zinc was considered low if it was <100 microgram/dl and <150 microgram/gm respectively. Children were excluded from the study showing genuine intolerance to drugs which includes vomiting and noncompliance to take drugs for specified period. Children taking zinc supplement during last three months were also excluded from the study. Children's mothers were supplied with questionnaires, which included feeding behavior and possible side effects they have observed during supplementation of the drugs. Children were enrolled in the study after taking informed consent from their mother.

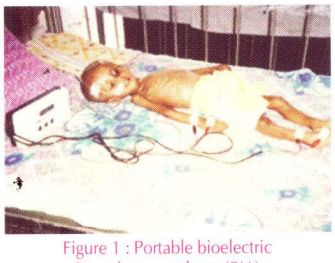

Figure 1 : Portable bioelectric impedence analyzer (BIA)

Eligible children were allotted to double blind randomized controlled trial to receive either oral zinc (Zn) supplement (20 mg/day, Group A) mixed with multivitamin syrup (Zn + MV) or multivitamin (MV) syrup (Group B) alone for 21 days. Simple randomization techniques were done using a computer programme. Medicines were supplied in bottles that were similar in size, shape and colours without any commercial label. Neither the patient nor the attending physician, appointed to the study knew which of the two drugs the patient received. The bottles were coded and only the principal investigator who was not directly involved in delivering drugs to patients knew which bottle contain which drug. Patients were followed up on 14th day, 21st day and at the end of one month of the study.

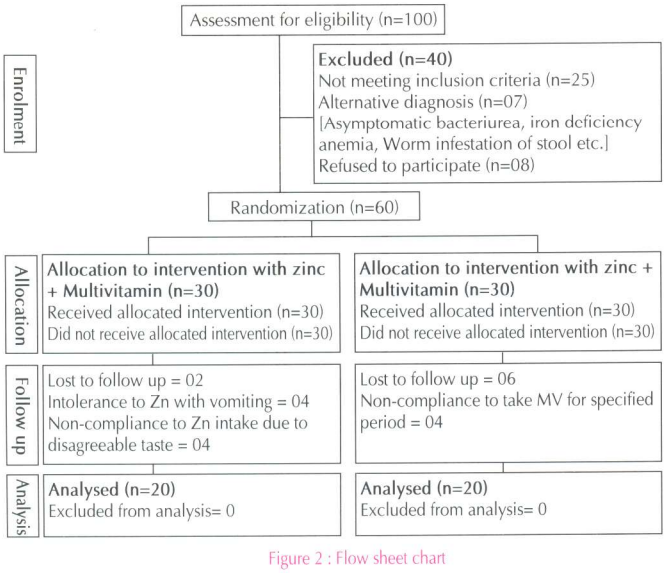

Figure 2 : Flow sheet chart

Patients appetite, adverse effects associated with drug intake and weight were assessed in each occasion. Body composition, serum & hair zinc status were assessed in all, finally analyzed children of both group A & B before intervention and at the end of one month of the study only to those children whose appetite improved associated with significant weight gain in group A only. Weight gain was considered significant if weight gain increased by more than 5% of body weight one month after the study. Strength of association (affect size) of improved appetite and weight gain associated with zinc supplement and precision of affect size were assessed by measuring risk ratio (RR) and 95% confidence interval (CI) of RR respectively. A RR was considered significant if 95% CI of RR did not include 1, excluding null hypothesis.

Results

Of 100 children assessed for eating disorder associated with failure to thrive, 40 children (Zn + MV=20, MV=20) completed the study (Fig 2). Baseline characteristics, anthropometric, BMI, body composition and serum and hair zinc in two groups were comparable (Table- 1, 2, 3, 4 & 5).

Table-1 : Sex distribution

Sex	Group- A (Zinc + MV)	Group-B (only MV)
Male	14	12
Female	6	8

Table-2 : Age distribution in months

Age	Group- A (n 20)	Group-B (n 20)
36-47	7	8
48-59	8	5
60-72	5	7

Table-3 : Anthropometric measurement

	Group- A	Group-B
Weight for age*	75.30 ± 6.25	78.50 ± 8.52
Height for age	90.47 ± 4.28	91.35 ± 3.78
Weight for height	85.42 ± 3.89	86.35 ± 3.48
Body mass index (BMI Wt kg/h^2 in meter	14.6 ± 1.70	14.8 ± 1.85 U

*% NCHS median

Table-4 : Initial zinc status

Group	Serum zinc (micro gm/dl)	Hair zinc (micro gm/gm)
A	141 ± 54.70	184 ± 48.60
B	152 ± 39.24	192 ± 82.54

Table-5 : Body composition & BMI

Group	% TBW	% FFBM	% FM	% Body solid	BMI	Impedance
A	60.83 ± 3.56	76.89 ± 8.29	23.10 ± 8.31	39.17 ± 3.38	14.06 ± 1.70	802 ± 141
B	62.22 ± 4.56	77.32 ± 7.31	22.68 ± 7.68	37.78 ± 4.42	15.8 ± 1.85	779 ± 132

Table-6 : Improved appetite evaluated after one month

Group	Yes	No
A	12 (60%)	8 (40%)
B	3 (15%)	18 (90%)

RR 8, 95% Ci 1.752, 36.48

Table-7 : Weight gain (>5% weight gain) after one month

Group	Yes	No
A	10 (50%)	10 (50%)
B	2 (10%)	18 (90%)

RR 9, 95% Ci 1.638, 49.41

According to mother's assessment in group A, improved appetite at the end of one month were found in group A (Zn+MV) in 12 (60%) children, of them 10 (50%) children achieved significant weight gain, in comparison to 3 children (15%) showing increased appetite of them 2(10%) children showing significant weight gain in group B (MV alone). This improvement of appetite and weight gain in children of group A were found statistically significantly in comparison to children of group B (Table 6 & 7).

Table-8 : Effect on body composition before & after zinc supplement of 10 children whose weight increased significantly associated with improved appetite with zinc supplement

Sl.	Age (Month)	Sex	Weight (kg)	BMI	TBW	% FFBS	% FAT	% IMP
1	50	M	14.50 15.20	15.4 16.2	60.30 63.72	79.40 83.16	20.60 16.84	967 695
2	61	M	15.00 16.50	13.9 15.3	59.62 63.71	76.83 82.10	23.17 17.90	869 733
3	48	M	14.50 16.00	13.4 14.8	55.38 56.2	71.37 72.40	28.62 27.60	974 862
4	46	M	12.50 13.50	13.6 14.7	61.4 65.28	79.00 84.14	21.00 15.86	871 752
5	57	M	12.80 14.10	14.2 15.1	58.41 59.20	73.80 76.00	26.20 24.00	892 780
6	68	M	18.00 19.20	14.4 15.1	54.19 59.45	68.8 75.49	31.2 24.51	940 780
7	55	M	14.50 15.80	15.4 16.2	60.83 53.78	79.04 70.20	20.60 29.80	**767** **798**
8	64	M	14.00 14.90	12.9 14.2	64.30 58.40	82.87 75.38	17.12 24.6	**863** **893**
9	66	M	15.20 16.00	14.3 15.1	58.92 62.32	76.92 81.36	23.10 18.63	851 760
10	41	M	12.80 14.00	14.2 15.00	57.50 59.62	73.81 76.53	26.19 23.47	892 780

Body composition of 10 children whose weight (Table-8) increased significantly by zinc supplement showed 8 (80%) children's weight gain were associated with increase of FFBM without increase in body fat. Serum zinc increased from initial 131±28.70 µg/dl to 184±45.20 µg/dl after zinc intervention while hair zinc before & after intervention was 178+42.24 µg/gm & 182±472.56 µg/gm in 10 children whose appetite increase with weight gain in zinc intervention group. No significant side effects were reported or observed of 12 children whose appetite increased. However, 6 out of 12 children mother, who showed improved appetite with zinc supplement for 21 days, reported reappearance of poor appetite of their children, when zinc supplement discontinued after 21 days.

Discussion

This pilot study revealed that zinc supplements improves appetite associated with weight gain significantly in children with nonspecific etiology of feeding refusal with failure to thrive, when compared with control children taking multivitamin only. Our study also found that increase appetite associated with weight gain do not adversely affect the body composition as evidenced by desirable increase in FFBM or lean body tissue without increase in undesirable increase in fat mass, in majority (80%) of children with weight gain. No significant side effects were observed during 21 days ingestion of zinc supplement. However mother of half of their children whose appetite improved, reported that eating disorder reappeared, when zinc supplement was discontinued after 21 days and weight gain was in their opinion was possibly due to increased appetite during the 21 days supplement of zinc. Beneficial effect of zinc in children in childhood diarrhea is well-established and routinely ed in Bangladesh as recommended by WHO. However zinc supplement is also occasionaly used by some medical practitioners in Bangladesh with unpublished observation that it improves poor appetite in children which is frequently the primary complaint by parents for which medical consultations are sought in private medical practice in particular. We realize that the relationship of improved appetite associated with weight gain by zinc supplementation remains controversial and its use in such condition is a matter of concern to some medical practitioners. Objective evidence of the effect of zinc supplementation on human appetite is however limited at this time. A milder form of zinc deficiency with slight growth retardation, poor appetite with impaired taste acuity was discovered in children of middle and upper income family, in Denever, Colorado, USA who were presumed to be in good nutritional status, whose taste acuity and anorexia hypogausia and pica improved with zinc supplement[10]. Krebs MF et al also observed increased food intake of young children receiving zinc supplement[11]. Anorexia, pica and poor growth in Chinese preschool children were associated with zinc deficiency in Beijing, China, which were corrected by zinc supplement[12]. Although unpublished observations by many health service providers in Bangladesh have demonstrated an increase appetite associated with weight gain with zinc supplement in children suffering from anorexia there is no published study in such condition. The study is unique in the sense that very few published studies done elsewhere on effect of zinc supplement on anorexia in human body were not placebo or case controlled and were not double or single blinded and no study demonstrated the effect of zinc on body composition in such conditions. An interesting finding of our study was that our study cases were not initially biochemically hypozincaemic, although weight gain and improvement of anorexia by zinc supplementation were associated with increase in serum zinc level. This is in disagreement with studies done elsewhere where anorexia were associated with low serum zinc level (serum zinc <100 µg/dl), which improved with zinc supplementation[10,12]. This finding can be explained by the fact, that since there is no single assay of zinc that can confidently and comprehensively assess zinc status of human body and there is no single reference range of normal serum zinc level, it is now widely recognized that the best way to demonstrate zinc deficiency is to observe clinical response with specific conditions with appropriate control[13,14]. Change in eating behavior found in our study with zinc supplement is useful in this regard just as growth response is observed with zinc supplement[13]. The beneficial effect of zinc supplement may be due to correction of latent zinc deficiency or direct stimulant effect of zinc on taste acuity or both, which may be analogous to immunostimulant effect of zinc supplement independent of zinc depletion[1,15]. Golden MHN et all found weight gain of zinc supplemented children associated with formation of lean tissue instead of adipose tissue[16]. This was consistent with our study where we found majority of our children weight gain was associated with increase in FFMS instead of fat mass. Two children weight gain associated with fat mass could be due to direct effect of increased appetite without any influence of zinc on body composition.

Zinc has physiological role in normal taste sensation and improves taste aquity[10]. Moreover many cases of zinc deficient and idiopathic hypogeusia have been corrected by zinc supplementation in adults[17]. Our study however revealed that 50% of children whose eating disorder improved with zinc supplement stopped feeding well when zinc supplement discontinues, which indicates short term benefit and high relapse rate of eating disorder in 50% children who responded well with Zn supplement for 21 days. This can be explained by the fact, that beneficial effect of zinc can be observed best in the presence of preexisting low serum zinc level[18,19]. Our study populations were not biochemically hypozincaemic initially. Pretreatment hypozincaemic status if found in our study could have more durable and beneficial effect on eating disorders. Instead of 21 days of zinc supplement, more prolonged course (3 to 6 months) of zinc supplement or zinc fortified food, may have long lasting effect as found by Chinese study[12]. No significant side effects were reported during 21 days zinc supplement of children who were finally analyzed. However 4 children showed intolerance

to zinc supplement with vomiting, who were excluded from final analysis. Our study has the weakness in the fact that sample size of study population was small. The result of our study once confirmed by the ongoing adequately powered placebo controlled multicentre studies, will raise the important question whether public health measures should be taken to improve appetite and growth in growth retarded eating disorder children, in the absence of acute or chronic medical or surgical illness.

Conclusion

From the study result we conclude, that zinc supplementation improves appetite and weight in significant number of children with poor appetite and growth failure due to nonspecific cause, even though they are biochemically not hypozincaemic without any adverse effect including adverse effect on body composition, which is consistent with our hypothesis that zinc supplement improves poor appetite associated with failure to thrive. However this beneficial effect was brief in half of the children, whose eating disorder reappeared when zinc supplement was discontinued. It is worth while giving a trial of zinc supplementation in children with eating disorders in the absence of any other nutritional deficiency or illness. However it was a pilot study and therefore further adequately powered multicentered randomized control trials are needed in order to validate our findings.

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Original Article

Effects of nutrition education on nutritional knowledge of the respondent mothers and STP of their hospitalised children

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Abstract

Malnutrition is a very common problem among under 5 children in Bangladesh. Though poverty plays the major role but lack of knowledge about proper utilization of available foods, superstitious beliefs and some social customs also contribute a lot to develop malnutrition among children. Mothers of 114 hospitalized under 5 malnourished children were taken for study purpose that was equally divided as case and control. Baseline knowledge of the mothers was tested by a standard questionnaire. After giving nutrition education, their knowledge was tested immediately and again after six months. About common foods, 37.5% of case group responded correctly initially but after six months it was 73%, where as 32% of control group initially responded correctly and after six months it was 36%. When considering knowledge of balanced diet, 44% of case group responded correctly and after six months it is increased to 71%, whereas in control group initially it was 52% and after six months it became 54%. Regarding false belief and food misconception, correct answers were given initially by 49% of case group and it went up to 66% after six months. But in the control group the corresponding rise was only 4%. Regarding cooking practices and wastage of food, initially 55% of the case group had answered correctly and after six months it rose to 78%. But 55% of the control group initially responded correctly and after six months it was 59%. Regarding Knowledge about iodized salt, 25% of the case group responded correctly initially and after six months it was 46%, whereas in control group it was initially 28% which increased to 32% after six months. Regarding knowledge about iodized salt, 25% of the case group responded correctly initially and after six months it was 46%, where as in control group it was initially 28% which increased to 32% after six months. Regarding deficiency diseases and their preventions, initially 49% of the case group responded correctly and after six months it rose to 88%, where as the result of control group initially was about 48% and after six months it was 51%. All of these findings indicated the impact of nutrition education which lead to improvements of knowledge among mothers of hospitalized under 5 children.

Introduction

With low resource base and almost perennial recurrence of natural calamities, Bangladesh is one of the most poor and densely populated countries of the world. Its population has now far exceeded the carrying capacity. Nutritional deficiencies constitute the major causes of morbidity and mortality among the children of Bangladesh. Bangladesh is a country of 123.1[1] million people of which about 40% is under 18 & about 14.5% is under- 5[2]. Here Infant mortality rate is 55/1000[3] and under-5 mortality rate is 77/1000[2] which are still far above the level of the developed countries. Current data taken from Bangladesh Bureau of statistics suggests that about 87.40% children is suffering from some sort of malnutrition and about 37.6% is suffering from moderate to severe malnutrition[4]. About 21.7% preschool children is suffering from sub clinical vitamin A deficiency and about 0.94% is suffering from xerothalmia[5]. About 17.2% children from aged 5 to 11 years is suffering from thyroid hormone deficiency[6]. Thyroid deficiency is one preventable cause of mental retardation and disability.

About 69.5% children aged from 0 to 4 yrs of Bangladesh is suffering from anaemia[3]. A child, who suffers from anaemia, may also suffer from many infectious diseases due to lowered body resistance. Anaemia is also a factor for contributing poor school performance of the children. "The dominant effect is loss associated with cognitive deficits in children[7]."

Each year about 13 million infant and children die in the developing countries. The majority of these deaths are due to infectious and parasite diseases and many if not most of the children die malnourished[8].

A malnourished child is great sufferer for himself and his parent. He or she will not grow properly both physically and mentally. When he or she will grow adult with these physical and mental handicaps, no way he would be able to perform optimum work for himself, his family and nation. So it has a long term impact on health and economic issue of a nation.

Etiology of malnutrition is complex. Primarily due to deficiencies and secondary due to medical reasons. Dietary deficiency may be due to poor economic condition i.e., parents cannot bye adequate food for their family due to poverty. Other reasons for dietary deficiencies are social and cultural factors due to lack of proper knowledge of mother about balanced diet, advantage of breast feeding and extra need for developing children the problem of malnutrition has further deteriorated in our country. Many deep rooted false beliefs customs, practices and ignorance are contributing significantly to malnutrition among the children of our country.

Methods and materials

Study Location: was Dhaka Shishu (children) Hospital and study population was mothers of hospitalized children (< 5 years).

Study design: The investigation was a case-control intervention study.

Study parameters: The parameters taken to assess the nutritional status of the studied children were-

1. Socio-economic information
2. Conduct of nutrition education sessions
3. Concentration of serum total protein

Nutrition education sessions: Mothers were exposed to nutrition education on following topics-

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a) Common easily available nutritious food
b) Balanced diet
c) Appropriate cooking process and avoidance of wastage of food
d) Superstitious beliefs and misconceptions about food
e) Necessities of iodized salts
f) Breast feeding, weaning and extra food for growing children to promote their proper growth and
g) Malnutrition related diseases, infectious diseases and adoption of preventive measures.

Mothers were taught sometimes in groups and sometimes at individual level within a period of one week. Materials used were posters, booklets pictures and models. Immediately after nutrition education session and again after six months, the nutritional knowledge of the respondents was evaluated. The socio-economic, knowledge, attitude and practice (KAP) regarding nutritional aspects were compared among the two groups (case-control).

Results

Table-1: Distribution of mothers by age

Age (year)	Number	Percent
< 20	5	4.4
20-24	36	31.6
25-29	40	35.1
30 & above	33	28.9
Total	114	100.0

Table-1 showed that around 65% of the total mothers were within the age range of 20-30 years of age and 30% of the total mothers are within the age range of 30 years and above. This table also showed that the average age of the mothers was about 27 years.

Table-2: Distribution of mothers by occupation

Occupation	Number	Percent
Housewife	90	78.9
Garments worker	10	8.8
Employee N.G.O, G.O	14	12.3
Total	114	100.0

Table-2 shows that among the mothers, 80% of them were homemakers, 10% of them were garment workers and the rest of them were NGO workers.

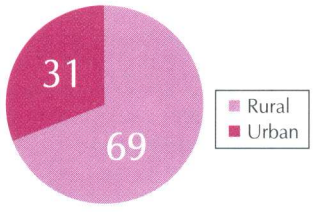

Figure 1: Distribution of mothers by residence

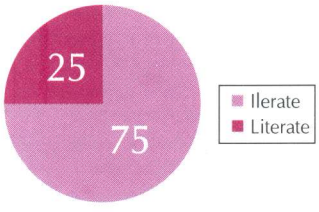

Figure 2 : Distribution of mothers by literacy

Figure 1, 2 show that about 69% of the total mothers lived in rural areas and the rest 31% lived in urban areas. From the study it was also found that around 25% mothers of total respondents were literate and the rest 75% were illiterate.

Table-3: Distribution of mothers by monthly income of households

Income (Taka monthly)	Number	Percent
< 4000	15	13.2
4000-5999	48	42.1
6000-7999	30	26.3
8000 & above	21	18.4
Total	114	100.0

Table-3 shows that 42% of the total households had income within the range 4000-5999 taka per month whereas 26% of them had income range 6000-7999 taka. From the table it was also seen that 19% of the total households have income of TK. 8000 & above and only 13% of them had income TK<4000.

Table-4: Distribution of respondents by knowledge

Topics	Case			Control	
	Baseline	Immediate after education	After six months	Baseline	After six months
Correct knowledge about common foods	37.5%	82%	73%	32%	36%
Answered correctly regarding knowledge about balanced diet	44%	85%	71%	52%	54%
Answered correctly regarding knowledge about food misconceptions	49%	78%	66%	52%	56%
Answered correctly regarding knowledge about cooking process & wastage of food	55%	96%	78%	55%	59%
Correct knowledge of testing iodine in salt	25%	67%	46%	28%	32%
Answered correctly regarding knowledge about deficiency diseases, infectious diseases & their preventions	49%	90%	88%	40%	51%

Table-4 shows that nutrition education increases the knowledge of case group mothers about common foods, balanced diet, food misconceptions, cooking process & wastage of food, testing iodine in salt, deficiency diseases, infectious diseases & their preventions.

Table-5: Nutritional status by Serum Total Protein (STP) of the study children

Age (Month)	Case (n=45)				Control (n=43)			
	Pre nutrition education		Post nutrition education		Base line		After six months	
	STP ≤ 62	STP > 62	STP ≤ 62	STP > 62	STP ≤62	STP > 62	STP ≤ 62	STP > 62
Age ≤ 5	2.22%	42.5%	-	44.46%	6.96%	39.54%	6.96%	39.54%
6-24	2.22%	28.6%	2.2%	28.87%	4.64%	34.86%	-	39.50%
25-59	2.22%	22.5%	-	24.44%	2.32%	11.68%	2.32%	11.68%
Total	6.66%	93.34%	2.2%	97.78%	13.92%	86.08%	9.28%	90.72%

Table-5 shows that among case group children (n=45) 6.6% of the children were STP≤62 before nutrition education was given and after 6 months of nutrition education was given it decreased to 2.2%. On the other hand, among control group children (n=43), initially 13.9% of the children were STP≤62 and after 6 months it decreased to 9%.

Discussion

Table-1 showed that around 65% of the total mothers were

within the age range of 20-30 years of age and 30% of the total mothers are within the age range of 30 years and above. This table also showed that the average age of the mothers was about 27 years. Among the mothers, 80% of them were homemakers, 10% of them were garment workers and the rest of them were NGO workers (Table-2).

About 69% of the total mothers lived in rural areas and the rest 31% lived in urban areas. From the study it was also found that around 25% mothers of total respondents were literate and the rest 75% were illiterate (Figure 1,2).

Table 3 showed that 42% of the total households had income within the range 4000-5999 taka per month whereas 26% of them had income range 6000-7999 taka. From the table it was also seen that 19% of the total households have income of TK. 8000 & above and only 13% of them had income TK<4000.

Among case groups 38% mothers had correct knowledge about common foods before nutrition education whereas 82% mothers immediately after education & 73% mothers after 6 months of education give correct answers about common foods. On the other hand about 32% mothers of control group (not exposed to nutrition education) had correct knowledge about common foods which was increased to 36% after 6 months which indicated that as no nutrition education was given to control group mothers, there was no marked improvement in knowledge about common foods. Thus it could be said that nutrition education had positive effect to increase the knowledge of case group mothers about common foods (Table-4).

Before nutrition education only 44% of the respondents of case group had correct knowledge about balanced diet while immediately after education it was moved to 85% and after 6 months of education it was 71% whereas about 52% of the respondents of control group (not exposed to nutrition education) had correct knowledge about balanced diet which was increased to 54% after 6 months. Therefore it can be inferred that nutrition education had positive role to increase the knowledge about balanced died (Table-4).

The study showed that only 49% of the respondents of case group answered correctly regarding KAP about food misconceptions before nutrition education while 78% of the respondents immediately after education and 66% of the respondents after 6 months of education answered correctly regarding KAP about food misconceptions but only 52% of the respondents of control groups initially and 56% of the respondents after 6 months answered correctly regarding KAP about food misconceptions. It was found that only 55% of the respondents of case group answered correctly regarding KAP about cooking process & wastage of food before nutrition education while 96% of the respondents immediately after education and 78% of the respondents after 6 months of education answered correctly regarding KAP about cooking process & wastage of food, on the other hand 55% of the respondents of control groups initially and 59% of the respondents after 6 months answered correctly regarding KAP about cooking process & wastage of food (Table-4).

Only 25% of the respondents of case group had correct knowledge of testing iodine in salt while 67% of the respondents immediate after education and 46 % of the respondents after 6 months of education had correct knowledge of testing iodine in salt but in case of control group only 28% of the respondents initially and 32% of the respondents after 6 months had correct knowledge of testing iodine in salt (Table-4).

The study stated that only 49% of the respondents of case groups answered correctly regarding KAP about deficiency diseases, infectious diseases & their preventions before nutrition education while 90% of the respondents immediately after education and 88% of the respondents after 6 months of education answered correctly regarding KAP about deficiency diseases, infectious diseases & their prevention whereas only 48% of the respondents of control groups initially and 51% of the respondents after 6 months answered correctly regarding KAP about deficiency diseases, infectious diseases & their prevention (Table-4).

Table-5 shows that among case group children (n=45) 6.6% of the children were STP≤62 before nutrition education was given and after 6 months of nutrition education was given it decreased to 2.2%. On the other hand, among control group children (n=43), initially 13.9% of the children were STP≤62 and after 6 months it decreased to 9%.

From the above discussion we find that nutrition education helped to improve the knowledge of case group mothers than that of the control group counterparts.

Conclusion

Nutrition education session helps a lot to improve the overall nutritional status of the children. It helps the mothers of the children to utilize the available food properly. Education group mothers showed significantly higher nutrition knowledge and better infant feeding practices than that of control group counterparts. From biochemical information it is seen that nutrition education reduces the rate of anaemia in the children of case groups. It also increases the knowledge of the mothers who exposed nutrition education session about type of food responsible for body growth and development. Nutrition education session also increases the knowledge of testing Iodine in salt of case group.

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Determination of MIC and MBC of selected azithromycin capsule commercially available in Bangladesh

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Abstract

Usually we consider that the azithromycin capsules in Bangladesh maintain standard MIC and MBC. But how much is this assumption is true; this will be evaluated through this research work. This is a cross sectional study to determine the minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) of selected azithromycin capsule. The collected samples were analyzed according to USP specifications[1]. The MICs of azithromycin were determined by broth dilution method. MBCs were determined by the drop plate method from the tubes, where apparently no visible growth found. This study showed that MIC & MBC values of azithromycin capsule found highest against *Pseudomonas* spp., *Shigella* spp. and *E. coli* were > 64.0 µg/ml (micro gram per milliliter) and lowest against *B. pumillus* was 1.0/2.0 µg/ml. MIC and MBC values higher than that of the peak serum concentration of azithromycin must have chance of therapeutic failure and development of azithromycin tolerance and resistance to the bacteria tested.

Introduction

To evaluate the efficiency of antibiotic there are two factors[2]. which influence potential utility of a antibiotics in a specific clinical situation. The first is the measure of potency of the antibiotic for the pathogen in question minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC). The second is relationship between the concentration time profile and potency of the antibiotics. This research work will play an important role to determine the MIC and MBC of selected azithromycin capsule in Bangladesh.

Materials and methods

Collection of sample: The azithromycin capsule collected from the retail seller and standard sample collected from a pharmaceutical company in the Dhaka city.

Collection of organisms: Pseudomonas spp., *Staphylococcus aureus, Shigella* spp. and *E. coli* collected from the patient sample of Dhaka Medical College Hospital and *Bacillus pumillus* from Microbiology department, University of Dhaka.

Reagents

1. pH 6 sodium phosphate buffer
2. Hydrochloric acid
3. Trypcin
4. Sterile water etc.

Media

1. Mueller Hinton Broth (MHB)
2. Mueller Hinton Agar (MHA)
3. Nutrient Agar (NA)
4. Mennitol Salt Agar (MSA)
5. Cetrimite Agar (CA)
6. Blood Agar (BA)

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Instruments and apparatus

1. Sterile 5 ml screw cap test tubes
2. 250 ml conical flask
3. 250 ml measuring cylinder
4. Inoculating loop
5. 1 ml and 0.1 ml micro pipette
6. 10 ml glass pipette
7. Beaker
8. Marker
9. Bunsen burner
10. Small and large (7" x 7") petri plate
11. Borer
12. Voltex mixture machine (FISONS-11777)
13. Shaking or rotator machine (FISONS-200)
14. Electrical digital balance (AJ 150 L)
15. Spatula
16. pH meter (HANNA)
17. Laminar air flow (C-901)
18. Incubator adjuster at 37°C. (SLI-600)
19. Spectrophtometer (Spectronic-20)
20. Freeze (MDF-U20806)
21. Micropepatte (GILSON)
22. Autoclave (HA-240M)

Preparation of azithromycin solution[5]

128 mg equivalent 305x128÷250= 156.16 mg azithromycin dihydrate capsule was dissolve in 1000 ml pH 6 sodium phosphate buffer prepare 100 ml of 0.1M dibasic sodium phosphate adjust with hydrochloric acid to pH 6 and at 0.10 mg trypcin and mix. rotated at the rate of 100 rpm for 45 minute at room temperature[1].

MIC and MBC determination procedure

Culture: Overnight Mueller Hinton broth cultures of *Staphylococcus aureus, E. coli, Bacillus pumillus, Shigella* spp. and *Pseudomonus* spp. at 37°C were prepared. The culture was adjusted to obtain turbidity comparable to that of the turbidity of MC, Farland 0.5 standard[3]. and then further diluted 1: 200 in Mueller Hinton broth. The inoculums thus prepared expected to obtain 105 to 106 C.F.U/ml.

Procedure[4]

1. An appropriate amount (0.128 g antibiotic plus 1000 ml respective solvent) of azithromycin capsule was dissolved in respective solvent to prepare an antibiotic solution containing 128 µg/ml.

2. Two fold dilutions of the antibiotic solution in Mueller Hinton broth were prepared and describe below:

(a) Ten sterile tubes were placed in a rack and were labeled each 1 through 8 and first one labeled as antibiotic control) and last one was labeled as G.C (growth control).
(b) 1 ml of Mueller Hinton broth was added in each test tube.
(c) 1 ml of antibiotic solution was added to test tube no 1 and A.C.
(d) With a sterile micropipette and tips, after adequate mixture 1 ml was transferred from tube no. 1 to tube no. 2.
(e) After a through mixing, 1 ml was transferred with a separate micro pipette from tube no 2 to tube no 3.

(f) This procedure was repeated through the next-to-next up to the tube no. 8. Except tube no G.C. (using fresh pipette for each dilution). From tube no 8 1 ml was removed and discarded. The last tube (tube G.C) received no antimicrobial agent and was served as a growth control. First A.C labeled test tube was served as a antibiotic control.

3. Each tube was inoculated (including the growth control except antibiotic control) with 1 ml of the culture of respective organism. The final concentration of antimicrobial agent in this test tube was half of the initial dilution series because of the addition of an equal concentration of inoculums in Mueller Hinton broth.

4. The tubes were incubated at 37°C for 24 hours.

5. The tubes were examined for growth and were determined the MIC of tested antibiotics, which is bacteriostatic for the test organism. The tubes were examined for visible growth (cloudy) and was recorded growth as (+) and no growth as (-).

6. For determination of MBC, the concentration which was bactericidal, was then found by sub cultured the contents of selective tubes into a series of Mueller Hinton broth, which did not contain any antibiotic and started from last two non-visible tube to the lst two visible tube (direction tube no. 1 to tube no. 8). Then was inoculated into Mueller Hinton agar containing Petri plate by 0.1 sterile micropipette and separate 0.1 ml sterile tips in drop method.

7. The plates were incubated at 37°C for 24 hours.

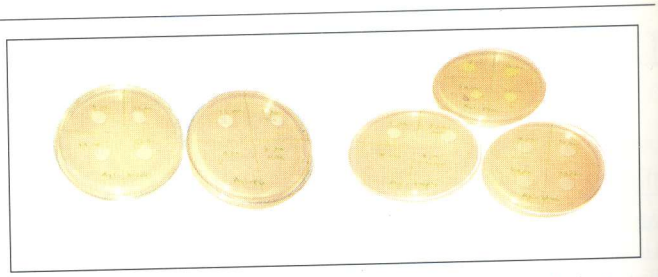
Tube No.	A.C	1	2	3	4	5	6	7	8	G.C
i) Mueller Hinton broth 1ml	1	1	1	1	1	1	1	1	1	1
ii) Antibiotic solution 1 ml	1	1	1	1	1	1	1	1	1	0
iii) Initial antibiotic concentration µg/ml	128	128	64	32	16	8	4	2	1	0
iv) Bacterial suspension 1 ml	0	1	1	1	1	1	1	1	1	0
v) Final Volume 2 ml	2	2	2	2	2	2	2	2	2	2
vi) Final antibiotic concentration µg/ml	64	64	32	16	8	4	2	1	0.5	0

A.C = Antibiotic Control, G.C = Growth Control

Table 1: MIC & MBC values of antibiotics tested against five organisms

Antibiotics tested	Test organisms MIC / MBC in µg/ml				
	Bacillus pumillus	*Pseudomonus* spp.	*Staphylococcus aureus*	*Shigella* spp.	*E. coli* spp.
Tetracycline	1.0 /2.0	8.0 / 16.0	0.5 / 1.0	1.0 / 2.0	> 64.0
Cephradine	1.0 /2.0	8.0 / 16.0	0.5 / 1.0	4.0 / 8.0	> 64.0
Cefixime	1.0 /2.0	> 64.0	1.0 / 2.0	2.0 / 4.0	> 64.0
Azithromycin	1.0 / 2.0	> 64.0	2.0 / 4.0	> 64.0	> 64.0
Ciprofloxacin	4.0 / 8.0	2.0 / 4.0	8.0 / 16.0	1.0 / 2.0	> 64.0

Photograph represents that the MIC of azithromycin against *Bacillus pumillus* spp. and *E. Coli* spp. was found 1µg/ml and resistant to azithromycin respectively



Photograph represented that the MBC values of azithromycin against *Bacillus pumillus, Staplylococcus aureus* was found 2 µg/ml, 4 µg/ml and *Shigella* spp., *Pseudomonas* spp., *E. coli* spp. were found resistant to cefixime

Discussion

The aim of this research work was to evaluate the MIC and MBC of azithromycin capsule commercially available in Bangladesh. This study showed some important findings like higher MIC values of antibiotics tested. The study informs the doctors communities the important information about the the MIC and MBC of condition of the antibiotics.

Table-1 showed that MIC and MBC values of azithromycin capsule found highest against *Pseudomonas* spp. and *E. coli* was > 64.0 µg/ml and lowest against *B. pumillus* was 1 µg/ml. According to Table-1 MIC values of antibiotics tested against *Staphylococcus aureus* were 0.5 µg/ml to 8.0 µg/ml. Nadia (2005)[5] showed that the MIC range of tetracycline, ciprofloxacin and azithromycin for same organism were 0.12 µg/ml to 32.0 µg/ml. Significant variation of MIC values seen in this study.

Limitation of the research works

The MIC and MBC values of selected azithromycin capsule evaluated in this study. Because of shortage of fund and Minimum research work result available regarding the MIC & MBC values of azithromycin in Bangladesh. For this reason it was difficult to obtain required amount of information for conducting this study. Even with all limitations, the research work provides useful information about the MIC and MBC values of selected azithromycin in Bangladesh.

Recommendation

To provide standard potent antibiotics in Bangladesh, suggestion and recommendations are as follows:

1. A complete study on biopotency of all antibiotics are essential.
2. A modern antibiotics testing laboratory have to be established.
3. Regular monitoring of the quality of antibiotics are essential.
4. Awareness must be created by using mass media about use and misuse of Antibiotics.

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Carotid angioplasty and stenting, an alternative to carotid endarterectomy

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Introduction

Carotid angioplasty stenting (CAS) was introduced as an option for treatment of carotid artery disease in early 90's. Purpose of this article to review the evolution of treatment of carotid artery disease and present day application of CAS.

Discussion

CAS is successful in 95-98% of the cases. Peri-procedure (30 days) and short term (4 years) stroke, myocardial complication, death and survival rates are comparable to Carotid Endarterectomy (CEA) in high risk patients. However results of CAS in all patients population and long term outcome yet to be determined. Stroke continues to be third leading cause of death in United States and is amongst top five major cause of death around the world. 50-60% of all strokes are because of extra cranial carotid artery disease and 40-50% of cerebral infract are from carotid bifurcation disease. Since early 70's extensive retrospective analysis as well as rigorous prospective randomized studies been done worldwide regarding carotid endarterectomy and been proven to be not only effective treatment for symptomatic carotid artery disease but also established the fact that carotid endarterectomy results in 50% reduction of stroke in asymptomatic carotid artery disease with >60% stenosis, especially in male. First surgical procedure for extracranial carotid disease was reported by Eastcott, Pickering and Rob in 1954 for hemispheric transient ischemic attack. The initial proposed surgical approach for relief of cerebral dysfunction and prevention of stroke was the excision of the lesion in extra cranial carotid artery. Surgical approach for extracranial carotid artery has evolved and matured to carotid endarterectomy (CEA). CEA is one of the most rewarding and technically satisfying procedure in vascular surgery. CEA has fulfilled the objective of minimizing the operative complications and maximizing the benefit for large group of population with carotid artery disease. CEA has achieved average combined morbidity and mortality of 1-4% for both symptomatic as well as asymptomatic carotid disease. The experience of the institution and operating surgeon, directly influences the rate of morbidity and mortality.

Complications of the procedure can be subgrouped into:

Operative or immediate

1. Acute bleeding
2. Intraoperative embolization resulting stroke
3. Intraoperative nerve injury- vagus, hypoglossal, recurrent and superior laryngeal, sympathetic chain and phrenic nerve
4. Thoracic duct injury

Delayed

1. Hematoma neck causing respiratory compromise
2. Intracranial bleed secondary to reperfusion injury
3. Recurrent stenosis
4. Cardiac and respiratory complication

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With tremendous improvement of technology and advancement of techniques of endovascular procedures during last few decades, carotid angioplasty and stenting (CAS) was introduced in early 90's for the management of carotid artery disease. Objective of this approach is to minimize the morbidity and mortality even less than carotid endarterectomy, if not at least match comparatively with CEA. If the procedure is deemed technically successful and clinically efficacious, it would even be applicable for the group of patients who otherwise are of significant high risk for CEA. Since CAS is considerably less invasive than CEA, pioneers of the procedure expected and promoted the procedure as good as CEA, perhaps would be superior in terms of morbidity and mortality. In fact initial anecdotal reports suggested CAS has significantly lower rate of stroke and cardiac complications as compared to CEA. During the last decade with wider acceptance of the procedure around the world and across various specialty, CAS has established its clinical applications and as an option for the management of carotid artery disease. There are numerous single and multi centers published reports regarding technical success and clinical outcome of CAS. Over all CAS is successful in 95-98% of the cases. Failure to complete the procedure is primarily because of anatomical configuration of aortic arch and tortuous carotid artery, henceforth, failure to maintain the access for deployment of embolic protection device, advancement of balloon catheter and placement of stent. Multiple published series reported 30 days morbidity and mortality (TIA's, Stroke, MI and Death) rate ranges from 1.29-4.9% in CAS for symptomatic and asymptomatic carotid disease. Comparatively CEA morbidity and mortality (TIA's, stroke, MI and death) rate ranges from 1.0-2.6% in symptomatic and asymptomatic carotid artery disease in same reported series. However the difference is statistically non significant. No significant difference was shown in longterm outcome ie stroke, death rate and recurrent stenosis in 4 years between patients who underwent CAS and those who underwent CEA, irrespective of low or increased surgical risk patients, symptomatic or asymptomatic carotid artery disease.

Deployment of embolic protection device (EPD) has become a standard for CAS. The embolic protection devices that are available for use:

A. Distal occlusion device: (PercuSurge GuardWire) has a low profile occlusion balloon at the tip of guide wire. The guide wire is advanced across the lesion then balloon is inflated distally. The occluding balloon diameter ranging from 3-6 mm, provides distal embolic protection. After completion of angioplasty and stenting of carotid artery, an aspiration catheter is advanced over the guide wire up to the occluding balloon. The debris collected against the occluding balloon is aspirated. Subsequently flow is restored by deflating the balloon. The occluding balloon itself can cause distal ischemia, depending on the occlusion time as well as patient condition, particularly the collateral circulation. The device preparation is some what cumbersome and also cause significant limitation of adequate angiographic visualization of carotid artery while balloon is inflated, thus making assessment of the artery and placement of stent more difficult.

B. Filters: (Accunet, AngioGuard, MedNova NeuroShield,

FilterWire EX and SipderWire) Filters are made of thin porous polymeric membrane capable of trapping embolic debris as small as 80 micromillimeter, supported by fine Nitonol metal skeleton of various configurations with diameter ranging 4-10mm. After crossing the lesion and reaching he distal internal carotid artery the filter is deployed, preferably in straight segment of distal internal carotid artery. During manipulation of balloon and stent the embolic debris is captured in the filter and at the end of the procedure the filter is collapsed into a retrieving catheter and the entire device is withdrawn with entrapped embolic debris. Filter devices are easy to prepare for deployment, has good visibility during the procedure. Unlike occlusion devices, the angiographic visualization of the lesion and stent is much easier with filter device since antegrade flow in the carotid artery is maintained. All of the filter device has nice crossing profile. However filter potentially can cause intimal damage at the site of deployment due to the vigorous movement of it during the procedure. Some of the filter can be potentially difficult in crossing the deployed stent during filter withdrawal because of fairly stiff retrieval pod and tortuous carotid artery.

C. Proximal suction device: (Parodi Anti-Embolic System, MO. MA) These are guiding catheter with a balloon at the distal end of the catheter. After the guiding catheter tip is advaced in common carotid artery proximal to the carotid targeted lesion, the balloon is inflated. External carotid artery is also occluded with a second balloon to cease reversal flow into internal carotid artery. Complete reversal flow is established in internal carotid artery with a mechanical device attached to guiding catheter. Suctioned blood volume is then infused back through a venous port. This technique allows protection before the lesion is manipulated and the risk of embolization is practically eliminated. The devices are bulky, there is potential for damage at the balloon inflation site and some time becomes difficult to advance the device to the desired site, importantly because of tortuous artery.

Several series has reported significant reduction of TIA'S and stroke rate with the use of EPD, however there is no prospective and randomized studies yet to show the use of EPD has significantly reduced the rate of TIA'S and stroke with CAS procedure. One comparative study indicated use of EPD resulted higher incidence of lesions on magnetic weighted lesions as compared to CAS without EPD. These lesions however were not clinically significant to cause any cerebral ischemic events. Increased MRI lesions were felt to be secondary to extra manipulation necessary to advance EPD across the carotid artery stenosis.

At present in United States CAS is approved for certain clinical scenario with significant carotid artery disease:

A. Patients with high risk for CEA and has symptomatic carotid stenosis >50%
B. Patients with high risk for CEA and has asymptomatic carotid stenosis >80%

Clinical conditions that qualify the patients as high surgical risk are:

1. Age at or above 80 years
2. Clinical significant cardiac diseases (CHF, NYHA class III or IV, Unstable angina & need for CABG, Recent myocardial infarction and ejection fraction <30%)
3. High grade recurrent carotid stenosis
4. High cervical carotid artery lesion
5. Contra lateral carotid artery occlusion
6. End stage renal failure
7. Severe chronic obstructive pulmonary disease
8. History of tracheostomy
9. Contra lateral laryngeal nerve palsy
10. History of previous neck radiation

CAS is increasingly performed because of presumed benefits of reducing peri-procedure complications and decreasing the hospital stay. At present CAS is at best non inferior to CEA in terms of clinical outcome and hospital stay. Procedural cost of CAS is significantly higher than those with CEA, mainly as result of high material (guide wire, catheters, balloon, stent and EPD device) cost.

Conclusion

CAS can be successfully performed in 95-98% of the cases and is accepted as an alternative option of treatment for carotid artery disease, especially in high risk surgical patients. Efficacy and outcome of CAS is comparable to CEA in high risk patients. CAS has not been proven yet as an option in low risk surgical patients with carotid artery disease. Long term results of CAS are yet to be determined especially since procedure is been widely accepted as an alternative to CEA only for few years. However multiple CAS studies are ongoing and are in various stage of study to assess the long term efficacy and the results.

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Managing postoperative pain

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Introduction

Despite recent advances in our knowledge of "multimodal" analgesics therapies for pain relief[1,2,3] many patients undergoing surgery continue to experience unacceptable levels of pain after their surgeries as postoperative pain is a complex and multi-factorial symptom which requires a considerate approach using a variety of treatment modalities to obtain optimal outcomes with respect to patient comfort and facilitating the recovery process. The approach to preventing postoperative pain involves administering a combination of opioid and non-opioids analgesics acting at different sites within the central and peripheral nervous system in an effort to eliminate side effects of each drug used[4].

The effects of unrelieved pain has tremendous importance as it affects the well- being, comfort and postoperative course of surgical patients. It had never been simple to implement a proper management plan as the cost benefit relationship remained a formidable factor. The focus always had been on patient safety and a large number of patients are being handled globally with about 90% satisfactory outcome. But nevertheless an approach involving specially assigned staff, capital investment and running costs in order to achieve such outcome had incessantly controlled the management plan. It is felt that unless the least of such extra resources is made available, more intensive postoperative pain control may not get delivered.

As we all know, pain is a response to stimulus and is a product of biological function. It usually indicates the presence of pathology within the body but in postoperative pain it is the consequence of the surgery depending on its magnitude. The objective for postoperative pain management is to attenuate or eliminate pain and discomfort with least side effects taking cost-benefit ratio into account. The management plan has to be need-based and individualized and the achievement is predicated on clinical, patient itself and local factors. The ultimate determinant of the satisfactory pain control will be patient's own perception of pain. However, it is generally agreed that if postoperative pain is not addressed at proper time or in proper manner the patient would be subjected to its adverse effect[5].

Postoperative pain can affect all organ systems and includes

- Respiratory- Decreased vital capacity, decreased FRC, decreased tidal volume (Reduced cough, atelectasis, sputum retention and hypoxaemia, Chest infection, pulmonary embolism)
- Cardiovascular- Increased myocardial oxygen consumption and ischaemia (Tachycardia, Hypertension etc.)
- Gastrointestinal- Decreased gastric emptying, reduced gut motility and constipation
- Genitourinary- Urinary retention
- Neuroendocrine- Hyperglycaemia, protein catabolism and sodium retention
- Musculoskeletal- Reduced mobility, pressure sores and increased risk of DVT
- Psychological- Anxiety and fatigue

The effects listed above are the pathological consequences and these can further have secondary effects if not interrupted at some stage. However, as mentioned earlier the provision of effective pain relief during the postoperative period is dependent on in general on the following.

- Anaesthetic technique
- Type and extent of surgery
- Patient's perception of pain

The increased interest which currently fill the medical literature in improving postoperative pain care is due to the wider availability of effective methods for pain relief, a growing awareness of beneficial effects of optimal postoperative pain relief as well as guidelines from authoritative national and international organizations. There is a social pressure and "consumer demand" from patients for better pain relief after surgery[6].

Benefits[7]

In addition to improving patient comfort, the immediate postoperative course as well as long term outcome may be influenced by the quality of pain relief after surgery or trauma. The benefits may be charted as follows:

- Less physical and mental stress
- Improved motivation and ability for active mobilization
- Pulmonary functions improved; pulmonary complications
- Less stress on cardiovascular system
- Thrombo-embolic complications reduced
- Less impairment of gastrointestinal functions
- Urinary retention less
- Less impairment of immunological functions
- Fewer septic complications
- Reduced mortality in high risk patients
- Faster recovery after surgery
- Less chronic neuropathic pain
- Reduced health care costs

Assessment of pain[8]

Pain scales are tools that can help to diagnose or measure pain's intensity. The information provided can help the clinician to choose the best modality for the treatment. The most popularly used scales are verbal, numerical, visual, or some combination of all three forms:

Verbal: Verbal scales describe the intensity or severity of the discomfort. These are useful for it relative terminology and one must focus on the most characteristic quality of the pain.

Numerical: Numerical scales are to quantify the pain using numbers, sometimes in combination with words. This with the name "Visual Linear Analogue Scale" (VLAS) currently has gained wide use in pain practice.

Visual: Good for assessing pain in children who cannot communicate well.

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Pain scales are best used as the pain is occurring for the sake of accuracy. With the continuation of the treatment, pain scales record how the pain is changing and if treatment is having the intended effect.

Verbal pain scale: Verbal scale describes the degree of discomfort by choosing one of the vertical lines that most corresponds to the intensity of pain felt. Clinicians can use this scale to determine if the recovery is progressing in a positive direction. But confounding results have been common especially with patients who have high anxiety level or very low threshold of pain.

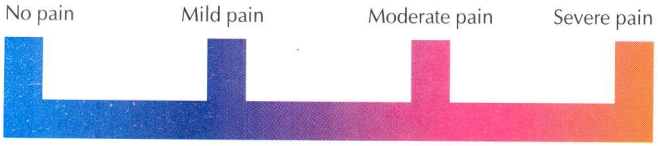

Figure 1: Verbal pain scale

Numerical pain scale (VLAS): A numerical pain scale describes the intensity of the discomfort in numbers ranging from 0 to 10 (or greater, depending on the scale). Rating the intensity of sensation is one way of expressing the discomfort due to postoperative pain.

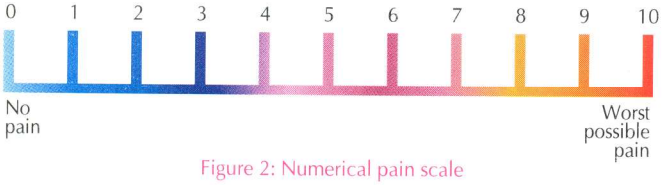

Figure 2: Numerical pain scale

Pain assessment in children or especially who cannot communicate can be difficult. Picture scales using varied facial expressions or by clinical observation (for example: sighing, groaning, sweating, ability to move) can be useful tools. The clinical assessment has the advantage of being independent of patient's cooperation to any great degree and can be carried out when other vital signs such as heart rate and blood pressure are being recorded. Few easy maneuvers like asking the patient to take a long deep breath or to cough or move may sometimes indicate the magnitude of the suffering. As mentioned earlier, measuring pain during rest and provision of analgesia on that basis often gives false positive outcome. It is, however, important that this is done when the patient is showing sign of distress and then a qualitative evaluation would provide some accuracy. Discomfort unrelated to the operating site may represent anxiety or generalized stress response and may act as confounders.

The early postoperative period presents special difficulty for any form of assessment so far described. Clinical signs (respiratory rate, haemodynamics etc.) are often the best guidelines under the circumstances. The assessment protocol should form part of the routine postoperative observations. The protocol should contain proper charts in graphical form rather than as a number. Supporting non-doctor medical staff should be trained and encouraged to use these tools of assessment of pain as a routine. Moreover, training should extend up to the administration of analgesics.

Visual scale: Visual scales show pictures of human body to help explain where the pain is located. A popular visual scale - the Wong-Baker Faces Pain Rating Scale- features facial expressions to help the clinician to understand how the pain makes the patient feel. This scale is particularly useful for children, who sometimes don't have the vocabulary to explain how they feel.

The Wong-Baker faces pain rating scale[10]: Designed for children aged 3 years and older, the Wong-Baker Faces Pain Rating Scale is also helpful for elderly patients who may be cognitively impaired. If offers a visual description for those who don't have the verbal skills to explain how their symptoms make them feel.

Figure 3: The Wong-Baker faces pain rating scale

If the patient is asleep, no further assessment is needed. If the patient is awake following is the protocol[9]

Table 1: Pain assessment for children under four years

Cry	Not crying	Score 0
	Crying	Score 1
Posture	Relaxed	Score 0
	Tense	Score 1
Expression	Relaxed or happy	Score 0
	Distressed	Score 1
Response	Responds when spoken to	Score 0
	No response	Score 1

(Total score 1 as slight pain, 2 as moderate pain, 3 as severe pain and 4 as the worst pain possible)

Management

The plan of anaesthesia should always include postoperative analgesia and should be safe, effective and convenient. This starts with a discussion with the patient during pre-operative visit[9].

Pain generally has been considered as a challenge for the clinicians. World Health Organization (WHO) however has dealt the issue globally and promoted a ladder attending 'pain' in general. The object of the WHO Analgesic Ladder was to control pain in patients with cancer. However, it has the potential for the management of acute pain as it has a logical strategy to pain management. The ladder has three steps; this along with VLAS may be used to address acute pain.

Analgesic ladder: The 'World Federation of Societies of Anaesthesiologists (WFSA) Analgesic Ladder' has been developed to treat acute pain in which pos-operative pain can be included. The ladder initiates with severe pain that can be expected to be controlled with strong analgesics in combination with local anaesthetic blocks and peripherally acting drugs[9]. The use of oral route for the administration of drugs may be limited because of the nature of the surgery and drugs may have to be given parenterally. Normally, postoperative pain should decrease with time and the need for drugs to be given by injection should cease. The second step on the postoperative pain ladder is the re-establishment of the use of the oral route for pain control. Strong opioids, now may pave the way for using combinations of peripherally acting agents and weak opioids. The final step is when the pain can be controlled by peripherally acting agents only.

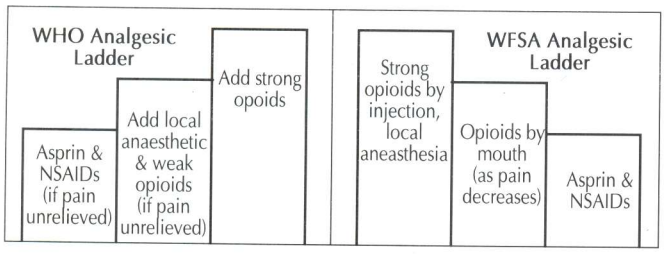

Figure 4: Analgesic ladder

The key to improving postoperative pain control and hasten recovery process, as suggested by many, is to use the "multimodal" approach in stages described above. It has indeed been considered as the benchmark for fast track clinical tool for acute pain by active workers in the field[4].

The effective pain control is of singular importance to clinicians treating patients undergoing surgery. Although this should be achieved for humanitarian reasons, but there is now evident significant physiological benefit. Not only does effective pain relief mean a smoother postoperative course with earlier discharge from hospital, but it may also reduce the onset of chronic pain syndromes. But clinicians often find difficulty in managing mild and moderate pain and as the combination therapy described above is getting more popular. A 4 step ladder is given below which may solve some of the problems.

Therapeutic measures should follow the reported intensity of the pain through VLAS.

Table 2: Pain intensity grade

Pain intensity	Therapeutic measures
1-3 (slight pain)	Paracetamol (not exceeding 4G/day), NSAIDS with adjuvants (antidepressants, tranquilizers etc.)
3-4 (mild pain)	Combinations Paracetamol and NSAIDS
5-6 (moderate pain)	Paracetamol + NSAIDS + weak opioid or mu receptor agonist (Codeine , Tramadol etc)
7-10 (Severe pain)	Paracetamol+NSAID+Potent opioid (Morphine, Pethidine etc)

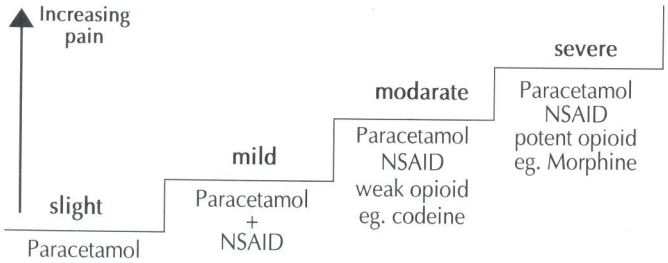

Figure 5: Analgesic ladder

Non-pharmacological methods of pain relief

- Preoperative explanation and education
- Relaxation therapy
- Hypnosis
- Cold or heat
- Splinting of wounds etc
- Transcutaneous electrical nerve stimulation (TENS)

Pharmacological methods of pain relief

Simple analgesia

- Paracetamol is a weak anti-inflammatory agent
- Modulates prostaglandin production in the central nervous system
- Can be administered orally or rectally
- Best taken on a regular rather than 'as required' basis.
- Overdose results in hepatic necrosis
- Often combined with weak opiates (e.g. dihydrocodeine, tramadol etc.)

Non-steroidal anti-inflammatory agents

- Inhibit the enzyme cyclo-oxygenase
- Reduces prostaglandin, prostacyclin and thromboxane production
- Also have weak central analgesic effect
- Often used for their 'opiate sparing' effects
- Side effects include: Gastric irritation and peptic ulceration, Precipitation of bronchospasm in asthmatics, Impairment of renal function, Platelet dysfunction and bleeding, Ulcerogenic effects, Bronchospastic respiratory failure, Injection site pain/ tissue necrosis.

Table 3: NSAIDs[9]

Drug name	Forms available	Daily dose range	Half life (h)
Ibuprofen	Tablet, syrup	600- 1200mg	1-2
Diclofenac	Tablet, suppository, injection, cream	75- 150mg	1-2
Naproxen	Tablet, suspension, suppository	500- 1000mg	14
Piroxicam	Capsule, suppository, cream, injection	10- 30mg	35+
Ketorolac	Tablet, injection	10- 30mg	4
Indomethacin	Capsule, suspension, suppository	50- 200mg	4
Mefenamic acid	Tablet, capsule	1500mg	4

Paracetamol: It is mainly analgesic and antipyretic agent. Being well absorbed orally and is metabolised by the liver. Side effects are negligible if used judiciously and has been found to be most effective in mild pain. Overdose may causes hepatic damage.Doses range from a minimum of 500mg, to 4g, orally in adult.

Opiates

- Most commonly used drugs morphine and pethidine
- Diamorphine is a prodrug rapidly hydrolysed to morphine and 6-monoacetyl-morphine (may have a very restricted use)
- More lipid soluble than morphine with greater central effects
- Pethidine has only about 10% the analgesic potency of morphine
- All act on mu receptors in brain and spinal cord
- Mu 1 receptors are responsible for analgesia
- Mu 2 receptors are responsible for respiratory depression
- Side effects of opiates include: Sedation, Nausea and vomiting, Vasodilatation and myocardial depression, Pruritus, Constipation, Urinary retention, Respiratory depression, Urinary retention, Gastrointestinal motility reduced.

Routes of opiate administration

- Oral - Available for codeine, dihydrocodeine and oral morphine
- Subcutaneous - Useful for chronic pain relief but has been used postoperatively
- Intramuscular - Produces peaks and troughs in pain relief (Break through pain)
- Intravenous - Reliable but can produce sedation and respiratory depression
- Patient-controlled analgesia (PCA) - Patient determines own analgesic requirement
  - "Lock-out" period prevents accidental overdose
  - Safe as sedation occurs before respiratory depression

- Epidural or spinal
  - Lipid soluble opiates (e.g. fentanyl) are normally used
  - Produces good analgesia with reduced risk of side effects

Weak opioids[9]

Codeine: Weak opium alkaloids; markedly less potent than morphine, administered orally and treats mild to moderate pain. Combining with paracetamol provides better result without complication if maximum recommended dose is not exceeded. Doses range: (15 mg to 60mg 4 hourly with a maximum of 300mg daily). Doses range from 32.5mg (in combination with paracetamol) to 60mg 4 hourly with a maximum of 300mg daily.

Combinations of weak opioids and peripherally acting drugs may be used in minor surgical procedures especially for outpatients: Paracetamol 500 mg/codeine 8 mg tablets. 2 tablets 4 hourly to a maximum of 8 tablets daily is considerd as a good combination.

Table 4: Strong analgesics[9]

Drug name	Route of delivery	Dose (mg)	Length of Action (h)
Morphine	Intramuscular/ subcutaneous	10-15	2-4
Methadone*	Intramuscular	7.5-10	4-6
Pethidine	Intramuscular	100-150	1-2
Buprenorphine	Sublingual	0.2-0.4	6-8

* not readily available in the Bangladesh

(Intravenous - half the IM dose slowly over 5 minutes)

Systemic local analgesic agents: Lignocaine as a local anaesthtic agents is being widely used and still remains a strong choice in most of the settings, but the potential benefits of intravenous lignocaine in reducing postoperative pain has recently drawn attention[11].

Patient Controlled Analgesia (PCA)[12] is a system whereby patients could administer their own intravenous analgesia and so titrate the dose according to the need. This is achieved by using a small microprocessor - controlled pump. Tthe patient has the control and can self-administer a small bolus dose of opioid and judging the benefit can organize the analgesic requirement. according to the severity of the pain. In theory, a steady state concentration in plasma can be obtained. Almost every opioid drug has been used for PCA., while the ideal drug should have rapid onset, moderate duration of action and a high margin of safety between effectiveness and troublesome side effects. PCA has been used intravenously and intramuscular, subcutaneous and epidural routes have also been practiced. The details of PCA delivery technique is beyond the scope of this article but in spite of the cost of the equipment it has been proved to be an effective way of handling acute pain. Less total amount of opioid is used with PCA than with intramuscular route. . The reported side effects is about the same with the two techniques but PCA has less incidence of respiratory depression.

Table 5: Guidelines for patient controlled intravenous opioid administration[9]

Drug (cone)	Size of bolus (mg)	Lock-out interval (min)
Morphine (1mg/ml)	0.5 -- 2.5	5-10
Pethidine (10 mg/ml)	5 -- 25	5-1
Methadone (not locally available) (1mg/ml)	0.5 -- 2.5	8-20
Fentanyl (1mg/ml)	0.01 -- 0.02	3-10

Local/regional anaesthetic techniques: Regional anaesthetic techniques are associated with possible better respiratory and cardiovascular effects, reduced blood loss and excellent pain relief. Technique that can be used for the surgery as well as postoperative analgesia may be considered near perfect. Following have been used.

- Local infiltration of incisions with long-acting local anaesthetics
- Blockade of peripheral nerves or plexuses and
- Continuous block techniques peripherally or centrally.

postoperative analgesia may be used as a part of a prepared plan for overall anaesthetic management with appropriate analgesic drugs. Pain being multifactorial in origin should follow a management that consist of a combination of approaches in order to achieve the best results. Bupivacaine Infiltration of an incision line can provide effective analgesia for several hours. Pain relief beyond that can be obtained with intermittent administration or by infusions via a thin catheter. Selective analgesia in various parts of the body supplied by the plexus or nerves can be achieved by conduction blockade. These are especially considered where a sympathetic block is desired or central blockade is contraindicated.

After the reintroduction of spinal anaesthesia it has been found to be excellent analgesia for surgery in the lower half of the body and pain relief can last many hours postoperatively. Continuous spinal analgesia using catheter has been tried but epidural analgesia is more popular and safer. But performing epidural technique needs competence and back up service if continuous epidural infusion or patient controlled epidural epidural analgesia (PCEA) is planned. A great deal of sterility care is mandatory for these techniques. A meta analysis of the epidural analgesia concludes that 'epidural analgesia, regardless of analgesic agent, location of catheter placement and type and time of pain assessment, provided better postoperative analgesia compared with parenteral opioids[13].

Intrathecal and epidural opioids have become popular in wide variety of surgical procedures. Administration is easy and on the top of providing surgical anaesthesia for a stipulated period it can act as postoperative analgesic means for several hours. It can be an additional technique with general anaesthesia. It has been reported that as long as 24 hours' comfortable analgesia has been achieved after a single injection of intrathecal morphine.

But there are side effects with these routes of delivery. Nausea, vomiting, itching (which is much more common with morphine than other drugs) and urinary retention are the main ones. Possibility of respiratory depression can be a serious concern for the clinicians. Assuming that all patients are at risk of this occasional complication and a high level of care and vigilance needs to be adopted. High dependency or intensive therapy unit, however, would be right place to keep this patient if there is a concern. Prescribing any other narcotics to this group patient (receiving intrathecal or epidural opioid) is prohibited.

Opioid/local anaesthetic combinations are becoming quite popular and have been adopted by many clinicians in order to achieve a synergistic effect and also to minimize the severity of the side effects of either agents. Dilute concentrations of local anaesthetic agents have been used in combination with opioids and delivered by infusion through an epidural catheter.

Other routes of delivery Transdermal, inhaled and intranasal opioids are among the routes of drug delivery currently used.

Table 6: Local anaesthetics for the treatment of acute pain[9]

Agent	% solution for analgesic blocks	Duration (hours)	Max. single dose mg/kg. (Total mg in adults*)	% solution for infusion	Comments
Lignocaine					
Infiltration	0.5-1	1-2	7	-	Rapid onset. Dense motor block
Epidural	1-2	1-2	(500)	0.3-0.7	
Plexus or nerve	0.75-1.5	1-3	-	0.5-1.0	
Mepivacaine					
Infiltration	0.5-1	1.5-3	7	-	Rapid onset. Dense motor block Longer action than lignocaine
Epidural	1-2	1.5-3	(500)	0.3-0.7	
Plexus or nerve	0.75-1.5	2-4	-	0.5-1.0	
Prilocaine					
Infiltration	0.5-1	1-2	8.5	-	Rapid onset. Dense motor block Least toxic amide agent. Methaemaglobinaemia > 600 mg
Epidural	2-3	1-3	(600)	0.5-1	
Plexus or nerve	1.5-2	1.5-3	-	0.75-1.25	
Bupivacaine					
Infiltration	0.125-0.25	1.5-6	3.5	-	Avoid 0.75% in obstetrics. Mainly sensory block at low concentration. Cardiotoxic after rapid IV injection
Epidural	0.25-0.75	1.5-5	(225)	0.0625- 0.125	
Plexus or nerve	0.25-0.5	8-24+	0.125- 0.25	-	
Chloroprocaine					
Infiltration	1	0.5-1	14	-	Lowest systemic toxicity of all agents. Motor/sensory deficits may follow intrathecal injection
Epidural	1.5-3	0.5-1	(1000)	0.5-1	

*For healthy patients with 1:200,000 adrenaline added to solutions. Maximum doses quoted should be reduced by 40% if solutions do not contain adrenaline. Much lower doses can be lethal if injected directly.

Table 7 : Intrathecal and epidural opioids for treatment of acute pain[9]

Drug	Single dose (mg)	Onset (min)	Duration of single dose (h)
Epidural			
Morphine	1-6	30	6-24
Pethidine	20-150	5	4-8
Methadone	1-10	10	6-10
Fentanyl	0.025-0.	1 5	2-4
Subarachnoid			
Morphine	0.1-0.3	15	8-24+
Pethidine	10-30	?	10-24+
Fentanyl	0.005-0.025	5	3-6

Factors influencing the outcome

The site of the surgery has a great deal of role in terms of degree of severity of pain. Surgery on the thorax and upper abdomen are more painful than on the lower abdomen. Surgeries in peripheral areas however, are least painful as compared to its former counterparts. Any surgery involving a body cavity, large joint surfaces or deep tissues should be regarded as painful. Surgeries on the thorax or upper abdomen may affect pulmonary, cardiovascular and other function adversely as described previously. As the choice of analgesic techniques may be influenced by the site of surgery, it may also be influenced by drug availability and familiarity with different methods of analgesia. Patient-controlled analgesia (PCA) paradigm, has produced publications indicating higher frequency of PCA demands for morphine following surgery. This is where Infusion through epidural route has been proved to safer.

In the past, the standard method of treating postoperative pain in the developed world has been intramuscular opioid (usually morphine) although individual variation in terms of response had been apparent. The effects of opioid drugs vary greatly among patients and thus individual responses cannot be predicted resulting under-treatment of acute postoperative pain as the pain management staff overestimate the length of action and the strength of the drugs for one and the fear of complication for another. In spite of the above, other factors may alter the amount of pain suffered by the individual patient. The attitude of the patient in terms of individual personality, nature and intended purpose of the surgery may be important. Proposed surgery with a positive outcome may obviate the use of more analgesics as compared to a procedure with unfavourable or doubtful result. Patients who are afraid of anaesthesia or surgery may complain of more pain.

Certain drugs, such as morphine, which are the mainstay of postoperative pain relief in many places, are either not available or unduly costly. Patient-controlled analgesia (PCA.) devices are expensive and not available in most of the centres in Bangladesh and that techniques of regional anaesthesia which employ continuous infusions through disposable catheters are not easy to introduce either. Techniques beyond local resources cannot be advocated for general use. It would be, however, advisable to maximise the effective use of local anaesthetic techniques and intermittent delivery of such analgesic drugs as are available.

Pain relief in children[9]

postoperative pain in children is often under-treated although there is nothing to suggest that pain is less intense in neonates and young children due to their developing nervous system. This is done only for the fear that the potent analgesics are dangerous when used in children because of the risks of side effects if not addiction. Fear and anxiety of the patients are usual contributory factors and the treatment of pain needs to take that into account.

Pain assessment has always been difficult, especially in those patients who cannot explain and express in intelligible terms. Nevertheless, ignoring the presence of pain in children can be dangerous and the course is to assess the pain and the patients response to treatment as thoroughly as possible. Children over four are better patients and are able to translate pain if proper assessment are used.

Management of pain in children needs more care, attention and precision than in adults. Anticipatation of pain postoperatively with its degree of severity is one of the clinical acumen as children are not best at pin pointing the problems but would ask for relief. One way is to follow a set protocol established on guidance from standards. Selection of route of administration will naturally depend on the drug to be used, the severity of the pain and the likely side effects. Oral route is by far the best if possible but rectal route is gaining popularity as it is well tolerated and vomiting is not a problem. The parenteral route should have its rightful indications.

Local anaesthetic creams EMLA are available that can be applied under an occlusive dressing to produce numbness of the underlying skin for up to an hour. These may allow painless placement of venous catheters or infiltration of the area with local anaesthetic. Some procedures for pain relief can itself generate pain. This, of course needs extra attention.

Infiltration of local anaesthetic agent into the incision lion before recovery from anaesthesia can reduce postoperative pain for long periods. This may act as preemptive analgesia allowing less amount of systemic algesics in subsequent period. Day care patients are best suited for this. Caudal extradural anaesthesia provides excellent analgesia for any surgery below the waist such as herniorrhaphy, orchidopexy or circumcision. But the parents ought to be warned about some of the side like, urinary retention and of transient weakness or numbness.

Dose schedule for caudal block with bupivacaine in children. 0.25% solution is satisfactory for blocks requiring a volume of 20ml or less. A more dilute solution (0.2% bupivacaine) should be used where volumes of 20 ml or more are required[9].

For short cases 1% lignocaine will be effective and the required volume can be calculated in a similar fashion[9].

Table 8 : Doses schedule for extradural block

Type of block	Volume (ml/kg)
Lumbosacral	0.5
Thoracolumbar	1.0
Mid-thoracic	1.25

Maximum doses of bupivacaine in any four hour period are 2-3mg/kg and for lignocaine 3mg/kg (without adrenaline), 6mg/kg (with 1:200,000 adrenaline).

Pain relief in the elderly

The geriatric group has special problems in the planning of pain management. Communication and assessment may not be possible as a degree of dementia would be present. The choice of analgesic techniques is predicated on this factor. A little, however, will go a long way as their distribution volume for drugs is shrunk. Many are anxious and may give false signal necessitating a careful assessment. Assessment of pain, however, may be carried out by normal methods and conventional methods. Impairment of higher intellectual functions may need observational techniques similar to those described earlier. Inefficient absorption and metabolism and excretion is usual in elderly and care is advised. NSAIDS and opioids need special precaution if prescribed. Drug interaction has greater chance to occur as these group of patients are usually on varieties of medication.

Local anaesthetics Regional blocks are effective and quite satisfactory for postoperative pain relief. Intercostal nerve blocks are pulmonary function friendly after chest or upper abdominal surgery and pain below the waist can be abolished by epidural blockade. His also helps in prevention of ileus postoperatively. Epiduar blocks have wider spread however and need reduction of doses. If proper precaution is taken regional blocks can be very effective in the elderly and give excellent analgesia postoperatively promoting quicker recovery and rehabilitation.

Conclusion

The postoperative pain control still remains an enigma as over the years changes in approach has taken place but no fool proof technique has been found so far. The multimodal techniques have been recommended by both American society of Anaesthesiologists (ASA) and World Federation of Society of Anaesthesiologists (WFSA) with an acceptable outcome. But the continuing quest for better strategies to confront postoperative pain should look beyond multimodal approach. Regardless of how the pharmacological armamentarium may change PCA with finer adjustments still seems to have a place in future. Transdermal application too seems a very potential technique as a non invasive effective method of treating acute pain.

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MSD News

Khulna

Soronkhola UHC, Bagerhat: On 25th August 2008, Soronkhola UHC, Bagerhat arranged a RTM on "Review on skin deseases" at room of UH & FPO. Dr. Md. Safiqul Islam, UH & FPO was the Chairperson. About 15 doctors attended the meeting.

Morolgonj UHC, Khulna: Morelgonj UHC, Khulna arranged a RTM on 23rd August 2008 on "Short review on skin diseases" at the seminar room. Dr. Md. Habibur Rahman, UH & FPO was present as the chairperson. About 15 doctors enjoyed the session.

Kotalipara UHC, Gopalgonj: A RTM was arranged by Kotalipara UHC on 7th August 2008 on "Role of ceftriaxone to treat various infections" at the room of UH & FPO. Dr. Zodh Nath Mondal, UH & FPO was present as the Chairperson. About 25 doctors attended the session.

Tungipara UHC, Gopalgonj: Tungipara UHC arranged a RTM on 5th August 2008 on "Role of ceftriaxone to treat various infections" at the room of UH & FPO. Dr. Mostafizur Rahman, UH & FPO chaired the meeting. About 20 doctors attended the seminar.

Fakirhat UHC, Bagerhat: On 24th December 2008, Fakirhat UHC of Bagerhat arranged a RTM on "Common skin problems in outdoor" at the room of UH & FPO. Dr. Alamgir Hossain, UH & FPO chaired the session. About 16 doctors attended the meeting.

Kochua UHC, Bagerhat: A RTM was arranged by Kochua UHC, Bagerhat on "Common skin problems in outdoor" on 27th December 2008 at the room of UH & FPO. Dr. Torun Kanti Halder, UH & FPO was present as the chairperson. About 15 doctors enjoyed the session.

Monirampur UHC, Jessore: Monirampur UHC, Jessore arranged a RTM on 25th November 2008 on "Common skin problems in outdoor" at the room of UH & FPO. Dr. Sk. Keramot Ali, UH & FPO, chaired the meeting. Dr. Nuruzzaman, AD, School Health was the Chief Guest and Dr. Nurul Islam, AD, Family Planning was the Special Guest. About 20 doctors attended the seminar.

Mymensingh

Jamalpur General Hospital: On 26th October 2008 Jamalpur General Hospital arranged a RTM on "CSOM its complication & management" at the conference room. Dr. AKM Shahidur Rahman, President, BMA Jamalpur chaired the session and Dr. Md. Dabimuddin Sarder, Civil Surgeon was present as the Chief Guest. Dr. Md. Kamruzzaman, Consultant, ENT, Jamalpur General Hospital was the Keynote Speaker. About 70 doctors attended the seminar.

Haluaghat UHC: A RTM was arranged by Haluaghat UHC on 15th November 2008 on "Comparative review on cephalosporin" at the conference room. Dr. Abdul Jabber, UH & FPO chaired the meeting. About 20 doctors attended the session.

Rest of MSD news at page- 638

Hepatorenal syndrome

Roy DK[1]

The ORION Medical Journal 2009 Jan;32(1):629-632

Summary

Hepatorenal syndrome (HRS) is a form of acute or subacute kidney injury which develops in patients with chronic liver disease. Kidney injury is caused by intense vasoconstriction of the renal circulation. In contrast to other forms of acute kidney injury it may be reversible using pharmacological agents. The diagnosis of HRS is currently based on exclusion of other causes of renal dysfunction. Pharmacological agents currently used include the vasopressin analogues telipressin and the alpha adrenoreceptor agonist midodrine. Intravenous albumin is an important adjunctive treatment both in the prevention and treatment of HRS. Increasing intravascular volume using TIPS (transjugular intrhepatic stent shunt) is also effective in some patient and may be useful in maintaining patients who have initially responded to pharmacological therapy. Recent findings suggest that the risk of developing HRS in the setting of spontaneous bacterial peritonitis may be reduced by the administration of albumin together with antibiotic therapy and that of HRS occurring in severe alcoholic hepatitis can be lowered by the administration of pentoxifylline. Despite improvements in survival, long term prognosis is still poor and generally depends on the degree of reversibility of the underlying liver disease or access to liver transplantation.

Introduction

Acute kidney injury (AKI) is a common complication of patients with advanced cirrhosis[1,2]. Acute kidney injury in patients with cirrhosis may be due to variety of causes including aetiological factors that can lead to AKI in patients without liver disease like severe dehydration, shock (septic, hemorrhagic), nephrotoxic drug, or intrinsic renal disease such as glomerulonephritis. Hepatorenal syndrome (HRS) is a functional renal failure without any specific aetiological factor and with normal renal histology. The true incidence of HRS is unknown. Most of the classic studies[1,3-6] were carried out many years ago and used non standard criteria for the diagnosis of HRS. The largest study by Gines et al[6] showed that approximately 18% patients of cirrhosis with ascites develop HRS at one year and 39% at 5 year. Although HRS was described more than 50 years ago, many features of its pathogenesis and natural history remained unknown. The past 15 years have witnessed major advances in the prevention and treatment of hepatorenal syndrome. Recent better insight into the pathophysiology of portal hypertension and HRS has allowed the rational application of new therapeutic strategies to this group of patients. Liver transplantation was the only treatment of HRS in earlier days but now it has been shown that pharmacotherapy may reverse HRS and that this improvement is maintained despite drug withdrawal in majority of patients. Therefore pharmacotherapy particularly vasocontrictors with intravenous albumin has become the first line therapy in majority of patients with HRS. This article will review the present status of diagnosis and management of hepatorenal syndrome.

Definition

Hepatorenal syndrome (HRS) is a functional acute or subacute renal failure with preserved tubular function and normal renal histology occurring mainly in patients with advanced cirrhosis and ascites, who have marked circulatory dysfunction[7] as well as in patients with acute liver failure[8] and alcoholic heapatitis. It is characterized by marked reduction in glomerular filtration rate (GFR) and renal plasma flow (RPF) in the absence of other identifiable causes of renal failure.

Classification of HRS

HRS can be subdivided into two types: Type-1 HRS and Type-2 HRS according to both the intensity and progression of renal failure[9]. Type-1 HRS is characterized by rapidly progressive renal failure. There is doubling of serum creatinine reaching value greater than 221 mol/l (2.5 mg/dl) in a period of less than two weeks in addition to other criteria of HRS[9]. Type-1 HRS usually occurs within the setting of an acute deterioration of circulatory function characterized by arterial hypotension and activation of endogenous vasoconstrictor system, and may be associated with impaired cardiac and liver function as well as encephalopathy. Prognosis of type-1 HRS is very poor, with an overall survival of less than 10% and a median survival of only 2 weeks in older studies[6]. Type-2 HRS is defined by more indolent rise in serum creatinine (>133 mol/l) with a steady and slowly progressive course which do not meet the criteria for type-1 HRS. Type-2 HRS usually arises in the context of patients with diuretic refractory ascites. Some patients with type-2 HRS eventually develop sudden rapid progression of renal failure after weeks or months of stable serum creatinine concentration and may than meet the criteria of type-1 HRS. Survival of patients with type-2 HRS is shorter than that of non azotemic cirrhotic patients with ascites but better than that of patients with type-1 HRS. 50% of type-2 HRS patients survive for approximately 6 months duration[7].

Pathogenesis

The pathogenesis of HRS is incompletely understood, although agreement exists that HRS is the consequence of intense renal vasoconstriction, presumably reflex in response to splanchnic vasodilatation[10-12] (Box-1). Peripheral arterial vasodilation particularly in the spalcnhnic circulation is associated with reduction in effective arterial blood volume. Reduction in effective arterial blood volume leads to counter regulatory activation of sympathetic nervous system (SNS), renin angiotensin aldosterone system (RAAS) and arginin vasopressin (AVP)[13-15]. As a result there is arterial vasoconstriction in other areas such as kidneys, brain and liver[16-17]. The initial stimulus to the development of HRS is portal hypertension, which leads to severe splanchnic vasodilatation probably through increased production and reduced clearance of vasodilators such as nitric oxide (NO), prostacycline, glucagon, atrial natriuretic peptide, adrenomedullin, carbon monoxide etc. There is growing evidence that sinusoidal portal hypertension directly affects renal function in cirrhosis giving rise to the so called hepato renal reflex. Jalan R et al[18] observed that when a transjugular intrahepatic porto systemic shunt (TIPS) is occluded acutely by angioplasty balloon there is reflex reduction in renal blood flow. Initially the kidneys are able to adapt to the decreased renal blood flow by local release of vasodilators such as prostaglandin E2[19]. However, as liver disease progresses or complication intervene, the kidneys are unable to maintain these adaptive responses in the face of intense vasoconstrictor stimuli and hepatorenal failure supervene.

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Box- 1: Pathogenesis of hepatorenal syndrome and site of action of therapeutic options

Pathogenssis	Therapeutic option
Cirrhosis	← Liver Transplant
↓ Portal Hypertension	← TIPS
↓ Splanchnic Vasodilatation	← Vasoconstrictors
↓ Reduced effective arterial blood volume	← Albumin infusion
↓ Stimulation of atrial natriuretic / Vasoconstrictor systems	
↓ Intense renal vasoconstriction	
↓ HEPATORENAL SYNDROME	

Precipitating factors

HRS may develop spontaneously or it may develop in close chronological relationship to some precipitating factors like bacterial infection especially spontaneous bacterial peritonitis, large volume paracentesis without plasma expansion, diuretic induced intravascular volume depletion, gastrointestinal bleeding etc[20-21]. Spontaneous bacterial peritonitis has been clearly established as a precipitating factor for HRS[20-22]. About 20% patients with SBP develop HRS during or immediately after the infection. Upto 15% patients of cirrhosis with ascites develop HRS when large amount (>5L) of ascitic fluid are removed without plasma expanders[23]. About 10% patients with cirrhosis and gastrointestinal bleeding develop HRS[24-25]. Although most of them develop renal failure due to acute tubular necrosis.

Diagnosis

The diagnosis of HRS is essentially one of exclusion and the diagnostic criteria set by the international ascites club are helpful in this regard. The definition and diagnostic criteria for HRS was initially established in 1994[9] and revised by the international ascites club during the 56th meeting of the American association for the study of liver diseases[26] (Box - 2).

Box- 2: New diagnostic hepatorenal syndrome criteria in cirrhosis

- Cirrhosis and ascites
- Serum creatinine > 133 mol/l (1.5 mg/dl).
- No improvement of serum creatinine (decrease to a level of =133 mol/l) after at least 2 days with diuretic withdrawal and volume expansion with albumin. The recommended dose of albumin is 1 gm /kg of body weight per day up to a maximum of 100 gm /day.
- Absence of shock.
- No current or recent treatment with nephrotoxic drugs.
- Absence of parenchymal kidney disease as indicated by proteinuria >500mg/day, microhaematuria (>50 RBC / HPF) and or abnormal renal ultrasonography.

The main differences between the old[9] and the revised[26] criteria are: i) Creatinine clearance has been excluded as diagnostic criteria because it is more complicated than simple serum creatinine ii) renal failure in the setting of ongoing bacterial infection, but in the absence of septic shock is considered HRS iii) Plasma volume expansion should be performed with albumin rather than saline iv) minor diagnostic criteria have been removed as they are not essential. In practice, however, making a clear diagnosis of HRS is often difficult because these patients may have multifactorial aetiology of renal dysfunction (Box - 3) which should be considered in the differential diagnosis.

Box- 3: Common causes of acute kidney injury in patients with cirrhosis

- Prerenal: Dehydration, Over Diuresis, Gastrointestinal bleeding, Sepsis, Hepatorenal syndrome.
- Parenchymal renal disease: IgA nephropathy, Cryoglobulinaemia.
- Nephrotoxins: NSAIDS, Aminoglycosides, Radio contrast media.

The initial step to the diagnosis of HRS is to determine the existence of renal failure (raised serum creatinine >133 µmol/l) in a patient with advanced hepatic failure and portal hypertension. Acute kidney injury of pre renal origin due to fluid losses (Vomiting, Diarrhoea or over diuresis due to excessive diuretic use) should be identified by history and physical examination in all patients. Even if there is no history of fluid loss, renal function should be assessed after diuretic withdrawal and volume replacement to rule out any subtle reduction of plasma volume as the cause of renal dysfunction. Diagnosis of HRS depends on failure of serum creatinine and urine volume to improve despite diuretic withdrawal and volume expansion with albumin. The presence of shock before the onset of renal dysfunction precludes a diagnosis of HRS and points towards a diagnosis of ATN. Septic shock may be difficult to diagnose because of lack of symptoms of bacterial infection in patients with cirrhosis. Therefore, bacterial infection should always be ruled out (Leucocyte count, examination of ascitic fluid, cultures, C-reactive protein etc) before the diagnosis of HRS is made. Treatment with NSAID and other nephrotoxic drugs in the days or week preceding the development of acute kidney injury should be ruled out. AKI due to parenchymal renal disease like glomerulonephritis to be excluded by the presence of proteinuria, haematuria or both. Differentiation of HRS from ATN is not an easy task. Tubular function is intact in HRS and therefore the intact concentrating ability of renal tubules and high level of circulating aldosterone level may lead to very low urinary sodium concentration (<10 mmol/l). In practice however, the urinary sodium concentration is unreliable and may be low even in ATN. Therefore, an international consensus was reached that this variable should not be used as a criterion to differentiate between HRS and ATN in cirrhosis. ATN in cirrhosis should be suspected when renal dysfunction develop in the setting of volume depletion, shock or use of nephrotoxic agents. Presence of such a condition immediately before the development of renal dysfunction favours the diagnosis of ATN not HRS. Ultrasonographic evaluation of the kidney should be performed in all cases to exclude post renal obstruction and the presence of small kidney size may suggest chronic kidney disease.

Hyponatremia is almost universal in HRS. So, if serum sodium concentration in a patient of cirrhosis and renal dysfunction is normal, than the diagnosis of HRS is unlikely[27-29]. Hypokalemia is also common but moderate in most cases. Severe metabolic acidosis is uncommon in HRS except for patients who develop severe infection. Arterial blood pressure is low in most cases despite pronounced activation of major vasoconstrictor mechanisms. Pulmonary oedema, a common complication of renal failure without liver disease is rare in patients with HRS unless they are treated aggressively with plasma expanders.

Most patients with HRS have sign symptoms of advanced liver failure and portal hypertension. The presence of ascites is universal in patient with HRS. So, lack of ascites in a patient with cirrhosis and renal dysfunction argue against the diagnosis of HRS.

Histology of the kidney may be helpful to confirm the diagnosis and to define prognosis in selected patients especially when liver transplantation is being considered. HRS is an example of functional renal failure that is renal histology is normal and an improvement in liver function can bring about improvement in

renal function. In patients with intrinsic renal disease, liver transplantation is unlikely to lead to recovery of renal function and consideration should be given to combined liver and kidney transplantation. Renal biopsy can be safely achieved by the transjugular route where coagulation abnormalities exclude the percutaneous approach[30].

Management of HRS

Definite evidence of reversibility of HRS come from liver and kidney transplant studies from 1960 to 1970s[31,32]. Improvement in liver function can bring about improvement in renal function. Unfortunately many patients die from renal failure before improvement in liver function takes place. Therefore, therapies are needed that can bridge a patient to liver transplantation or recovery from precipitating event. Patients with suspected HRS should be managed as inpatients. Vital signs, urine output, and blood chemistry should be closely monitored. Because most patients have dilutional hyponatremia, total fluid intake should be restricted to avoid positive fluid balance and thus further reduction in serum sodium level. The administration of saline solution can increase ascites and oedema greatly because of renal sodium preservation and therefore is not recommended. For this reason and the absence of severe metabolic acidosis administration of sodium bicarbonate is not advisable. Potassium sparing diuretics should be withdrawn to avoid the risk of hyperkalemia. Early identification of infection and treatment is essential as infection is an important contributor of death in these patients. Spontaneous recovery from HRS occurs in only 3.5% of patients[33]. The most important treatment goal in HRS is improvement of renal perfusion and GFR. On the basis that HRS results from reduction in effective arterial blood volume due to arterial vasodilatation, attempts have been made to correct this by the administration of vasoconstrictor drugs. Best results have been obtained with systemic vasoconstrictors in combination with plasma volume expanders. They reduce massive splanchnic vasodilatation, increase mean arterial pressure (MAP) and thus suppress the vasoconstrictors activated in HRS .

Vasoconstrictor agents: Vasoconstrictors used in HRS include Vasopressin analogue (Ornipressin and Telipressin), and alpha adrenergic agonists (Midodrine, nor-epinephrine). Both ornipressin and telipressin act on V_1 receptors present on vascular smooth muscle cells in the mesentery and skin. They are more effective vasoconstrictors of the mesenteric than the renal circulation, a property which is useful in hepatorenal syndrome by favoring renal blood flow[34,35]. They reduce blood flow to splanchnic organs and hence portal blood flow and pressure. Ornipressin has a short half life whereas telipressin has a prolonged half life of 2-10 hours. The higher frequency of ischemic side effects with ornipressin limits its use[36,37]. Telipressin has been evaluated in the management of HRS-1 in a number of studies and has been found to be effective in reversing HRS in majority of patients[36,38-40]. Predictors of lack of response to telipressin include old age, severe liver failure (child pugh score ≥ 13) and omission of concomitant albumin administration[40,41]. The improvement in GFR occurs slowly over several days. Recurrence of HRS after treatment withdrawal in responders is uncommon (about 15%) and re-treatment is effective in most cases. The frequency of ischemic side effects requiring the discontinuation of telipressin treatment (5-15%) is lower than that with ornipressin (30-50%). There are two major short comings of treatment with telipressin, the drug is not available in some countries and the cost is high. Because of these limitations alpha adrenergic agonist (Midodrine and Nor-epinephrine) is attractive alternative. Alpha adrenergic agonists are cheaper, widely available and as effective as telipressin[42,43]. Midodrin is an orally active alpha adrenergic agonist, which has been shown to increase renal plasma flow and GFR in patients with ascites[44]. In most studies both type of vasoconstrictors have been given in combination with volume expanders like albumin, fresh frozen plasma or both to improve arterial under filling. The use of volume expanders appears to increase the efficacy of vasoconstrictor drugs.

Other drugs: The efficacy of drugs with renal vasodilator activity, such as dopamin or prostaglandins, has not been proven and they are therefore not recommended. Serum level of Endothelin, a potent renal vasoconstrictor is found higher in patients with HRS[45]. In three patients who received the endothelin-A receptor antagonist BQ123 showed improvement in GFR and renal plasma flow without significant effect on systemic haemodynamics[46]. Furher studies with this drug would be valuable.

Transjugular Intrahepatic Portosystemic Stent Shunt (TIPS): Given that portal hypertension is necessary for the development of HRS, attempts to reduce portal pressure by techniques like TIPS have been employed in the treatment of HRS. This procedure consists of insertion of an intrahepatic stent between portal and hepatic veins by a transjugular approach. In HRS, TIPS improve circulatory function and reduce the activity of vasoconstrictor systems[37,47]. Brensing et al[47] treated 31 non transplantable HRS patients with TIPS, of whom 14 had HRS-1. There were significant improvement in urine volume, serum creatinine, sodium excretion and creatinine clearance. Median survival in the TIPS group was significantly better compared to non-TIPS group (49 Vs 2 weeks). The efficacy of TIPS was also confirmed by Wong et al[48] in their series. In the TIPS group renal function, serum sodium, and sodium excretion normalized. TIPS insertion was also successful in increasing central blood volume and reducing plasma rennin activity. Refractory ascites is a feature of type-2 HRS. The use of TIPS in these patients was found to have improved renal function, better control of ascites, and reduced risk of progression from type-2 to type-1 HRS[49]. Gines a et al[49] in a randomized trial compared TIPS and repeated paracentesis plus IV albumin in patients with cirrhosis and refractory ascites showed that the use of TIPS was not associated with an improved survival compared to the patient treated with repeated paracentesis plus IV albumin. However, the main limitation of this treatment is that it is considered to be contraindicated in in patients with severe hepatic failure (Child pugh score>12) or severe hepatic encephalopathy because of the risk of inducing irreversible hepatic failure or chronic disabling hepatic encephalopathy. The use of TIPS can be considered for patients unable to use vasoconstrictors.

Extra corporeal detoxification: The molecular absorbent recirculating system (MARS) has been proposed as a therapy for HRS-1. This is a system using an albumin containing dialysate which is recirculated and perfused through charcoal and anion exchanger columns. By this method toxins that are implicated in the pathogenesis of HRS such as tumour necrosis factor -α (TNF-α), interleukin-6, and NO are removed by selective binding to dialysate albumin[50]. In a small randomized trial of 13 patients with severe underlying liver disease (mean child pugh score-12.5, serum bilirubin >15mg/dl) were treated. Eight of them were treated with MARS with 5 controls (Hemodiafiltration and standard medical treatment). A mean of 5 treatments were given. Mortality was 100% in the control arm by day 7 compared to 62.5 % at day 7 and 75% at day 30 in the MARS group[51].

Renal replacement therapy: Most patient with HRS do not tolerate hemodialysis and develop complications like hypotension, bleeding, infection etc, which can lead to death during treatment. Moreover, findings indicate that the need for renal replacement therapy (severe fluid overload, acidosis, hyperkalemia) is less common at least in early stages of HRS. Continuous veno venous

hemofiltration is found safer and effective and may be chosen as the preferred form of renal replacement therapy when needed.

Liver transplantation: Liver transplantation was the only effective therapy for patients with HRS before the introduction of vasoconstrictors and TIPS, and is still the treatment of choice for these patients[52,53]. Majority of HRS patients show improvement in creatinine clearance post transplant. However, most patients do not regain normal renal function. Those transplanted with HRS, the incidence of end stage renal disease after 11 year follow up is 10% compared to<1% in those transplanted with normal renal function[52]. Patients with HRS who undergo liver transplantation tend to have more complications, spend more days in intensive care unit and have higher inhospital mortality rates than liver transplanted in patients without HRS[54,55], although long term probability of survival is only slightly lower. The haemodynamic and neuro hormonal abnormalities associated with HRS disappear within the first month after transplantation and patients regain their ability to excrete sodium and free water[56]. Reversal of type-1 HRS by pharmacological treatment before liver transplantation may improve survival after transplantation. Therefore consideration should be given to strategies which can reduce the impact of impaired renal function on long term post transplant survival. The use of calcineurin inhibitor sparing drug regimens or the treatment of HRS prior to transplantation with vasoconstrictors has been suggested.

Prevention: One studies have shown that HRS can be prevented effectively in two specific clinical settings: spontaneous bacterial peritonitis (SBP) and alcoholic hepatitis. The incidence of renal failure is approximately 30% in patients developing SBP. Sort P et al[22] in a study showed that this can be ameliorated by the administration of intravenous albumin in addition to antibiotics (10% in the albumin group Vs 33% in the non albumin group) The mode of action of albumin is thought to be the prevention of further circulatory disturbance[57]. In patients with alcoholic hepatitis, the administration of pantoxifylline (400 mg three times daily) decreases the rate of occurrence of HRS and mortality (8% and 24%) respectively[58]. The mode of action of pantoxifylline is thought to be by the inhibition of TNF-α release, levels of which are elevated in alcoholic hepatitis.

Conclusion

Hepatorenal syndrome is a functional renal failure occurring mainly in patients with advanced cirrhosis and ascites. HRS is the consequence of intense renal vasoconstriction presumably reflex in response to splanchnic vasodilatation. The diagnosis of HRS is essentially one of exclusion. HRS can be prevented effectively in two specific clinical settings like - spontaneous bacterial peritonitis and alcoholic hepatitis. Liver transplantation was the only treatment of HRS in earlier days. With significant advances in past 15 years, it has been shown that pharmacotherapy can reverse HRS and that improvement is maintained despite withdrawal of drugs in majority of patients.

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Clinical problems related to anti-tubercular drug therapy

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Introduction

Tuberculosis is an ancient disease that continues to haunt as we step into next millennium. Tuberculosis is the most common cause of death worldwide due to a single infectious agent in adults and accounts for over a quarter of all avoidable deaths globally. One third of our population is infected with Mycobacterium tuberculosis along with 5 lakhs new cases and 70,000 deaths annually. Bangladesh ranks 5th in disease burden of tuberculosis worldwide. Tuberculosis is the only infectious disease to be declared as a global emergency by WHO.

TB morbidity by country 2000 Bangladesh ranks 5th in tuberculosis disease in the world

Country	Estimated case no.	Case rate/100,000
India	1.85	184
China	1.36	102
Indonesia	0.59	280
Nigeria	0.35	305
Philipines	0.25	330
Bangladesh	0.60	238
Pakistan	0.25	175

Treatment of tuberculosis poses a different clinical problem in special situations like renal insufficiency, liver disorder, pregnancy etc. Sometimes patient develops hypersensitivity to anti-tubercular drugs. Diabetic patients often present atypically and they need special attention. Drug resistance is a growing problem in managing tuberculosis. The emergence of drug resistance has jeopardized the efficacy of control programme and treatment protocols worldwide. The present article highlights the issue and addresses the clinical problems and quarries.

Treatment of tuberculosis in renal insufficiency

Treatment of tuberculosis in renal insufficiency poses a difficult problem as various anti-tubercular drugs are cleared by kidney. British Thoracic Society advocates dose reduction for dugs which are excreted by renal route, while American Thoracic Society prefers increasing the dosing interval instead of decreasing the dose. Administration of drugs which are excreted by kidney should be changed by increasing the dosing interval if the creatinine clearance falls below 30 ml/min.

Rifampicin and isoniazide are eliminated by liver and they can be given in usual dose. Ethambutol is excreted 80% by kidney. So when the CCR is below 70 ml/min the dose of ethambutol should be altered and a dose of 15-20 mg/kg is given 3 times a week. Pyrazinamide is metabolized by the liver, but its metabolites - pyrazinoic acid and 5-hydroxy- pyrazinoic acids are excreted by kidney. Thus to avoid toxicity, the drug should be given three times a week in a dose of 25-35 mg/kg body weight if the CCR is below 30 ml/min. Apart from this, the risk of developing hyperuricemia is increased in case of renal insufficiency. Streptomycin is predominantly excreted by renal route and removed by haemodialysis to a significant extent (about 40%). So it should be given three times in a week in dose of 12-15 mg/kg body weight if the CCR is below 30 ml/min and for those on hemodialysis.

Table 1: Dose recommendation for adults with renal insufficiency (CCR <30 ml/min and on haemodialysis

Drug	Change in frequency	Dose and frequency
Isoniazide	No change needed	300 mg/ day
Rifampicin	No change needed	600 mg/ day
Pyrazinamide	Yes	25-35 mg/kg body weight/dose 3 times a week
Ethambutol	Yes	15-25 mg/kg body weight/dose 3 times a week
Streptomycin	Yes	12-15 mg/kg body weight/dose 3 times a week

Presently there is no data to guide the administration of anti-tubercular drugs in patients undergoing peritoneal dialysis and for this sub-set of patients recommendations as for haemodialysis are applicable. The safest regimen that is advised to new cases of tuberculosis with renal insufficiency is - Rifampicin, isoniazide and Pyrazinamide for 2 months and rifampicin with isoniazide for next 4 months.

Hepato-toxicity in tuberculosis treatment

Effective anti-tubercular therapy is an important step in prevention of tuberculosis. Yet all are potentially hepatotoxic. At least 1-2% of patients develop hepatitis which causes difficulty in management may lead to discontinuation of therapy leading to defaulter.

Table 2: Classification of drugs in relation to hepato-toxicity

Hepato-toxic	Non hepato-toxic
Isoniazide (H)	Ethambutol (E)
Rifampicin (R)	Streptomycin (S)
Pyrazinamide (Z)	Kenamycin, Amikacin
Ethionamide	Cyclosporine
Para-amino salicylic acid (PAS)	Fluoroquinolone

High risk patients for hepato-toxic reaction to anti-tubercular drug

1. Persons more than 35 years age
2. Persons from areas where hepatitis is endemic
3. Postpartum African-American and Hispanic women
4. Persons with -
   a. Alcohol induced liver disease or a history of substance abuse
   b. History of malnutrition or kwashiorkor

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c. AIDS or HIV infected
d. Acute or chronic viral hepatitis
e. Chronic drug consumption (hepatic enzyme inducing drug)

Treatment of patients with liver disorder

The patients with the following conditions can receive short course chemotherapy regimen provided there is no clinical evidence of - chronic liver disease, hepatitis virus carriage, past history of acute hepatitis, excessive alcohol consumption. However hepato-toxicity is more common among those and requires close monitoring.

Established chronic liver disease

Isoniazide, rifampicin along with one or two non-hepatotoxic drug such as streptomycin and ethambutol can be used for total treatment duration of 8 months. An alternative regimen is streptomycin, isoniazide and ethambutol in the initial phase followed by isoniazide and ethambutol in the continuation phase with a total duration of 12 months. Patients with CLD should not receive pyrazinamide. Therefore the recommended treatment regimen is the following - 2SHRE/ 6HR or 2SHE/10SE.

Treatment of tuberculosis during acute hepatitis

Acute Viral Hepatitis: If possible defer anti-tubercular treatment until acute hepatitis has resolved. When it is necessary to treat tuberculosis during acute hepatitis, such as in case of tubercular meningitis, disseminated tuberculosis, miliary tuberculosis, the combination of streptomycin and ethambutol till resolution of hepatitis is the safest option. When hepatitis has resolved, restart the treatment as initially given and the continuation phase of 6 months with isoniazide and rifampicin is appropriate. If the hepatitis persists, streptomycin and ethambutol should be continued for a total of 12 months.

Flow chart for managing hepatitis during anti-tubercular therapy

LFT increased > 2.5 times normal/ Patient clinically icteric/ symptomatic

↓

Stop the anti-tubercular drugs

↓

Do viral markers to exclude viral hepatitis

↓

Repeat LFT in one week

↓

LFT abnormal and treatment resumption essential

↓

Start modified protocol with S, E and Fluoroquinolone

↓

Once LFT returns to normal rechallenge with INH, R and PZA once at a time

↓

Continue treatment with combination ultimately chosen. Duration will be longer than usual short course chemotherapy

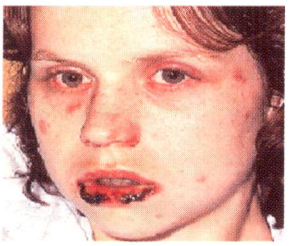
Drug (Anti-tubercular) induced hepatitis : Most anti-tubercular drugs can damage the liver. Pyrazinamide, isoniazide and rifampicin are most commonly responsible. Once decided that it is drug induced hepatitis due to anti-tubercular drugs, all the drugs should be stopped and kept withheld until hepatitis resolves or LFT becomes normal. It is strange but fortunate, that in most cases the same regimen can be re-started without further hepatitis. However a seriously ill patient should be treated with two of the least hepato-toxic drugs, streptomycin and ethambutol until the hepatitis has resolved. A fluoroquinolone may be added to the regimen. Once drug-induced hepatitis has resolved, the same drugs are reintroduced one at a time.

Treatment of tuberculosis in pregnancy and lactation

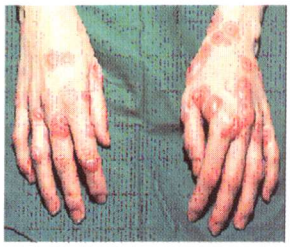
Tuberculosis in pregnant lady may lead to underweight infant or congenital tuberculosis. Risk of miscarriage is much higher in active tuberculosis than in drug treatment. So, standard drug treatment should be given to a pregnant lady with tuberculosis. Treatment regimen for drug sensitive tuberculosis should include rifampicin, isoniazide, ethambutol and pyrazinamide. Streptomycin should not be given due to fetal oto-toxicity. According to WHO, 6 month regimen based upon INH, rifampicin and PZA should be used whenever possible and ethambutol should be given if a 4th drug is needed during initial phase. Women who received rifampicin during pregnancy should be given vitamin K at delivery to avoid post-partum bleeding. All anti-tubercular drugs can be given during lactation except fluoroquinolone because of possible risk of cartilage damage of infant. Women taking oral contraceptives should be counseled for possible contraceptive failure, especially in rifampicin based regimen, as there is increased metabolism of contraceptive drug due to hepatic enzyme induction. Such women should use alternate contraceptive methods.

Hypersensitivity (allergic) reaction due to anti-tubercular drugs

Like many drugs, anti-tubercular drugs may also cause hypersensitivity reactions. This is common in 2nd to 4th week of treatment. More commonly they occur with aminoglycosides like streptomycin, thioacetazone, but less commonly with isoniazide, rifampicin and ethambutol.



Picture 1: Ulceration of the lips & mouth due to anti-TB induced hypersensitivity (Stevens - Johnson syndrome)



Picture 2: Rash (Erythema multiforme major) due to anti-TB induced hypersensitivity

Various degrees of drug reaction are as follows:

1. Mild- itching of the skin only.
2. Moderate- fever with rash. The rash is often mistaken for measles or scarlet fever. If severe the skin looks blistered or resembles urticaria.
3. Severe- in addition to fever and rash, there may be generalized lymphadenopathy, hepato-splenomegaly, peri-orbital swelling and angio-edema. There may be generalized erythema multiforme with ulceration of the mucous membrane of the mouth, genitalia and eyes (Stevens-Johnson syndrome). This is very rare but dangerous reaction, particularly to thioacetazone.

Management

Management is done in two steps- immediate management followed by desensitization if required.

Immediate management

- If only mild itching- oral antihistamine; continue drug treatment as the patient desensitizes himself.
- Fever with rash- stop all anti-tubercular drugs; give antihistamine.

- Very severe reaction -
  - Stop all drugs
  - Hospitalization
  - Inj. Hydrocortisone 200 mg IV or IM stat, or
    Inj. Dexamethasone 4 mg IV or IM until the patient can take oral feeding, then
  - Tab. Prednisolone 40 mg/day; reduce the dose gradually over 2 days depending on patients response.
  - Intravenous fluid
  - Nutritional support
  - Care of bowel, bladder, skin and eye

Desensitization

- It should not begin till hypersensitivity reaction has disappeared.
- Desensitization is done in hospital.
- If possible give two anti-tubercular drugs which the patient did not receive previously.
- Start prednisolone (1-2 mg/kg body weight) 3 days before reintroduction of anti-tubercular therapy; continue up to 2 weeks and then gradually taper off.
- Sccording to IUALTD recommendations, reintroduction should be with one drug after another and with progressively increasing dose.
- The ideal approach is to administer one sixth of the total dose followed by gradual increment of one sixth dose each day. Thus reaching the full dose by one week.
- Once one of the anti-tubercular drugs has been reintroduced in one week, additional drugs are reintroduced each week in the same way.

Tuberculosis with diabetes mellitus

Tuberculosis is 2-7 time more common in diabetic patients. Nearly 30% of diabetic patients have tuberculosis and it has been seen that tuberculosis is the most common (5-9%) complicating illness in diabetes. Atypical presentation is common in diabetes and diagnosis of tuberculosis must be considered when lower zone infiltration or cavitations are seen on chest X-ray. Investigations and treatment of tuberculosis remains the same as in case of non-diabetics. Strict glycaemic control is essential for the successful treatment of tuberculosis. Addition of insulin to the treatment regimen would be a good option for attaining best glycaemic control without causing significant interaction or augmentation of side effects of anti-tubercular drugs. There must be no hesitancy to use steroid along with anti-tubercular therapy if indicated in a patient with diabetes; glycaemic control would then require an increment of dose of hypoglycemic agent.

Management outline of chronic and multi-drug-resistant tuberculosis

The most common cause responsible for development of resistance has been the practice of bad prescription. These include - administration of single drug, inadequate dosage & duration, prescription of drug by unqualified person. The government should ensure adequate drug supply.

Chronic tuberculosis: A patient with tuberculosis who is sputum positive at the end of a standard retreatment regimen with essential anti-tubercular drugs.

Multi-drug resistant tuberculosis (MDR-TB): A patient who has active tuberculosis with bacilli resistant to at least both rifampicin and isoniazide. MDR-TB can rarely be observed in new cases; it is more frequent in re-treatment cases, especially in treatment failure cases.

For treatment of MDR-TB special attention is needed -

- Financial resources.
- Capacity of the NTP to maintain on regular treatment.
- Availability of laboratories that can perform high quality drug susceptibility tests.

Treatment of chronic and MDR-TB with reserve drugs are more expensive and more toxic than with essential drugs.

Table 3: Reserve anti-tubercular drugs

Reserve drug	Mode of action
Amikacin	Bactericidal
Capreomycin	Bactericidal
Kenamycin	Bactericidal
Ciprofloxacin	Bactericidal
Ofloxacin	Bactericidal
Cyclosporine	Bacteriostatic
Para-amino-salicylic-acid (PAS)	Bacteriostatic

Management protocol

- Patient should be isolated in a hospital.
- Treatment should be daily and directly observed.
- Standard treatment regimen include 5/6 drugs including at least 4 drugs that were never used by the patient, including an injectable drug (Amikacin, Capreomycin or Kenamycin) and a fluoroquinolone.
- The initial phase should be at least 6 months and continuation phase of 12-18 months with at least 3 most active and best tolerated drug.

Role of surgery in MDR-TB: Surgical therapy should be considered in patient with MDR-TB who has a poor response or unfavorable prognosis with medical therapy alone.

Conclusion

Compliance with anti-tubercular therapy in an individual patient is difficult to predict and non-compliance represents a major public health hazard. The burden is upon the treating physician to ensure compliance. Program of directly observed therapy can improve compliance and are associated with a lower frequency of secondary drug resistance & relapse.

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Lasers in dermatology : Four decades of progress

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Summary

Advances in laser technology have progressed so rapidly during the past decade that successful treatment of many cutaneous concerns and congenital defects, including vascular and pigmented lesions, tattoos, scars and unwanted hair- can be achieved. The demand for laser surgery has increased as a result of the relative ease with low incidence of adverse postoperative sequelae. In this review, the currently available laser systems with cutaneous applications are outlined to identify the various types of dermatologic lasers available, to list their clinical indications and to understand the possible side effects.

Abbreviations used

- APTD : Argon-pumped tunable dye
- CO2 : Carbon dioxide
- CW : Continuous wave
- Er:YAG : Erbium:YAG
- FDA : Food and Drug Administration
- IPL : Intense pulsed light
- KTP : Potassium titanyl phosphate
- LP : Long-pulsed
- Nd : Neodymium
- PDL : Pulsed dye laser
- PDT : Photodynamic therapy
- QS : Quality-switched
- YAG : Yttrium-aluminum-garnet

Laser history

The term laser is an acronym for light amplification by the stimulated emission of radiation. The first laser was developed by Maiman[1] in 1959 using a ruby crystal. The concept of stimulated light emission was initially introduced by Einstein[2] in 1917. In 1963, Dr. Leon Goldman pioneered the use of lasers for cutaneous applications by promoting ruby laser for various cutaneous pathologies[3-5]. The development of the argon & CW carbon dioxide (CO_2) lasers soon followed and served as the focus of cutaneous laser research during the next 2 decades[6].

Cutaneous laser surgery was revolutionized in the 1980s with the introduction of the theory of selective photothermolysis by Anderson and Parrish[12]. During the past decade extensive advances in laser technology have refined cutaneous laser surgery to the point that it is now considered a first line treatment for many congenital and acquired cutaneous conditions.

Laser principles

The therapeutic action of laser energy is based on the unique properties of laser light itself and complex laser-tissue interactions[13-15]. At certain wavelengths of light, specific absorption of laser energy can be achieved by distinct cutaneous targets. Laser light can be focused into small spot sizes allowing precise tissue destruction. When a laser is used on the skin, the light may be absorbed, reflected, transmitted or scattered. Once laser energy is absorbed in the skin 3 basic effects are possible: photothermal, photochemical or photomechanical effects. The depth of penetration of laser energy into the skin is dependent upon absorption and scattering. Scattering is minimal in the epidermis and greater in the dermis. In general, the depth of penetration of laser energy increases with wavelength. Therefore, on the basis of these principles, laser parameters (wavelength, pulse duration, and fluence) can be tailored for specific cutaneous applications to effect maximal target destruction with minimal collateral thermal damage. Because cutaneous lasers have different clinical applications related to their specific wavelengths and pulse duration, the choice of laser should be on the basis of the individual absorption characteristics of the target chromophore[17,18].

Vascular-specific lasers

Vascular-specific laser systems target intravascular oxyhemoglobin to effect destruction of various congenital and acquired vascular lesions. Lasers that have been used to treat vascular lesions include: Argon (488-514 nm), APTD (577 and 585 nm), KTP (532 nm), Krypton (568 nm), Copper vapor/bromide (578 nm), PDL (585-595 nm), Nd:YAG (532 and 1064 nm).

The flashlamp-pumped PDL was the first laser specifically developed for treatment of vascular lesions based on the principles of selective photothermolysis[12]. The PDL has revolutionized the treatment of many vascular lesions and is considered the laser of choice for most benign congenital and acquired vascular lesions because of its superior clinical efficacy and low risk profile[17]. This laser has been used to successfully treat a variety of vascular lesions such as port-wine stains, facial telangiectases, hemangiomas, pyogenic granulomas, Kaposi's sarcoma and poikiloderma of Civatte[18,19].

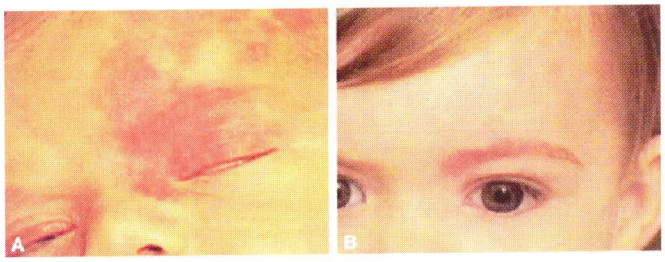

Figure 1: Port-wine stain in infant before treatmet (A) and resolution after 8,585-nm pulsed dye laser treatment (B)

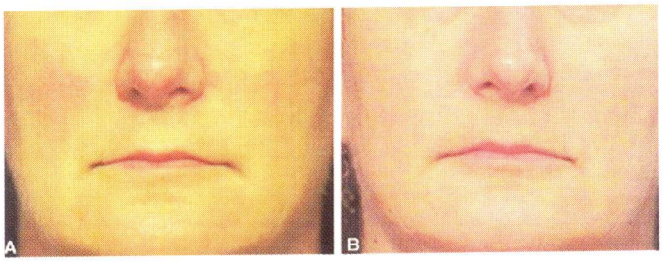

Figure 2: Facial telangiectases before (A) and after (B) improvement with 2 pulsed dye laser treatments

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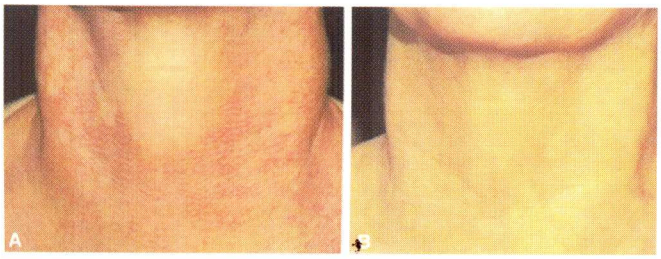

Figure 3: (A) Poikiloderma on neck and chest before treatment. (B) Improvement seen after series of intense pulsed light treatments.

PDL with longer wavelengths (585, 590, 595 and 600 nm) and extended pulse duration have been developed to effect relatively deep tissue penetration.

Laser treatment for hypertrophic scars, keloids

Hypertrophic scars and keloids develop as an abnormal response to cutaneous injury and are characterized by an over abundance of collagen. These types of scars are notoriously difficult to eradicate and have a high rate of recurrence after traditional treatments including surgical excision, dermabrasion, radiation and intralesional therapy[20,21]. Progress in laser technology and refinements in technique have made laser therapy one of the most advantageous modalities for the treatment of hypertrophic scars and keloids. In 1995, Alster and Williams performed the first controlled study of the response of hypertrophic scars and keloids to the PDL on median sternotomy scars.

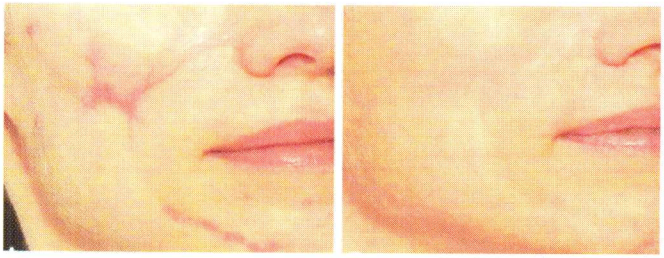

Figure 4: Hypertropic facial scars before (A) and after (B) improved scar color, height, and plability after two 585-nm pulsed dye laser treatments

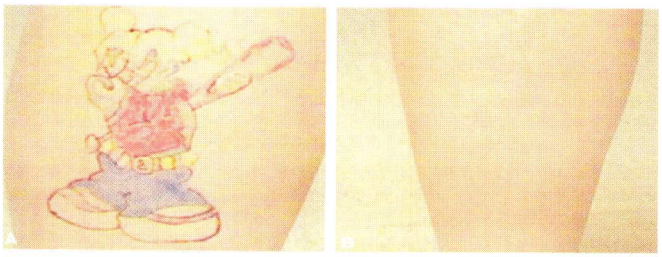

Figure 6: Multicolored professional tatto before (A) and after (B) lesional clearance after 9 treatments with quality-switched 755-nm alexandrite laser (blue/black inks) and 4 treatments with frequency-doubled 532-nm neodymium:yttrium-aluminum-garner laser (yellow/red inks)

Lasers use for the treatment of hypertrophic scars and keloid are CW Lasers (CO_2, 1argon, Nd:YAG) and PDL. The PDL has become a first line treatment for hypertrophic scars and keloids.

Pigment-specific lasers

Melanin-specific, high-energy, QS laser systems can successfully lighten or eradicate a variety of benign epidermal and dermal pigmented lesions and tattoos with minimal risk of untoward effects. Epidermal lesions (solar lentigines, ephelides, cafe´-au-lait macules, and seborrheic keratoses); dermal and mixed epidermal/dermal lesions (melanocytic nevi, blue nevi, nevi of Ota/Ito, infraorbital hyperpigmentation, drug-induced hyperpigmentation, Becker's nevi, and nevus spilus); and amateur, professional, and traumatic tattoos have all been shown to be amenable to laser treatment[22]. Laser systems used for eradication of benign pigmented lesions and tattoos have included not only CW and quasi-CW lasers (argon, CO2, copper vapor, krypton, KTP). But also the 510-nm PDL and various QS systems (532-and 1064-nm Nd:YAG, 694-nm ruby, 755-nm alexandrite). LP laser systems (ruby, alexandrite, 810-nm diode, and 1064-nm Nd:YAG) have also been used to better target some dermal pigmented lesions.

Photoepilation

Excessive hair growth in cosmetically undesirable locations may be the result of a variety of factors, ranging from hereditable causes and endocrine disease to exogenous drug therapy. Until recently, electrolysis was the only method for long-lasting hair removal; however, it is associated with as much as 50% hair regrowth and the potential for scarring and dyspigmentation[23, 24]. Laser systems and IPL sources currently approved by the FDA for the reduction of hair include: LP ruby (694 nm), LP alexandrite (755 nm), Pulsed diode (800 nm), LP Nd:YAG (1064 nm) lasers, IPL (590-1200 nm) sources. LP Nd:YAG laser systems are more effective particularly in patients with darker skin phototypes.

Ablative laser systems

Cutaneous laser resurfacing has experienced unparalleled growth in the field of aesthetic operation during the past decade. High energy, pulsed and scanned CO_2 and erbium:YAG lasers have been in widespread use since the mid-1990s and the success of these lasers in photodamaged facical skin has been well documented[25]. Because of flexibility and low side effect profile, the high energy, pulsed and scanned CO_2 has been considered the gold standard for facial rejuvenation system.

Nonablative laser systems

One of the newest trends in dermatology has been the development of nonablative laser systems. The infrared systems that have been used for nonablative dermal remodeling include: Nd:YAG laser (1320 and 1064 nm), Diode laser (1450 nm), Er:glass laser (1540 nm).

Laser phototherapy

UV phototherapy has long been a mainstay in the treatment of psoriasis. Recently, a 308-nm xenon chloride excimer laser has demonstrated clearing of psoriatic plaques with fewer treatments than traditional narrow-band UVB therapy. The laser only targets the affected areas of the skin, thus sparing the surrounding tissue from unnecessary radiation exposure. The 308-nm excimer laser has also been used to treat problems of dyspigmentation. In a pilot study, Spencer et al[26] demonstrated slight to complete repigmentation in 57% of 23 patches of vitiligo that received at least 6 treatments during 2 to 4 weeks. These results are encouraging because conventional phototherapy often requires months of treatment before improvement is seen. Acne vulgaris is another cutaneous condition amenable to phototherapy. Investigators have reported a decrease in acne lesions after exposure to blue, red, violet, or UV light. The mechanism of action by which blue light is thought to be effective is its absorption by endogenous porphyrins produced by Propionibacterium acnes with subsequent phototoxic effects[27]. More recently, 1450 nm diode lasers have been used to target sebaceous glands in the treatment of acne[30].

Optical imaging

Diagnostic, noninvasive imaging is one of the most exciting developments in laser technology. Confocal scanning laser microscopy allows real-time imaging of tissue in vivo and can provide rapid, high-resolution imaging of skin cytology including the epidermis, microvascular blood flow and inflammatory cells[28]. Potential clinical applications include non invasive skin imaging, detection of tumor margins and diagnosis of lesions without biopsy.

Laser safety

Of paramount importance is the general safety of both the patient and the operating room personnel during laser irradiation. Key laser safety issues include flammability, ocular safety, electric hazards, laser plume and infectious agents and controlled access to the laser suite.

Anesthesia

Most dermatologic laser procedures can be performed without any form of anesthesia. The most commonly used topical anesthetic compounds for cutaneous laser procedures are: EMLA Cream (Lidocain 2.5% & Prilocain 2.5%), Ela-max Cream (Lidocain 2.5%)[31], S-Cain Peel (Lidocain & Tetracain).

Side effects and complications

PDL treatment of port-wine stains, hemangiomas, telangiectases, and vascular ectasias typically result in a variable degree of short-term purpura formation. Pigmented lesions may lighten, darken, or recur after QS laser irradiation. Transient pigmentary alteration is the most common postoperative side effect and may last for several months after treatment. Complications of laser-assisted hair removal using LP lasers are usually minor and transient. The most common adverse reactions include pain during treatment, erythema and perifollicular edema.

Conclusion

Although lasers capable of cutaneous application have been available for more than 4 decades, it has been only within the past several years that their use gained widespread acceptance within the medical field. Lasers have essentially revolutionized cosmetic dermatology, providing safe and reliable means for treating a variety of cutaneous pathologies. With continued research and development, it is expected that new discoveries will continue to emerge leading to significant treatment advances in laser surgery.

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MSD News

Iswargonj UHC: Iswargonj UHC arranged a RTM on 18th November 2008 on "Comparative review on cephalosporin" at the room of UH & FPO. Dr. Mohammad Ieliyas, UH & FPO chaired the session. About 15 doctors attended the meeting.

Bhaluka UHC: A RTM was arranged by Bhaluka UHC on "Common skin problems in outdoor" on 17th November 2008 at the conference room. Dr. M. Shajahan, UH & FPO was present as the chairperson. About 20 doctors enjoyed the meeting.

Boxigonj UHC, Sherpur: Boxigonj UHC, Sherpur arranged a RTM on "Common skin problems in outdoor" on 27th October 2008. Dr. Siddeshar Saha, UH & FPO was present as the chairperson of the occasion. About 15 doctors attended the meeting.

Rajshahi

Orthopaedic Department, RMCH: Department of Orthopaedic, RMCH arranged a RTM on 24th December 2008 on "Habitual dislocation of patella & its management" at Nanking Chinese Restaurant. Professor Dr. B. K. Dam, Head of the Department chaired the meeting. Dr. Imam Gaziul Haque, Assistant Professor; Dr. Debasis Roy, Consultant; Dr. Poli Dam were the special guests and Dr. Md. Abdur Rahman, IMO was the keynote speakers. About 40 doctors enjoyed the seminar.

Mohonpur UHC: On 21st December 2008, Mohonpur UHC, Rajshahi arranged a RTM on "Role of omeprazole" at the seminar room. Dr. Sajedur Rahman, UH & FPO was present as the chairperson. About 20 doctors attended the meeting.

Health Camp (HC)

Saidpur Kuchiamara, Sreenagar: A health camp was arranged on 14th November 2008 at Saidpur Kuchiamara, Sreenagar, Munshigonj. The health camp was chaired by Professor Dr. Jalal Uddin and 12 other doctors were present. About 300 patients were treated on that day.

Launching of New Products

Combivit injection

Vitamin B-complex injection

...meets the parenteral nutrition

Orion introduces Combivit injection; each 2 ml injection contains Thiamine Hydrochloride BP 50 mg, Riboflavin BP 4 mg, Pyridoxine Hydrochloride BP 10 mg, Nicotinamide BP 100 mg, D- Panthenol USP 5 mg. Combivit injection contains the most important members of the vitamin B group in pure form and in therapeutically balanced proportions. The members of the vitamin B group contained in Combivit injection are components of enzyme systems that regulate various stages of carbohydrate, fat and protein metabolism, each of the components playing a specific biological role. Deficiency of vitamin B causes glossitis, stomatitis, cheilosis, beriberi, pellagra and vascularization of cornea. Combivit is indicated for prophylactic or therapeutic nutritional supplementation in physiologically stressful conditions. These include: condition causing depletion or reduced absorption or bioavailability of essential B-vitamins manifested by glossitis, stomatitis, cheilosis, beriberi and polyneuritis, the maintenance of normal growth and health during the early days of children, apathy and anorexia in elderly patients, prevention of vitamin deficiencies particularly when depletion is suspected, pregnancy and lactation, patients on restricted diets. Combivit injection is for intramuscular or intravenous administration. Usual recommended dose is 2 ml (1 ampoule) daily. Combivit injection is presented in a box containing blister pack of 2 X 5's ampoules. MRP of Combivit injection is Tk. 4.00/ ampoule.

Baclon

Baclofen BP 10 mg tablet

Managing life in motion

Orion Laboratories Ltd. has launched Baclon tablet containing Baclofen BP 10 mg per tablet. Baclofen is approved by USFDA for management of both Spasm and Spasticity. Baclon, an analogue of gamma-aminobutyric acid, is a centrally acting skeletal muscle relaxant. Baclofen is an active spasmolytic and acts as a GABA agonist at $GABA_B$ receptors. Baclon is indicated for long term management of Spasm and Spasticity in various pathphysiological conditions like injuries, Cerebrovascular disorders, Musculoskeletal disorders. Baclon is also indicated as in adjunct management for neurogenic bladder, in management of refractory trigeminal neuralgia. Baclofen is superior to commonly used muscle relaxants such as Diazepam, Dantrolene, Tolperisone, Tizanidine. The optimum dosage in adult generally ranges from 30 mg to 80 mg in 3 divided doses daily. Treatment should be always initiated with small, gradually increasing dosages. Therefore, treatment should be started with doses of 5 mg three times daily, increasing every 3 days by 5 mg 3 times daily until an optimum response is achieved. Upto 200 mg daily dose has been used for the control of severe spasticity in patients with spinal cord lesions although doses of more than 100 mg per day are not generally recommended. For children, treatment should usually be started with a very low dose, e.g. 0.3 mg/Kg daily in 4 divided doses. The recommended daily maintenance doses are: 12 months to 2 years: 10 to 20 mg; 2 to 6 years: 20 to 30 mg; 6 to 10 years: 30 to 60 mg. Baclon is supplied in a box containing 3 X 10 tablets in blister strip. MRP of Baclon is Tk 8.00/ tablet.

Medi News

Nobel prize in physiology or medicine 2008

Harold Zur Hausen

Francoise Barre-Sinoussi

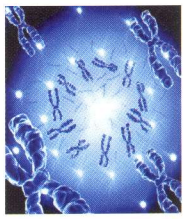
Luc Montagnier

Looking back over the two discoveries rewarded with the 2008 Nobel Prize in Physiology or Medicine reveals two different timelines for discovery research. One, Harald zur Hausen's realization that subtypes of a virus that produces harmless warts can also lead to cervical cancer, took a decade of work to prove, initially against a backdrop of considerable skepticism. The other, Françoise Barré-Sinoussi and Luc Montagnier's identification of the virus associated with AIDS, occurred within just a few months amid a flurry of global research activity directed to finding the cause of the then-new epidemic. Harald zur Hausen's suggestion that human papilloma virus (HPV) infection might lie behind cervical cancer flew in the face of general opinion in the early 1970s, which held that another commonly present virus, herpes simplex virus, might be the cause. Realizing that there were a multitude of different HPV subtypes, and hypothesizing that unknown subtypes might cause the cancer, zur Hausen's group began a painstaking search for such novel viruses. By the early 1980s they found novel viruses in genital warts. Their subsequent identification of two novel HPV subtypes in cervical cancers formed the essential piece of evidence linking HPV infection to the onset of the disease. Françoise Barré-Sinoussi and Luc Montagnier's discovery of the virus that later came to be known as human immunodeficiency virus (HIV) occurred just two years after the first reports of cases of what we now know as AIDS. An infective agent was suspected by many to cause the disease, and they decided to test whether it might be a so-called retrovirus. Retroviruses are relatively uncommon among the viruses that infect humans and rely on the host's cellular machinery to make their viral DNA. The gamble proved correct; their studies revealed retroviral activity in cells taken from a patient's lymph nodes, and demonstrated that virus from these cells could infect and kill white blood cells. Within the year, Barré-Sinoussi and Montagnier had isolated HIV from several patient groups.

nobelprize.org

Gene behind childhood anemias found

Scientists have identified a gene mutation that inhibits the production of fetal hemoglobin and causes two life-threatening anemias -- sickle cell disease and thalassemia. The finding could eventually lead to new treatments that could restore some hemoglobin production, turning these life-threatening diseases into manageable chronic conditions. "We have identified a gene that directly silences the fetal hemoglobin gene," said lead researcher Dr. Stuart Orkin, an investigator at the Howard Hughes Medical Institute and Children's Hospital Boston. "The regulation of fetal hemoglobin is probably the most important modifier of the severity of sickle cell anemia and thalassemia." Targeting that gene could be the key to treating both diseases, Orkin said. "We now have a target that if we could modulate it directly, we could increase fetal hemoglobin and reverse the silencing and reawaken the fetal gene in an adult," Orkin said. "That would have tremendous therapeutic implications in both of those disorders." While he does not see such treatment as a cure, "it would certainly be a very effective treatment," Orkin said. The report was published in the Dec. 4 online edition of Science. In an earlier study, Orkin's team identified five gene variants involved in hemoglobin production and the severity of disease in 1,600 people with sickle cell anemia. They identified one variant that had the most effect on hemoglobin in a gene called BCL11A, located in chromosome 2. In the current study, the researchers show that BCL11A directly blocks the production of hemoglobin. To prove the connection, Orkin's group blocked BCL11A and red blood cells started producing large amounts of hemoglobin. Hemoglobin is a protein in red blood cells that transports oxygen throughout the body. In sickle cell disease, there is an abnormality in hemoglobin that makes red blood cells stiff and sickle-shaped. In thalassemia, the ability to produce hemoglobin is severely compromised. Both diseases result in anemia that can range from mild to life-threatening. Sickle cell disease can cause severe pain and eventual organ damage. Treating thalassemia requires frequent blood transfusions and then chelation therapy, which gets rid of excess iron that can lead to organ failure. At birth, fetal hemoglobin makes up between 50 percent to 95 percent of a child's hemoglobin before switching to adult hemoglobin production. The fetal hemoglobin may be an adaptation to the low oxygen in the fetal environment. Fetal hemoglobin has a higher affinity for oxygen, allowing it to take oxygen more easily from the mother. Dr. Cage S. Johnson, director of the Comprehensive Sickle Cell Center at the University of Southern California Keck School of Medicine, agreed that this finding will lead to new therapies. "This research adds to our understanding of the genetic mechanisms underlying gamma-globin production," Johnson said. "Increased understanding of the genetic control of globin will provide the basis for gene therapy of these disorders. This research is another step in the process of developing gene therapy."



Health Day

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Zinc intervention programs can help achieve the Millennium Development Goals

The United Nations agencies have recently proposed Millennium Development Goals (MDGs). Zinc intervention programs can help to achieve all of the four health-related MDGs:

MDG 1: Reduce extreme poverty and hunger: The target that has been set for reducing hunger is to decrease the prevalence of children aged less than 5 years who are underweight. Zinc deficiency is one of the major causes of growth retardation and zinc intervention programs have repeatedly found increased growth of underweight children. Therefore, zinc supplementation can help to reduce the prevalence of underweight children. *MDG 4:* Reduce child mortality: Zinc supplementation substantially reduces the rates of diarrhea and pneumonia, which are the most common causes of death among children in developing countries. Therefore, interventions to enhance the zinc intake of children in low-income countries are a useful strategy for reducing child mortality rates. *MDG 5:* Reduce maternal mortality: Zinc deficiency can result in protracted labor, which increases maternal mortality rates and adversely affects the fetus. Therefore, improving the zinc intake of women before and during pregnancy may help to reduce maternal mortality and benefit infant growth and survival. *MDG 6:* Combat HIV/AIDS, malaria and other diseases: There is evidence that zinc supplementation may reduce the severity of malaria. In addition, zinc supplementation of HIV-positive children reduces their risk of both diarrhea and pneumonia, which frequently complicate HIV infections. Therefore, zinc supplementation may reduce fatalities from these diseases.

IZiNCG secretariat, Program in International Nutrition, University of California

Zinc therapy for diarrhoea increased the use of oral rehydration therapy and reduced the use of antibiotics in Bangladeshi children

Abdullah H. Baqui, Robert E. Black, Shams El Arifeen, Mohammad Yunus, K. Zaman, Nazma Begum, Amira A. Roess, Mathuram Santosham

Abstract

Excessive use of antibiotics for diarrhoea is a major contributing factor towards increasing rates of antimicrobial resistance in developing countries. Zinc therapy for diarrhoea has been shown to be beneficial in controlled efficacy trials, and it is of interest to determine if availability of zinc syrup for treatment of diarrhoea would satisfy the demand for a `medicine' for diarrhoea, thus reducing the use of antibiotics, without competing with the use of oral rehydration therapy (ORT). This community-based controlled trial was conducted from November 1998 to October 2000, and all children aged 3-59 months in the study area were included. In this trial, the availability of zinc supplements, along with ORT and appropriate education programmes, was associated with significantly higher use of ORT and lower use of antibiotics.

J health popul nutr. 2004 Dec;22(4):440-442

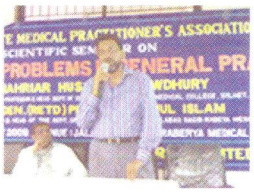
Medical Services Department (MSD) of ORION Laboratories Ltd. successfully arranged significant number of Round Table Meetings, Scientific Seminars, Intern Doctors Reception Programs, Health Camp in different venues of all over Bangladesh during August to December 2008.

Scientific seminar (SS)

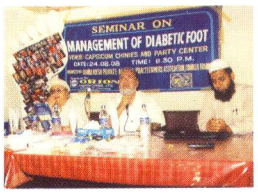
NITOR, Dhaka: On 17th December 2008, National Institute of Traumatology & Orthopaedic Rehabilitation (NITOR), arranged a Scientific Seminar on "Spasticity management" at the Conference Room-1. Professor Dr. Sk. Nurul Alam, Director, NITOR chaired the seminar. Professor Abdul Awal Rizvi, Academic Director; Professor M. A. Samad, Green Unit-1 and Professor Md. Sajjad Husain, Violet unit-1 were in the Panel of Experts. Dr. G. M. Shahidul Islam, Assistant Registrar, Blue Unit-1, was the keynote speaker. About 100 doctors enjoyed the seminar.

Department of Cardiology, SSMCH: Department of Cardiology, SSMC & Mitford Hospital arranged a scientific seminar on 13th November 2008 on "Use of lipid regulating dugs in cardiovascular diseases" at the seminar room. Professor Syed Azizul Haque, Professor & Head of the Department chaired the meeting. Dr. Anisur Rahman Khan, Assistant Professor was present as the Moderator and Dr. K. Asaduzzaman was the Keynote Speaker. About 50 doctors attended the seminar.

CCU, DMCH: Coronary Care Unit (CCU), DMCH arranged a scientific seminar on "Use of lipid regulating drugs in cardiovascular diseases" at the class room of CCU on 29th October 2008. Professor H. I. Lutfur Rahman Khan, Head of the Department chaired the session. Dr. Md. Faruque, Associate Professor; Dr. Md. Abdus Salam, Associate Professor; Dr. Mahibur Rahim, Associate Professor; Dr. Md. Serajul Haque, Assistant Professor; Dr. M. Shomsher Ali, Assistant Professor and Dr. A. E. M. Mazharul Islam, Assistant Professor of Cardiology were present as the Panel of Experts on that seminar. About 50 doctors enjoyed the session.



BPMPA, Sylhet: Bangladesh Private Medical Practitioners Association (BPMPA), Sylhet arranged a scientific seminar on 27th August 2008 on "Common skin problems in general practice" at the lecture gallery of JRRMCH, Sylhet. Major General (Retd.) Professor Dr. Md. Nazmul Islam, Principal, JRRMCH chaired the meeting. Dr. Azizur Rahman, President, BPMPA, Sylhet was the Chief Guest and Dr. Shahriar Hussain Chy, Associate Professor, Dept. of Dermatology, North East Medical College, Sylhet was the Keynote Speaker. About 175 private practitioners of Sylhet attended the scientific seminar.



BPMPA, Comilla: Bangladesh Private Medical Practitioners Association (BPMPA), Comilla arranged a scientific seminar on 24th August 2008 on "Management of diabetic foot" at Capsicum Chinese Restaurant and Party Centre, Comilla. Dr. Zobaida Hannan chaired the seminar and Dr. M. S. Alam, Senior Consultant (Rtd.) was the Chief Guest. Dr. Tawfiqun Nabi Khan, Secretary, BPMAPA, Sylhet was present as the Rapporteur and Dr. Mahbub Murshed, Consultant (Surgery), Diabetic Hospital, Comilla was the keynote speaker. About 60 doctors of Comilla Private Medical Practitioners enjoyed the session.

Round Table Meeting (RTM)

Dhaka

Sreenagar UHC, Munshigonj: On 11th November 2008, Sreenagar Upazilla Health Complex, Munshigonj arranged a RTM on "Common skin problems in outdoor" at the UHC Seminar Room. Dr. Lokman Hakim, UH & FPO chaired the meeting and Dr. Prodip Biswas was present as the Chief Guest. About 25 doctors attended the session.

Hepatology Department, BSMMU: Department of Hepatology, BSMMU arranged a RTM and iftar party on "Role of ceftriaxone to treat various infections" on 23rd September 2008. Dr. Fakuruddin, Consultant, Dept. of Hepatology chaired the meeting. About 45 doctors attended the occasion.

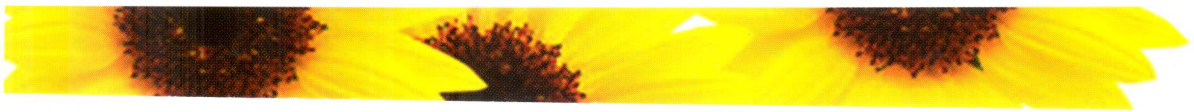
Medicine Unit-3, SSH: A round table meeting was arranged by Medicine Unit-3 of Shahid Shuhrawardy Hospital on 24th September 2008 on "Fluid management of dengue fever" at the conference room. Dr. Kamal Syed Ahmed Chowdhury, Head of Medicine Unit-3 chaired the seminar and Dr. M. Kanruzzaman Mazumder, HMO, was the keynote speaker. About 35 doctors enjoyed the meeting.

Neurosurgery Department, BSMMU: On 21st September 2008 a RTM and iftar party was arranged by the Department of Neurosurgery of BSMMU on "Role of ceftriaxone to treat various infections". Professor Aftabuddin, Chairman, Dept. of Neurosurgery chaired the meeting. About 45 doctors attended the occasion.

HCDP, South Bashabo: A RTM was arranged by HCDP, South Bashabo on 21st December 2008 on "Use of lipid regulating drugs on Diabetes Mellitus" at China Park Chinese Restaurant, Khilgaon. Dr. Arun Chandra Singh, Centre Director was the chairperson of the occasion. About 8 doctors enjoyed the session.

Probin Hospital, Agargaon: Probin Hospital, Agargaon, Dhaka arranged a RTM on 27th December 2008 on "Nutritional supplements in different age group" at the Conference Room. Dr. Sk. Lutfur Rahman, Director, Probin Hospital was the chairperson of the occasion. About 20 doctors attended the meeting.

Rest of MSD news at page- 628



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