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Editor's Choice

The Orion Medical Journal is celebrating fifteen years of trust and service to the medical community of Bangladesh. This enormous achievement is possible because of vigorous effort of our valued authors and boundless contribution of the respective members of the Advisory & Review Board. The Orion also accredits its esteemed reader and well-wishers for enduing such immense asseveration. This medical journal is exclusively emphasizing the local research work and endorsing national diseases with native treatment protocol. In this issue we published two Original Articles, two Review Articles and four Case Reports with adequate references. Latest and breakthrough news of modern Medical Science are also incorporated.

Editorial (P-02) of this issue focuses on the simplified diagnostic criteria with five step management of migraine headache. This editorial serves as an introduction to current accepted therapeutics for migraine treatment and an overview of pharmacological prophylaxis in the modern management of migraine.

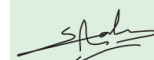
The first original article (P-10) reviews the infection rate among 30 patients, who underwent percutaneous kirschner-wire fixation for open Colle's fracture. "Association of Chlamydia trachomatis infection in females with tubal factor infertility" - the second Original Article (P-13) demonstrate genital C. trachomatis infection as the single most common cause of tubal potential damage.

First review article nicely sketches 'Danazol' as an effective agent in the treatment of aplastic anemia where treatment expense appears to be the primary factor in the third world country like Bangladesh. "Danazol as a first line therapy in Aplastic Anemia" - establishes Danazol, an effective drug for the treatment of aplastic anemia who could not afford the treatment cost of bone marrow transplantation or injection ATG and or cyclosporine. In the astounding second review article "Pitfalls of National Tuberculosis Control Program (NTP) in Bangladesh" illustrates relapse and failure cases of tuberculosis through DOT, increasing day by day. Some recommendations were drawn by the author in this regard.

Surgical management of a 32 years, married woman with Atrial Septal Defect and Severe Pulmonary Hypertension explained in a very fascinating case report (P-23). The second case report (P-27) stands with a story of a pregnant woman with Systemic Lupus Erythematosus (SLE). "Acute Inversion of Uterus" - an interesting case (P-29) also incorporated in this issue. In the last case report (P-30) an uncommon malignant soft tissue tumor, Rhabdomyosarcoma of the uterus of 72 years widow has been illustrated.

With Volume: 15, Issue: 1, No. 38, the Orion accomplishes the choice of thousand readers nationally and also in the international arena. Every effort has been made to make this issue interesting. We thank all our readers and reviewers for their continuous support. At the same time we expect your valuable opinion and suggestions to make "The Orion" medical journal ameliorated steadily.

May the Almighty bless in the spirit of good health.



DR. MD. SHAFIUR RAHMAN
Chief Editor
The ORION Medical Journal

Migraine headache: an overview

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Abstract

The history of headache can be traced almost to the beginning of the history of humankind. Among the many causes of it, migraine headache is a debilitating disorder affecting millions of people in the United States and worldwide. The diagnosis of migraine can significantly affect quality of life, health care costs and daily productivity. Hundreds of trials and many guidelines have documented various approaches to migraine management, whether via acute treatment or chronic migraine prophylaxis. Acute or abortive migraine management encompasses specific and nonspecific migraine therapeutics including non-opioid and opioid analgesics, triptans and ergotamines. Prophylactic migraine management data span the pharmacological spectrum from antiepileptic and antihypertensive agents to botulinum toxin type A. Special considerations for migraine management also must be applied in various populations including children, pregnant women and the elderly. Although hundreds of clinical trials are available regarding migraine treatment modalities, this review serves as an introduction to current accepted therapeutics for migraine treatment and an overview of pharmacological prophylaxis in the modern management of migraine.

Introduction

Headache affects nearly everyone at least occasionally and it is among the most common reasons that patients seek medical attention.¹ Migraine is an important cause of it and an estimated 187,000 attacks are experienced every day, and almost 90,000 people are absent from work or school because of migraine every working day² and approximately 13 million

visits each year in the United States to physicians' offices, urgent care clinics and emergency departments with headache disorders.³ Migraine occurs in 12-15% of the UK population, in women more than men in a ratio of 3:1.⁴ WHO ranks migraine in its top 20 disabling conditions. It is estimated that migraine costs the UK almost £2 billion a year in direct and indirect costs.⁵

Diagnosis

Migraine (with and without Aura) are diagnosed on the basis of diagnostic criteria proposed by International Headache Society in 'The International Classification of Headache Disorders'.⁶

Diagnostic Criteria

Simplified Diagnostic Criteria for Migraine is repeated attacks of headache lasting 4-72 hrs in patients with a normal physical examination, no other reasonable cause for the headache and: At least 2 of the following features:

1. Unilateral pain
2. Throbbing pain
3. Aggravation by movement
4. Moderate or severe intensity

Plus at least 1 of the following features:

1. Nausea/vomiting
2. Photophobia and phonophobia.

Investigations

Patients with migraine often do not require to perform investigations unless the history and neurological findings are suggestive of structural disease. Occasionally neuro-imaging may be required on an individual basis if a patient is disabled by fear of serious pathology and in most cases, CT scan and MRI are equally sensitive.⁵

Management

A stepped approach to migraine management consists of avoidance of any precipitating factors together with symptomatic and prophylactic treatment and assurance as well.³ During acute attacks, many patients find it helpful to rest in a quiet, darkened room until symptoms subside. To prevent medication overuse, use of simple analgesics should be limited to 15 days or less per month and combination analgesics should be limited to less than 10 days per month³. Successful treatment of migraine involves 5 steps:⁸

Step 1

An accurate clinical diagnosis based on the IHS criteria with full neurologic examination during the first visit.

Key words: Migraine headache

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Step 2

A disability assessment to quantify the extent of disability on the first visit as well as follow-ups.

Step 3

Step 3 consists of stratified care for the acute treatment of headache. Patients who have mild symptoms and disability can be adequately treated with acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), propoxyphene or a combination of these. Acute treatment is most effective when given within 15 minutes of pain onset and when pain is mild.¹⁰ Patients with moderate disability need migraine-specific oral medications. The 2 categories of such

medications are triptans and ergot alkaloids. The specific triptans are sumatriptan, rizatriptan, zolmitriptan, naratriptan, almotriptan, eletriptan, and frovatriptan.¹¹ Patients with severe headaches need oral, subcutaneous or intravenous formulations of these drugs. Patients with severe nausea and vomiting at the onset of an attack may respond best to intravenous prochlorperazine. These patients may be dehydrated and adequate hydration is necessary.

Approximately 40% of all attacks do not respond to a given triptan or any other substance. If all else fails, an intractable migraine attack (**status migrainosus**) or an attack lasting longer than 72 hours should be addressed in an urgent care or emergency department. In rare cases, patients may need to be hospitalized for a short period and may need to be treated with intravenous valproate or dihydroergotamine (subcutaneously/intramuscularly/intravenously) for a few days¹²

Step 4

Step 4 is to individualize treatment on the basis of the patient's profile. No two patients with migraine are the same. Each patient has a unique psychosocial environment that heavily influences his or her treatment.

Step 5

Step 5 is patient education, which is key to successful long-term management. It includes teaching the patient to avoid trigger-factors that precipitate a migraine attack (eg, lack of sleep, fatigue, stress, certain foods, use of vasodilators) and a lifestyle change at some level.

Emergency treatment at home

This usually falls to general practitioners. If an effective therapy has not been established previously, the options are: intramuscular diclofenac 75mg (not pethidine) and/or intramuscular chlorpromazine 25-50mg (potent antiemetic and sedative). Early follow-up is recommended.

Treatment of recurrence within the same attack after initial home treatment

Symptomatic medications (steps one and two) may be

repeated within their dosage limitations. In the case of triptans, there is evidence of efficacy of a second dose for recurrence but no evidence that it is the most appropriate treatment. There is informal evidence that repeated dosing with these drugs quickly gives rise to repeated rebound, perhaps over several days. Instead diclofenac may be tried where recurrence is usual and expected. DHE or ergotamine may be useful for this purpose but safety and efficacy have not been formally established; they should not be used within 12 hours after any triptan.

Patients who consistently experience recurrence

There is some evidence that this occurs more in those whose untreated attacks last longer than 24 hours. Naratriptan may be the triptan of choice. Ergotamine has a prolonged duration of action and trials suggest that it is associated with significantly less recurrence.

Long-duration migraine

Migraine lasting longer than 3 days is uncommon.

Apparently long-duration attacks may be migraine with a superseding tension-type headache for which naproxen or diclofenac are preferable to specific anti-migraine drugs.

Status migrainosus is extremely rare. Multiple recurrences with repeated doses of a triptan are now a well-recognised complication and correct management is withdrawal of triptan. Diclofenac should be used until symptoms settle. Patients who show susceptibility to this problem should try ergotamine instead, but be very cautious in repeating the dose.

Slowly developing migraine

Some patients develop attacks slowly and are initially uncertain whether a headache is migrainous or not. If treatment is required at this stage, simple analgesics are recommended and may prevent further development. Triptans should not be used, if at all, until it is certain that the headache is migrainous (there is some evidence that delayed use of triptans does not significantly impair their efficacy).

Migraine in pregnancy and lactation

Paracetamol in moderation is safe throughout pregnancy and breastfeeding. Aspirin is safe except near to term. For nausea, prochlorperazine is unlikely to cause harm throughout pregnancy and lactation. Metoclopramide and domperidone are probably safe in second and third trimesters.

PREVENTION OF HEADACHE DISORDERS

Migraine prophylaxis is rewarding to some extent and when indicated, prophylactic therapy is used in addition to, not instead of, acute therapy.

Indications¹³

Therapy to prevent migraine is indicated if

- (1) the patient has more than 2 migraine attacks per month,
- (2) the patient has single attacks that last longer than 24 hours,

- (3) the headaches cause major disruptions in the patient's lifestyle,
- (4) abortive therapy fails or is overused,
- (5) the patient has complicated migraine and
- (6) Over-frequent use of acute therapy.

Goals of preventive therapy

The goals of preventive therapy are:

- (1) to reduce attack frequency, severity, and/or duration,
- (2) to improve responsiveness to acute attacks, and
- (3) to reduce disability.

Classes of Migraine Prophylaxis

There are 3 classes of medications that are effective for migraine prevention -antiepileptics, antidepressants, and antihypertensives. Botulinum toxin A may be another effective medication^{13,14}

First-line prophylactic drugs

Beta-adrenergic blockers without partial agonism, propranolol, metoprolol, atenolol etc if not contraindicated.¹⁵ Cardiospecificity and hydrophilicity both improve the side-effect profile and are to be preferred. Once-daily dosing is associated with significantly better compliance. On these grounds, bisoprolol 5-10mg od may be the beta-blocker of choice. Sodium valproate 0.6-2.5g daily¹⁶

Pizotifen 1.5mg daily is sedative and should be taken at bedtime.

Amitriptyline 10-150mg daily, usually at night, is first-line prophylactic when (a) migraine coexists with tension-type headache (b) there is associated depression; or (c) there is disturbed sleep. It may be used concomitantly with a beta-blocker as second-line. Desipramine, nortriptyline, protriptyline etc may also be used.

Second-line prophylactic drugs

Methysergide 1-2mg tds

Beta-blocker and amitriptyline together used in prophylaxis but with limited efficacy. Calcium channel antagonists are of uncertain value. Verapamil modified release, 120-240mg bd is well tolerated, with headache sometimes a side-effect. Clinical trials evidence of efficacy is limited.

Selective serotonin reuptake inhibitors are second-line to tricyclics. Fluoxetine 20mg alter die to 40 mg od is best studied. Clinical trials evidence of efficacy against migraine is inconclusive (against depression, its efficacy in higher doses is established).

Prophylaxis for hormone-related migraine

An effect of hormones on migraine is common, and greater for migraine without aura. Empirical evidence suggests oestrogen withdrawal triggers migraine in some women¹⁷

Menstrual migraine, defined as attacks of migraine without

aura that occur regularly on day 1 of menstruation + 2 days and at no other time, is rare¹⁸. Correct diagnosis of menstrual migraine is essential for successful hormonal management. The diagnosis is clinical and confirmed by diary card evidence over three months.

Depending on need for contraception, several options can be tried in whatever order seems appropriate. Prophylaxis should be tried for a minimum of three cycles at maximum dose before it is deemed ineffective.

A) Non-hormonal prophylaxis does not depend on regular menstruation. Mefenamic acid 500 mg tds-qds can be given from the onset of menstruation until the last day of bleeding. It is recommended as first-line in migraine occurring with menorrhagia and/or dysmenorrhoea.

B) Hormones for menstrual migraine are supplements: if the woman has an intact uterus and is menstruating regularly, no progestogens are necessary. oestradiol 1.5 mg in 2.5g gel is applied daily from day-3 for 7 days.

C) Combined oral contraceptives (COCs) and injectable depot progestogens inhibit the ovarian cycle. Migraine in the pill-free interval is most notable with high-progestogen contraceptives¹⁹ Oral progestogen-only contraception does not inhibit ovulation.

Migraine and hormonal contraception

Headache is a common side-effect of COCs and many women report onset of migraine after starting them. Others report improvement of pre-existing migraine²⁰. There is concern that migraine and COCs are both independent risk factors for stroke in young women, in the latter case related to the ethinylloestradiol component. This has led to the development of opinion-based recommendations for the use of COCs in migraineurs.²¹ although not all experts agree.

Progestogen-only contraception is acceptable with any type of migraine contraindicating synthetic oestrogens. The progestogen-only pill has a higher failure rate but Depo-Provera and the Mirena intrauterine system both have lower failure rates than COCs. Women can switch immediately from COCs to progestogen-only contraception.

Migraine in pregnancy and lactation

Most women with migraine improve during pregnancy. If not, prophylactics should be restricted but, when necessary, propranolol has best evidence of safety during pregnancy and lactation.²²

Women should be counselled with regard to the relative risks and benefits.

Migraine and hormone replacement therapy (HRT).²³ Hormone replacement therapy is not contraindicated After hysterectomy, oestrogen implants are an option.

Duration of use

There is no good guide for what should be the minimum period but once a drug has been found to help, it should be continued for several months. If the patient remains headache-free, the dose can then be tapered and the drug eventually withdrawn. Uninterrupted use over a year or longer is rarely appropriate. Prophylactic drugs that are apparently not effective should not be discontinued too soon or patients must not be labeled non-responders prematurely. and 3 cycles in the case of specific therapy for hormone-related migraine. Patients should be discouraged from stopping too soon unless they have unacceptable side-effects.²³

If prophylaxis fails

If prophylaxis fails, review diagnosis, compliance (often poor) and concordance (often very poor, especially with multiple daily doses). Review other medication, especially for medication overuse. Consider combinations if any. If prophylaxis still fails to have measurable benefit, discontinue it.⁶

Referral: When to Refer a patient with migraine are:³

- Frequent migraines not responsive to standard therapy.
- Migraines with atypical features.

Conclusion

A stepped approach for acute treatment of migraine is required since it is associated with significant disability and is often undertreated. Medication overuse results in the development of chronic daily headache. The risks of medication-overuse headache should be discussed with all patients when initiating acute treatment for migraine. Stopping medication-overuse may result in improvement in headache frequency and severity. The great frequency of migraine-headache in clinical practice coupled with a very low relative incidence of serious causes makes it difficult to maintain an appropriate level of suspicion. If it is approached with a standard operating procedure that supplements history with fundoscopic examination, brief but comprehensive neurological examination and the use of diaries to record headaches, associated symptoms and medication use and an awareness of the few important serious causes, errors should be avoided. Clinician's review and analysis of a prospective diary that records headache symptoms over a few weeks can improve management.

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Infection rate of percutaneous Kirschner-Wire fixation for Open Colle's fracture

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Abstract

Records of 13 men and 17 women aged 35 to 80 yrs (average 57 yrs) who underwent open reduction and percutaneous kirschner wire fixation for open unstable colle's fracture. Each fracture was fixed with 2 - 3 kirschner-wires of 1.8 mm diameter, kirschner wires left protruding through the skin for easy removal with their ends bent outside the skin to prevent migration. The wounds were cleaned through surgical toileting and wound debridement. There was one patient who presented with partial radial artery injury (longitudinal) contused and suture done with 6-0 vicryl. The wound was left open for 2-3 days and later delayed primary suture done.

Purpose

To review the infection rate in 30 patients, who underwent Percutaneous kirschner wire fixation for open Colle's fracture.

Introduction

Colle's fractures are more common in post menopausal osteoporotic women and old aged men. Extraarticular fractures are more common than intraarticular fractures.¹ The wound was cleaned through surgical toileting and open reduction and kirschner-wire fixation done.

The kirschner wires passing through styloid process from distal fragments to the medial border of proximal fragments,² and another kirschner wires passing through distal to the proximal fragment centrally.³ It is a common practice to leave kirschner wire protruding through the skin for easy removal. We reviewed the infection rate in 30 patients, who underwent open colle's fractures and fixation by percutaneous Kirschner wire.

Key words: Colle's fracture, Kirschner-Wire, Percutaneous fixation

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Materials and Methods

This prospective study was done between April 2008 and March 2009. Records of 13 men and 17 women aged 35 to 80 yrs (average 57yrs) were considered, who underwent open reduction and percutaneous kirschner wire fixation.

At first each fracture was cleaned through surgical toileting and debridement done and all dead and devitalized tissue

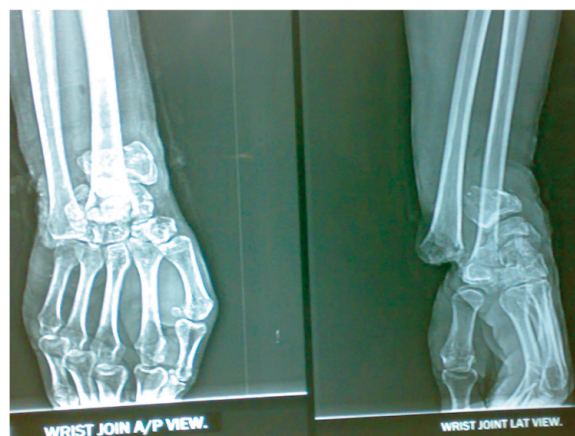


Fig. no-1. AP view of wrist joint

Fig. no-2. Lateral view



Fig. no-3 Open wound.

removed meticulously. The wound was cleaned by copious amount of normal saline. Each fracture was fixed with 2-3 kirschner-wires of 1.8mm diameter. Each wire was inserted from a stab wound made by a number 11 blade knife. The kirschner wire fixation was used in 30 patients. Fixation done in radial styloid process to the proximal shaft of radius. kirschner-wires were left protruding through the skin for easy removal, with their ends bent outside the skin to prevent migration. The wound was left open for 2-3 days for observation after 1st and 2nd post operative follow up, the wound was in very good color, (bright red) viable and no infection occurred, then in 3rd post operative day the wound was closed by delayed primary suture with 3-0 prolene. The



Fig. no-4 -K-wire fixation.



Fig. no-5. 3rd post operative day.



Fig. no- 6. After wound closed.

wounds were cleaned and dressed with gauze, and plaster of paris cast was applied posteriorly with pamer flexion position. The patients were followed up at 2, 4 and 6 weeks. Pin site and stitches site were examined at 2, 4 week.

Result

Five (16.66%) of the patients developed pin tract infection, early removal of kirschner wires at 3 - 4 wks. and our observation the infection rate is higher (60%) in between the age of 46 to 60 years. (Table no 1), and female is higher than male 40% (Table no 2.) And more affected in poor socio economic conditioned patient, 50%. (Table no 3.)

Table No-1
Age distribution

Age	No of patients	percentage
35-45yrs	4	13.4%
46-60yrs.	18	60%
61-80yrs.	8	26.7%

Table No-2
Sex distribution

Sex	No of patients	percentage	Sex	No of patients	percentage
Male (35-45yrs)	2	6.6%	Female(35-45yrs)	2	6.6%
Male (46-60yrs.)	6	20%	Female(46-60yrs)	12	40%
Male(61-80yrs)	3	10%	Female(61-80yrs.)	5	16.7%

Table No-3
Socio-Economic Condition
(On the basis of monthly income)

	No of patients	percentage
Poor	15	50%
Middle Class	10	33.33%
Upper Class	5	16.66%

Table No-4
Infection Rate

Sex	No of patients	percentage	Sex	No of patients	percentage
Male (35-45yrs)	0	0%	Female(35-45yrs)	0	0%
Male (46-60yrs)	0	0%	Female(46-60yrs)	2	6.66%
Male(61-80yrs)	1	3.33%	Female(61-80yrs)	2	6.66%

Discussion

The colle's fracture is common in post menopausal women and elderly male patients, fall on out stretched and dorsiflexion of the hand is the usual mechanism of injury¹ and we commonly manage by close reduction under G/A and immobilization by short arm back slab for 4 to 6 wks. The colle's fractures is usually displaced posterolaterally and fracture line runs through the corticocancellus junction of the distal radius. In this studies the open colle's fracture and we managed early with in 4-8 hours (Average 6 hours) by open reduction and pcutaneous kirschner wire fixation, and wound properly toileting and left open for 2-3 days and then closed delayed primary suture.

Infection after pcutaneous kirschner wire fixation rang from a minor erythematosis reaction to osteomyelitis, septic arthritis, and septicaemia.⁴ Reported infection rates vary from 7%⁵ (in a cohort of 137 patients, 2 of whom developed osteomyelitis) to 35%⁶ (in patients with percutaneous fixation). In our study, infection rate was 16.66%, slight decrease to the 20% quoted for hybrid external fixators.⁷ The pin sites of the external fixator can be cleaned and dressed regularly, but pin sites in our percutaneous kirschner wire fixation were covered by a cast. The longer of the kirschner wires were left protruded, the greater the risk of pin tract infection.

In our observation the 5 (five) patients had mild pin tract infection, and wound is viable (no infection), the infection rate after percutaneous kirschner wire fixation is unacceptable. The kirschner wires should be buried under the skin to decrease the infection rate.

Conclusion

The infection rate of open colles fracture is more common, the presence of foreign implant also enhance the infection rate. But it can be reduced by proper toileting. In this prospective study infection rate reduced up to 16.66%.

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Association of Chlamydia trachomatis Infection in Females with Tubal Factor Infertility

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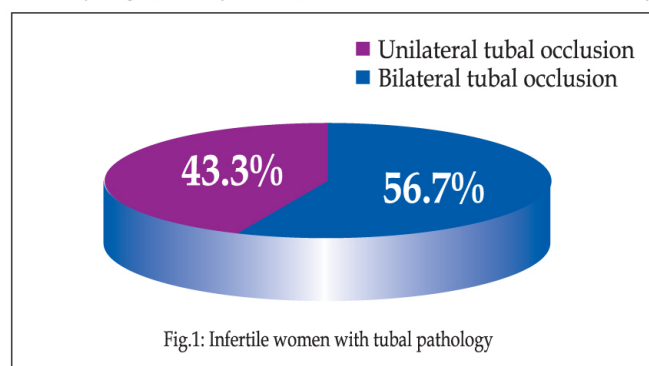
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Abstract

The commonest causes of infertility in the females are tubal and ovulatory factors. Tubal damage underlies infertility in approximately 14% couples and 40% infertile women. The main causes of tubal damage are either pelvic inflammatory disease (PID) or iatrogenic causes. PID remains the major cause of tubal damage in the western world, with *Chlamydia trachomatis* infection being the prime pathogen in most cases. We tried to find out the role of *C. trachomatis* infection in female with tubal factor infertility in our context.

This prospective case control study included 60 women who underwent laparoscopic examination for subfertility at BSMMU during July 2005 and June 2006. During laparoscopy, endometrial curettage was done and histopathological examination AFB staining and culture sensitivity test were also carried out. The patient immune status ratio was also interpreted.

We found bilateral tubal occlusion in 56.7% and unilateral in 43.3% in infertile women with tubal pathology. Chlamydial antibody (IgG) study was positive in 56.7% cases and only



6.7% control subjects ($P < 0.001$). Highly significant difference ($P < 0.001$) was also observed when mean ($\pm$ SD) immune status ratio (ISR) was compared between control (0.46 ± 0.29) and case (1.33 ± 0.91). These findings strongly suggests that *Chlamydia trachomatis* is the major cause of tubal occlusion in the infertile women.

Key words: Infertile women, Tubal occlusion, Chlamydia trachomatis

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Introduction

Reproduction is a basic human right and is essential for continuation of species. Without reproduction, life in general sense, ceases. Infertility is defined as inability to conceive within one year of regular unprotected coitus. Infertility is said to be primary when the woman has never conceived and secondary if the woman has conceived in the past.

Eighty percent of patients conceive within one year and another ten percent conceive in the next two years. Remaining ten percent have some problems to conceive and for them, investigations and treatment is necessary.^{1,2}

Infertility is the problem of couple and both partners should be investigated. The goals of the infertility evaluation are to determine the probable cause, accurate information regarding the prognosis, counselling support, and education throughout the process of evaluation, and guidance regarding treatment options.

The commonest causes of infertility in the females are tubal and ovulatory factors.³ Endometriosis may account for 15 percent infertility in women.⁴ Tubal damage underlies infertility in approximately 14 percent couples and 40 percent infertile women.³ The main causes of tubal damage are either pelvic inflammatory disease (PID) or iatrogenic causes. PID remains the major cause of tubal damage in the western world, with *Chlamydia trachomatis* infection being the prime pathogen in most cases.³

Chlamydia trachomatis is the major cause of tubal occlusion and is also associated with in vitro fertilization (IVF) failure or spontaneous abortion.⁵ These infections can be asymptomatic in 80 percent cases and persists in the genital tract for long period of time in the form of resistant to immune destruction.⁶ Significant percentage of couples seeking treatment for infertility might, therefore, harbour *C. trachomatis* in their genital tract.

Chlamydial infection is also responsible for 40 percent ectopic pregnancies, while 60 percent women with tubal factor infertility have serological evidence of past infection with chlamydia.⁷ Thus, it is important to detect and treat lower genital tract infection to reduce the incidence of PID and screening for chlamydia, which has received much attention recently. A report by the Department of Health, United Kingdom in 1998 showed that the major sequelae of PID include ectopic pregnancy, tubal factor infertility and chronic pelvic pain.⁸ The incidence of ectopic pregnancy is increasing, and it remains the principal cause of maternal death in the first

trimester of pregnancy. The asymptomatic nature of chlamydial infection makes screening essential if control of this infection is to be achieved. In Sweden, policies to reduce the prevalence of infection have been in place since 1980, and rates of chlamydial infection and its complications have fallen significantly.⁶ In the present study, we tried to find out the association between *C. trachomatis* infection in the female and tubal factor infertility.

Materials and Methods

This prospective case control study included 60 women who underwent laparoscopic examination for subfertility (both primary and secondary) in the Infertility Unit, Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period of July 2005 to June 2006. Women above 40 years, and women whose laparoscopic examination revealed other pelvic pathology, e.g. chocolate cyst, old ectopic pregnancy, broad ligament fibroid with distorted tube, etc., and also women whose husbands had semen abnormalities were excluded from the study. The selected 60 women on laparoscopic evaluation were divided into two groups: (a) Group A (n=30, normal tubes), and (b) Group B (n=30, tubal pathology).

Serological tests (IgG antibody to *C. trachomatis*) were carried out in the Department of Immunology, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka.

Table I
Interpretation of patient immune status ratio

ISR value	Results	Interpretation
≤0.90	Negative	No detectable IgG chlamydial antibody, suggests no prior immunological exposure to chlamydial species, result does not rule out recent exposure and collection of test sample prior to development of IgG. Culture or other direct methods are recommended for determining current infections.
0.91-1.09	Equivocal	Immunological exposure cannot be assessed. Samples that remain equivocal after repeat testing should be retested by an alternate method. If results remain equivocal upon further testing, an additional sample may be collected.
≥1.10	Positive	Detectable IgG chlamydial antibody indicates presence of detectable IgG antibody. Suggests immunological exposure to one or more chlamydial species.

The assessment was based on a careful analysis of the history and clinical examination of the women. In the history, particular emphasis was given on pelvic pain along with per vaginal discharge, menorrhagia, dyspareunia, post coital bleeding, intermenstrual bleeding, septic abortion, puerperal sepsis, intrauterine device (IUD) usage, lower abdominal surgery (e.g. appendicectomy, ectopic pregnancy, ovarian cystectomy, etc.) and tuberculosis. On per speculum examination, emphasis was given whether cervix was unhealthy, friable or normal looking. On bimanual pelvic examination, emphasis was given on normal size uterus with restricted mobility, tender adnexae. All investigations were reviewed.

During laparoscopy, endometrial curettage was done and sent for histopathological examination, AFB staining and culture sensitivity test.

Tests were carried out in the laboratory of BIRDEM hospital. IgG antibodies to *C. trachomatis* level of all the samples were tested using ELISA method.

The patient immune status ratio (ISR) was interpreted as outline in Table I (Chlamydia antibody IgG assay Capita™ chlamydia IgG):

Collected data was compiled and statistical analyses were done using computerbased software SPSS.

Results

In this prospective study, 60 women were recruited from Infertility Unit of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Sampling was done in selected groups of infertile women who underwent laparoscopic examination; 30 were infertile women with normal fallopian tubes and 30 were infertile women with tubal pathology.

Table II
Basic data of the study subjects

Parameters	Group A (n=30) Mean±SD	Group B (n=30) Mean±SD	P value
Age (years)	26.30±4.92	26.60±3.48	ns
Duration of marriage (years)	7.60±3.40	7.68±3.49	ns
Duration of infertility (years)	5.58±3.31	6.13±3.02	ns

Unpaired Student's 't' test, ns = not significant

Table II shows comparison of age, duration of marriage and duration of infertility. None of the parameters showed significant difference between case and control. Mean ($\pm$ SD) age was 26.30 ± 4.92 and 26.60 ± 3.48 years, duration of marriage 7.60 ± 3.40 and 7.68 ± 3.49 years, and duration of infertility 5.58 ± 3.31 and 6.13 ± 3.02 years, respectively, in control (group A) and case (group B) groups.

Table III
Laparoscopic findings of fallopian tubes in cases (n=30)

Findings	Right No.	(%)	Left No.	(%)
Adhesion	9	(30.0)	11	(36.7)
Elongated	1	(3.3)	1	(3.3)
Tortuous, beaded,	8	(26.7)	8	(26.7)
Hydrosalpinx	6	(20.0)	6	(20.0)
Dilated/congested	2	(6.7)	2	(6.7)
Normal	4	(13.3)	2	(6.7)

Table III shows laparoscopic findings of right and left fallopian tube of case group of women. Adhesion was common finding in both right and left fallopian tubes (30% vs 36.7%). Other pathologies were equally distributed between right and left fallopian tubes, such as elongation (3.3%), tortuous, beaded (26.7%), hydrosalpinx (20%) and dilation/congestion (6.7%). Laparoscopic findings was normal in 4 (13.3%) right fallopian tubes and 2 (6.7%) in left fallopian tubes. Fallopian tubes were normal in all (100 %) women of control group.

Table IV
Tubal patency test results in cases (n=30)

Tubal patency	Number of patients	Percentage
Only right side negative	7	23.3
Only left side negative	6	20.0
Both (right and left) side negative	17	56.7

Table V
Findings of antibody to Chlamydia trachomatis in serum

Findings	Control (n=30) No.	(%)	Case (n=30) No.	(%)	P value
Positive	2	(6.7)	17	(56.7)	<0.001***
Negative	28	(93.3)	13	(43.3)	

Fisher's exact test, *** = Significant

In all 30 control women (100%), fallopian tubes were normal. Tubal patency test in 30 case group of women showed 7 (23.3%) blocked right tube, 6 (20%) blocked left tube and 17 (56.7%) both right and left tube blocked (Table IV)

Table V Shows Antibody to Chlamydia trachomatis in serum was positive in 2 (6.7%) & 17 (56.7%) women in control & case groups, respectively. The difference was statistically highly significant ($P < 0.001$)

Table VI
Comparison of immune status ratio

	Control (n=30)	Case (n=30)	P value
Mean $\pm$ SD	0.46 ± 0.29	1.33 ± 0.91	<0.001***
Range	0.19 1.44	0.20 3.62	

Unpaired Student's 't' test, *** = Significant

Table V shows mean ($\pm$ SD) immune status ratio of control and case groups were 0.46 ± 0.29 and 1.33 ± 0.91 , respectively. In the case group, the ratio was significantly high ($P < 0.001$).

Discussion

Infertility is a fairly common problem in our country and which has social and clinical significance in a basically pronatalist society like Bangladesh. The hospital admission rate of infertility cases at the Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, was 26.5 percent of all gynaecological admission.⁹

One of the major cause of infertility is tubal factor. Das found tubal block in 35 percent cases in her study at BSMMU10. Begum found tubal block in 34 percent cases in her study at BIRDEM hospital.¹¹ Ochoa et al. found pelvic pathology in 34.8 percent cases in their study.¹²

The sharp worldwide increase in the incidence of pelvic inflammatory disease (PID) during the past two decades has led to the secondary epidemics of tubal factor infertility. The most common cause of tubal factor infertility is occlusion of the fallopian tubes due to an infection by a sexually transmitted agent, by *C. trachomatis*. The prevalence of diagnosed case of tubal factor infertility can be correlated to the epidemiological situation regarding this agent, that was prevailing several years ago. This is partly due to the trend seen in many western countries that women often postpone to try to get pregnant. Therefore, there is often a time lag between the acute PID and when women first consult because of fertility problems. Subclinical salpingitis is today regarded as even more common than symptomatic PID. Persistent tubal infections by *C. trachomatis* are also a common feature, even despite courses

of antibiotic therapy. Many cases of chlamydial salpingitis have a more or less subclinical course. The tubal infection may become chronic in spite of antibiotic therapy. Immunological processes may continue after microbiological cure, which stresses the importance of screening for *C. trachomatis* in order to detect and treat carriers to hinder spread to still uninfected women.

Ullah *et al.* showed that chlamydial antibody was positive in 70.97 percent cases in blocked fallopian tube and 6.67 percent cases in normal (patent) fallopian tubes.¹³

Dele Davies & Wang reported that 60 % women with tubal factor infertility had serological evidence of past infection with chlamydia.¹⁴ Akande *et al.* reported that antibody (IgG) titre in women with tubal damage were significantly higher than women without tubal damage & past infection with *C. trachomatis* was associated with a significantly increased risk of women suffering from tubal infertility.¹⁵

Moore *et al.* found 73-79 percent prevalence of *C. trachomatis* antibody (IgG) among infertile women with tubal abnormalities.¹⁶ Chlamydial antibodies were unaffected by such variables as age, race, duration of infertility and parity. Cervix was significantly abnormal in cases than control, also the size and mobility of uterus. Fornix was not free in significantly large number of cases than controls.

In our study, out of 30 cases, 53.3 percent had primary infertility and 46.7 percent secondary infertility. Most common tubal pathology was adhesion in 11 (36.7%). Other common diagnosis were beaded and tortuous tube in 8 (26.7%) and hydrosalpinx in 6 (20%) cases. Tube was dilated in 2 (6.7%) cases.

In our study, bilateral tubal occlusion was present in 56.7 percent and unilateral tubal occlusion was present in 43.3 percent infertile women with tubal pathology. This result was higher than the study reported by Ullah *et al.* who found 37.5 percent and 10.94 percent cases, respectively.¹³

Comparison between case and control groups regarding age, duration of marriage and duration of infertility showed no significant differences between the two groups.

We found that the IgG antibody to *C. trachomatis* in serum was positive in 56.7 percent cases and mean ($\pm$ SD) ISR was 1.33 ± 0.91 . Mean age of the cases was 26.30 ± 3.48 years, duration of marriage 7.68 ± 3.49 years, duration of infertility 6.13 ± 3.02 years, duration of contraceptive use 15.80 ± 12.45 months. Chlamydial antibody (IgG) study showed highly significant difference between the cases and control, which was positive in 56.7 and 6.7 percent cases, respectively, and ISR was 1.33 ± 0.91 and 0.46 ± 0.29 , respectively. The significantly higher percentage of chlamydial antibodies (IgG) positive in infertile women with tubal blockage

compared with those with tubal patency strongly supports the hypothesis that *C. trachomatis* is the major cause of tubal occlusion in the infertile women. *C. trachomatis* antibody testing is simple, inexpensive and causes minimal inconvenience to the patient. Therefore, *C. trachomatis* antibody testing deserves to become an integral component of the initial fertility workup.

Conclusion

Genital *C. trachomatis* infection has a worldwide distribution and is now recognized as the single most common cause of tubal peritoneal damage.^{17,18} Screening programs for *C. trachomatis* will be of paramount importance in the prevention for long term sequelae. The cost of screening is only a fraction of the healthcare costs incurred due to complications resulting from undiagnosed and untreated chlamydial infection. The selection of a diagnostic test for the detection of chlamydial genital infection depends on availability of local expertise and prevalence of *C. trachomatis* in the test population. Infection with *C. trachomatis* results in the formation of antibodies detectable in serum or detecting evidence of past chlamydial infection using serology is noninvasive, simple and quick to perform.¹⁹ As such, chlamydia serology may be used as a screening test for tubal damage in infertile women.

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Danazol as a first line therapy in Aplastic anaemia

Kamruzzaman AKM¹, Siraj S², Haque MA³

The ORION Medical Journal 2012 July;15-1(38): p14-15

Abstract

Aplastic anaemia is defined as the presence of pancytopenia in the peripheral blood and a hypocellular marrow in which normal haemopoietic marrow is replaced by fat cells. The diagnosis of aplastic anaemia requires at least two of the followings in addition to a hypocellular marrow 1) Hb <10 gm/dl 11) Platelet count <100 X 10⁹/L 3) Neutrophil count <1.5X10⁹/L. At least two thirds of the patients no aetiological agents can be identified i.e idiopathic. In about one third of patients drugs, chemicals, virus may be responsible. Pathogenesis remain unclear but an autoimmune mechanism appears to be important.

Definitive treatment of aplastic anaemia is bonemarrow transplantation. Although ATG plus cyclosporine is the therapy of choice for aplastic anaemia without a donor, when neither HSCT nor immunospressive therapy is available, danazol remain an acceptable therapeutic option for aplastic anaemia.

Mizanur Rahman, 30 years from South Maheshpur, Kaharul, Dinajpur diagnosed as a case of Aplastic anaemia on the basis of history, clinical examination, complete blood count, peripheral blood film. Platelet count and bone marrow examination. He was initially treated by Tab. Anapolone and prednisolone for 6 months but not improved. Cyclosporine did not given due to poverty. Then he was treated by Tab. Danazol and prednisolone daily and blood transfusion 2-3 months interval. He was followup monthly interval by clinical feature and complete blood count. After 9 months his Hb level increased and later on persist. His total WBC count and platelet count become increased after 1 year of treatment. Then treatment was continued with danazol and steroid and did not require blood transfusion. He was then follow up 3 months interval. During each follow up patient was symptomless and complete blood count was normal. After 18 months patient is stable both clinically and laboratorically. Then dose of danazol was reduced and steroid was withdrawn. After 3 months of reducing dose of danazol, patient was stable and danazol was continued.

Key words: Danazol, Aplastic anaemia

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Introduction

Aplastic anaemia is defined as the presence of pancytopenia in the peripheral blood film and a hypocellular marrow in which normal haemopoietic marrow is replaced by fat cell.¹ The diagnosis of aplastic anaemia requires at least two of the followings in addition to a hypocellular marrow

- 1) Hb% <10gm/dl
- 2) Platelet count <100000/cmm
- 3) Neutrophil count <1500/cmm.¹

At least two thirds of patient have no aetiology i.e idiopathic. In about on third of patients drugs, chemicals, virus may be responsible.¹ Pathogenesis remain unclear but most causes are acquired and immune mediated and there are also inherited form. Annual incidence of aplastic anaemia is about 2 cases per million population.²

The onset is at any age, with a peck incidence around 30 years and a slight male predominance. Acquired aplastic anaemia most commonly presents between ages of 15-25 years but there is second peak incidence after 60 years.^{2,3}

The disease is diagnosed by clinical feature, complete blood count, platelet count, bone marrow examination and trephine biopsy.

The disease may turn to PNH, MDS, or leukaemia during the course of disease. Severity of disease may be 3 types-

- (a) Non severe aplastic anaemia
- (b) severe aplastic anaemia
- (c) very severe aplastic anaemia.

Severe aplastic anaemia, very severe aplastic anaemia does not improve with out definitive treatment. Non severe aplastic anaemia may remain stable or slowly worsen with times.

Definitive treatment of aplastic anaemia is bone marrow transplantation, and immunosuppressive therapy. Androgen may be given. Historically androgen or anabolic steroids were the first specific form of therapy used in aplastic anaemia. If there is no response after 6 months, then androgen should be stopped. If response occurs androgen should be slowly reduced. Although ATG plus cyclosporine is the therapy of choice for aplastic anaemia with out a donor, when neither HSCT nor immunosuppressive is available, Danazol remain an acceptable therapeutic option for aplastic anaemia. Untreated aplastic anaemia is an illness that leads to rapid death typically within 6 months.⁴ Older people or who are generally too frail to undergo bonemarrow transplantation, who undergo immunosuppression have five years survival rate of upto 75%.⁴ With immunosuppressive treatment more than half of patients with aplastic anaemia will achieve remission.⁵

Case Report

Mizanur Rahman 30 years, from south Maheshpur, kaharul, Dinajpur presented with weakness for 6 months, gum bleeding for 2 months and 4 units of blood transfusion. He gives history of jaundice 5 years back and exposure to insecticides for 15 years but no history of radiation.

On examination patient is anaemic, not icteric, bony tenderness absent, no lymphadenopathy, rash present, liver and spleen are not enlarged. Heart and lungs are normal.

On investigation total count of WBC -4000/cmm, differential count of WBC-Neutrophil-55%, lymphocyte-40%, eosinophil-4%, monocyte-1%. Hb%-6gm/dl, ESR-110, platelet count -15000/cmm. Bonemarrow examination shows -Hypocellular marrow consistent with aplastic anaemia. HBsAg-negative, Anti HCV- negative, Serum creatinine-0.9mg/dl, X-ray chest P/A view-normal.

Patient was treated initially with Tab. Anapolone and prednisolone for 6 months but not improved. Cyclosporine could not be given due to poverty. Then he was treated with Tab. Danazol 200mg 3 times daily and Tab. Prednisolone 60 mg daily, with fresh blood transfusion 2 months interval. He was follow up monthly intervals by clinical feature and complete blood count with platelet count. After 9 months his Hb% become raised. Danazole 600mg daily and prednisolone was continued. After 1 year his WBC count and platelet count become increased. Drug was continued, he was follow up 3 months interval and after 18 months his Hb% become 10.2gm/dl, total count of WBC-7000/cmm, differential count of WBC: neutrophil-80%, lymphocyte-15%, eosinophil-4%, monocyte-1%, platelet count-150000/cmm. Then dose of danazol was reduced and prednisolone stopped. After 3 months patient is stable both clinically and laboratorically i.e Hb%-10.5gm/dl, total count of WBC-6000/cmm, platelet count-180000/cmm. Danazol was continued.

Discussion

Aplastic anaemia defined as pancytopenia in the peripheral blood film and hypocellular marrow. It is idiopathic but one third cases drugs, chemical and virus may be responsible i.e autoimmune mechanism. Definitive treatment of aplastic anaemia is bone marrow transplantation and immunosuppressive therapy but androgen i.e Danazol may be given. When neither HSCT nor immunosuppressive therapy is available danazol remain an acceptable therapeutic option for aplastic anaemia

The onset is at any age, with a peak incidence around 30 years and a slight male predominance. Long term outcome is variable. Untreated patient may die within 6 months. Patient who undergo immunosuppression, have 5 years survival rate upto 75%.

Patient was diagnosed by history, clinical examination, Hb%, TC, DC, platelet count, peripheral blood film and bone marrow examination. To find out causes of aplastic anaemia viral markers was done and drug history was taken.

Aplastic anaemia may be responded with danazol. Response to danazol is slow and it usually takes time 3-6 months. We treated the patient with danazol 600mg daily, as dose required to induce remission is 600mg daily. Patient was follow up monthly interval. After 18 months of treatment patient was clinically stable and his blood picture was Hb%-10.2gm/dl, total count of WBC-7000/cmm, Neutrophil-80%, lymphocyte-15%, eosinophil-4%, monocyte-1%, and platelet count-150000/cmm. Danazol was tapered slowly within 3 months and patient was also clinically and laboratorically stable.

During treatment patient develops fungal infection. Daily dose of danazol was given 600mg which was given in other studies such as Jaime-perez JC, Almaguer D and Tatsuya Chuhjo, Shinji Nakao. Time taken to response occur in this patient was 12 months which showed in other studies such as Jaime-perez JC, Almaguer D and Emmanuel C Besa, MD; Koyamangalath Krishnan. As response occurs in this patient, other studies also showed responses such as Jaime-perez JC, Almaguer D which shows response rate 46% and Emmanuel C Besa, Koyamangalath Krishnan which shows response rate 45%.

Conclusion

Danazol is effective for the treatment of aplastic anaemia who could not afford treatment with bone marrow transplantation or injection ATG and or cyclosporine.

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Pitfalls of National Tuberculosis Control Program (NTP) in Bangladesh

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Abstract

Tuberculosis is a major public health problem in Bangladesh. Annual death rate due to a single infectious agent is 70,000. More than 45 lac. Patients prevailing in the community with annual increment of more than 300,000. NT along with its partners are working to detect at least 70% of new Smear Positive Patients and to cure at least 85%. As per recommendation of WHO. NTP is running with the DOTS strategy for control of Tuberculosis.

Treatment Regimens in our national guidelines.

Standardized treatment regimen for each diagnostic category (Adults)

TB Diagnostic Category	Patient Category	Treatment Regimen	
		Intensive Phase (daily)	Continuation Phase (daily)
I	• Extra Pulmonary TB Patients • New Smear (+) positive PTB Pts. • New Smear (-) Negative PTB Patients • Concomitants/Associated HIV/AIDS	2 (HRZE)	4 (HR)
II	• Sputum Smear (+) positive PTB with history of treatment of more than one month • Relapse • Treatment failure after Cat-1 • Treatment after default • Others	2 (HRZE)/1 (HRZE)	5 (HR)E

Bangladesh Introduced DOTS Strategy in 1993 and had expanded at all upazillas in collaboration with different partner NGO's by June 1998.

But as days passes we are getting more relapse and failure cases. But why failure and relapses? There are many reasons. Most important of them are-

- (1) Non adherence to treatment regimens which can be minimized by DOT. But practically DOT is not maintained at all.
- (2) More extensive cavitory lesions. Patients with more extensive cavitory lesions have higher failure and relapse rates in such patients special consideration should be taken for enhanced treatment regimens.³

Key words: NTP, Tuberculosis, NTP in Bangladesh

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- (3) HIV positive patients and immune compromised patients though rare in Bangladesh are more likely to relapse.⁴

Standardized TB drug regimens as described in treatment guidelines cannot address every possible situation. They need good clinical judgments. Several papers have addressed TB drug mal-absorption.^{5,6,7} at some extremely low concentration any drug functions just like a placebo.

It is very difficult to understand which patient will with low serum concentrations. It is logical to consider the outcome upon the extent of disease immune function and the virulence of the organisms. A rational approach should be considered to increase the dosages to achieve normal concentrations to improve patient's outcome.

So by using standardized regimens unifications as well as high quality treatments may be available for the majority of patients but it is to be considered that one size does not fit all patients.

Principles of Chemotherapy in Tuberculosis

- (1) At least two agents to which the organism is susceptible must be used in the treatment of achieve tuberculosis to prevent the emergence of drug resistance.
- (2) A single drug should never be added to a failing regimen because this could result in the development of resistant to that new drug.
- (3) The duration and effectiveness of a treatment regimen will depend on the drugs used.
- (4) Non adherence to the treatment regimen is the most important cause of treatment failure, relapse and acquired drug resistance.

Now if we see the regimens in our national guideline, one can find Cat-II regimen which is against the principles of

chemotherapy just mentioned above. In case of failure in Cat-II or relapse after treating in Cat-I we retreat the same patient in Cat-II where only one drug i.e, Inj. Streptomycin is added which is in judicial and against the concept of principles of Chemotherapy in tuberculosis. Moreover, the rate of resistance against Inj. Streptomycin in our country is very high.

WHO recommends this regimen for less affluent countries and for those countries where resource is limited. Previously they also recommended only HT/HE in continuations phase which did much harm evidenced by more relapse rates treating in that regimen.

Use of FDC Tablet

Use of FDC Tablets against tuberculosis may simplify the prescription of drugs and may also limit the risk of drug resistant tuberculosis arising as a result of inappropriate

drug selection and monotherapy.

Dosages of FDC Tablets

FDC tablets are composed as follows.

4FDC: Isoniazid 75 mg + Rifampicin 150mg + Pyrazinamide 400 mg. + Ethambutal 275mg

2FDC: Isoniazid 75 mg + Rifampicin 150mg

After introduction of FDC tablets. Dosages of antitubercular drugs are rescheduled as follows:

District	<30 Kg	30-37 Kg	38-58 Kg	55-70 Kg	>70Kg	Total
Rangpur	100	600	1973	170	08	2851
Lalmonirhat	10	270	812	78	03	1173
Total	110	870	2785	248	11	4024

Dosages schedule for adults (number of tablets)
Recommended by WHO.

Patient body weight (Kg)	Initial phase		Continuation		
	2 Months		4 Months		6 Months
	RHZE Daily	RHZ Daily	RH Daily	RH Three Weekly	EH Daily
30-37*	2	2	2	2	1.5
38-54**	3	3	3	3	2
55-70***	4	4	4	4	3
71 and more	5	5	5	5	3

*Only a small proportion of adult TB patients will fall into the categories with body weights from 30 to 37 Kg. or body weights above 70 Kg. Therefore, in practice most patients taking rifampicin containing FDC tablets will receive either three or four tablets daily.

** Some countries traditionally use a cut-off point at 50 Kg. as proposed here. The dosage schedule presented here can be used also with a cut-off point at 50 Kg. i.e. patients with body weights from 35 to 49 Kg. receives three tablets and those body

weights from 50 to 70 Kg receives 4 tablets.

Now as for example we presented here age distribution of adult TB patient in two districts of Bangladesh.

Adult as patient registered in Rangpur and Lalmonirhat District from 1st January, 2009 to 31st December, 2009.

Pretreatment weight (kg)	Intensive phase Daily First 2 months. No.of 4FDC tab.	Continuation phase. Daily (Next 4 months) no. of 2FDC tab
30-37	2	2
38-54	3	3
55-70	4	4
>70	5	5

Below 30Kg.	110
30-37Kg.	870
Total	980

Total patient in two district --- 4024

% of patent receiving under dosages. 42.35%

WHO assumed only small proportion of adult TB patient will fall into the categories with body weight from 30-37 Kg. They hope most patients taking Rifampicin containing FDC tablets will receive either three or four tablets daily.

But the scenario is different in our country. A significant no. of adult TB patient fall in to the categories with body weight from 30-37 Kg or less then 30 Kg. We have shown in Rangpur and Lalmonirhat District. Their number is 24.35% which is statistically significant.

Patients treated in this category receive drugs in under dosages or in sub therapeutic dosages. Most of the relapse and failure cases we recently noticed are this sub group.

The dosages schedule presented in our national guideline can be used with a cut-off point at 50 Kg. i.e. patient with body weight from 30 to 49 Kg receives three tablets and those with from 50-70 Kg receive 4 tablets.

The efficacy of these formulations has not been extensively investigated, although in at least one study, a combined formulation of Isoniazid, Rifampicin, and Pyrazinamide was less effective then a regimen in which the same medications were given separately.

Another important thing which should be remembered that Ethambutal when used as primary agent in the treatment of tuberculosis should be given at dose of 25mg/Kg instead of 15mg/Kg.⁹

By using FDC tablets and as per dosages schedule in the national guideline dosage of Ethambutol is not maintained.

What we need to do?

The national guideline should be corrected and dosage schedule should be revised according to the need of our country. More Medical Graduates either in the Govt. side or in the NGO's should be involved in TB treatment and

management. They should have adequate knowledge and proper training. Treatment should be started by Medical Graduates instead presently practicing by paramedics or non medical personnel. Difficult and complicated cases should be consulted with chest specialists and they should have an active role in TB control program. A steering committee consisting of multiple relevant disciplines should be formed to look after the on-going activities of NTP and to monitor any change in the plan of action on the basis of scientific reasons not by the unethical suggestion of Donor agencies.

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Surgical Management of an Adult Patient with Atrial Septal Defect and Severe Pulmonary Hypertension

Tarik KM¹, Hoque KZ², Zahangir NM³, Kabir AHM⁴, Talukder MQI⁵, Haider MZ⁶

The ORION Medical Journal 2012 July;15-1(38): p19-22

Abstract

Secundum type atrial septal defect (ASD) is one of the commonest forms of congenital cardiac malformation. In ASD blood will flow from left atrium to the right atrium, through pulmonary circulation once again to the left atrium. Most of the patients live with no or minimal symptoms. But in some individuals, who are susceptible to the development of pulmonary vascular disease, there may be decrease in left to right shunt and by late teenage years or third decade of life, there may be shunt reversal when surgical correction is considered contraindicated. In these patients, use of Sildenafil will reduce pulmonary pressure, and with other necessary measures, this group of patients can be treated successfully by surgical correction. Here we report such a case which was treated with Sildenafil in pre and post operative period and other aggressive measures were taken to reduce pulmonary hypertension.

Introduction

Secundum ASDs represent 6% to 10% of all cardiac anomalies and are more frequent in females than males by about 2:1.¹ ASDs occur in 1 child per 1,500 live births.² Most ASDs occur sporadically; however, a few families have the defect as a genetic abnormality. As endocardial cushion tissue closes the ostium primum, the ostium secundum forms via fenestrations in the anterosuperior position of the septum primum. The septum secundum then develops and eventually provides partial closure of the ostium secundum. At the completion of atrial septation, the limbus of the fossa ovalis is the septum secundum and the septum primum is the valve of the fossa ovalis. Secundum ASDs occur when there is inadequate

septum primum. The underlying cause of this malformation is usually multifactorial, although there are a few recognized genetic defects that result in secundum ASD, such as Holt-Oram syndrome. ASD is commonly diagnosed at early life but sometime missed due to lack of symptom.³

Through ASD blood passes from left atrium to right atrium resulting increased flow to right ventricle and to pulmonary arteries. However, increased blood flow through the pulmonary arteries increases shear stress on the arterial wall and can lead to changes in the pulmonary vasculature that result in increased pulmonary vascular resistance and pulmonary hypertension. In the setting of severe pulmonary hypertension, a right-to-left shunt at the atrial level results in systemic desaturation that is unresponsive to supplemental oxygen. This right-to-left shunt in the setting of pulmonary vascular disease is called Eisenmenger Complex and occurs in approximately 5% of secundum ASDs, most commonly in women. Left atrial enlargement will occur,

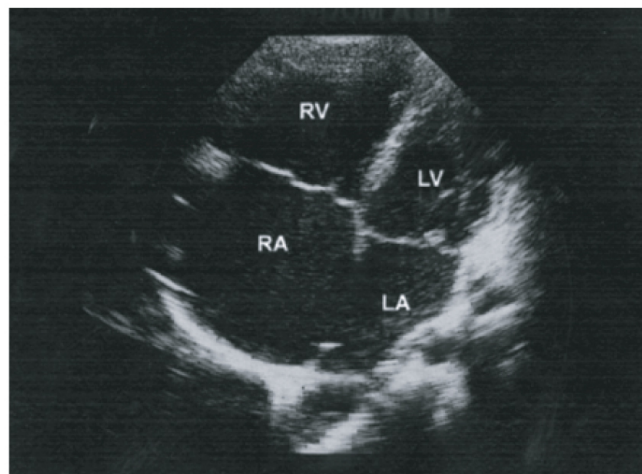
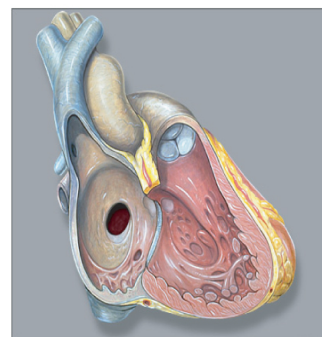


Figure 1. Secundum Atrial Septal Defect

Key words: ASD, Atrial Septal Defect, Pulmonary Hypertension

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but left ventricular enlargement is unusual given the compliance characteristics of the left ventricular myocardium.⁴ Here we present a case of ASD with severe pulmonary hypertension, which was diagnosed lately, went through surgical management in Apollo Hospitals Dhaka and encountered various peri and post operative events.

Case Report

A 32 years, married lady admitted in this hospital with the complaints of breathlessness, palpitation, repeated respiratory tract infection since long time back. According to her statement she has been suffering from same type of illness since her early childhood. But she did not visit to doctor for treatment till few months back. Recently she has been

diagnosed as ASD with severe PH, was receiving sildenafil for two month and came to our hospital for further treatment. Her menstrual cycle was irregular, last menstrual period was in March. She has two children. She has been receiving Diuretics and Sildenafil since her diagnosis in last March 2011.

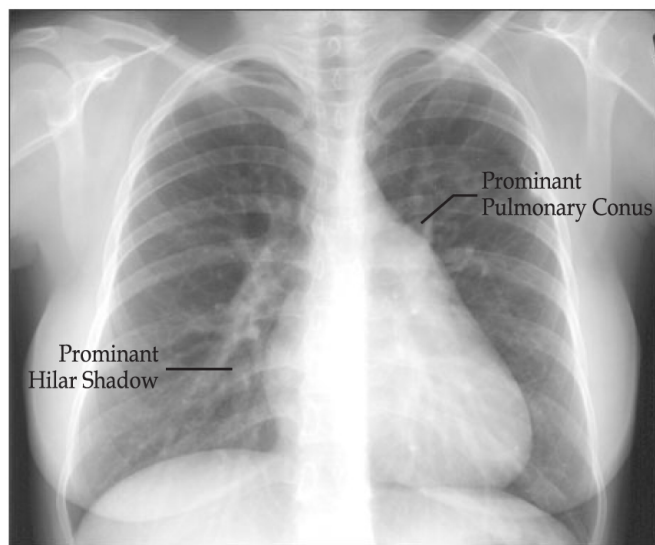


Figure 2: Plain X Ray Chest

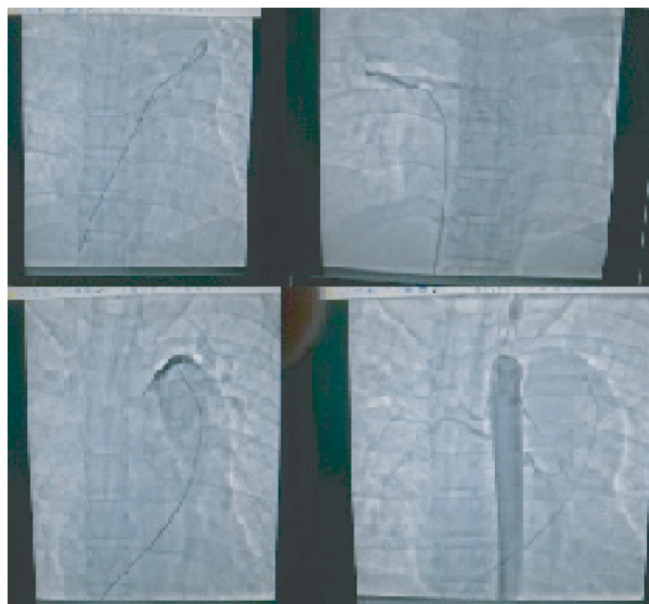


Figure 3. Cardiac cath showing hugely dilated pulmonary artery

In the outside hospital, she performed a 2-D echocardiography, with diagnosis of Secundum ASD, bidirectional shunt, moderate Pulmonary Regurgitation with severe Pulmonary Hypertension (PH). Pulmonary artery systolic pressure was (PASP) 112mm.Hg. She has also undergone a cardiac catheterization study. It was found that severe PH and R~L shunt, after giving O₂ for 10 minutes. PA pressure came down to 100 mm Hg with bidirectional shunt. On admission we have clinically examined her. Other investigations were in normal limit.



Patient's SpO₂ was 100% on FiO₂ 60%, PO₂ 303 mm Hg, PCO₂ 38 mm Hg, PA Pressure 40/30 mm Hg. thoroughly and found no cyanosis, mild clubbing, Pulse 70/min, BP 100/60 mm Hg, Respiratory rate 20/min.

In our hospital we did a 12 lead ECG with findings of RBB, mild RVH no Q wave, a chest X-ray with huge protruding Pulmonary Conus with plethoric lung field and RV type cardiomegaly. We again did a 2-D Echocardiogram. Finding was a large ASD (26mm ×21mm) with bidirectional shunt, good LV function and PASP was 100 mm Hg.

The Patient was undergone Pericardial patch closure of ASD in CPB, and cardiac arrest kept in the pericardial patch intended to prevent sudden rise of pulmonary pressure. Cross clamp time was 53 minutes and extracorporeal circulation time was 93 minutes.

Then the patient came on ICU and in post operative period the scenario of the patient was eventful. On 0 post operative day (POD) patient was on ventilator and receiving inotropic support (Dobutamin, Adrenalin) GTN, Insulin and sedation in infusion.

On 1st POD with previous drug patient was extubated in the afternoon, his PA pressure was 100/60 mm Hg, became suddenly unstable, then again re-intubated several hour later due to increased HR and decreasing saturation, Patient was disoriented, SpO₂ came down to 92%, PO₂ came down to 72 mm Hg, After intubation SpO₂ became 100% at 60% FiO₂,

Dobutamin stopped and infusion Milrinon started continued till two days without any significant change of PA pressure. (100/60 mm. Hg).

A CT scan of Brain performed on next day and found mild infarct in the temporal cortical zone. At 9th POD tracheostomy was done and ventilation was continued.

After tracheostomy significant improvement was observed of patient, SpO₂ 95% at 70% FiO₂, PO₂ 72 mm Hg, PCO₂ 35 mm Hg, On 10th POD sedation was gradually off and patient with down from ventilator. On 12th POD (28/05/11) patients look good, She took her meal orally we removed tracheostomy tube at 15th POD. We discharged the patient 20th POD advised to take Sildenafil, some diuretics and Digoxin orally. Patient came to hospital for follow up after one month with a 2d Echocardiogram. Where we found a tiny residual ASD (which

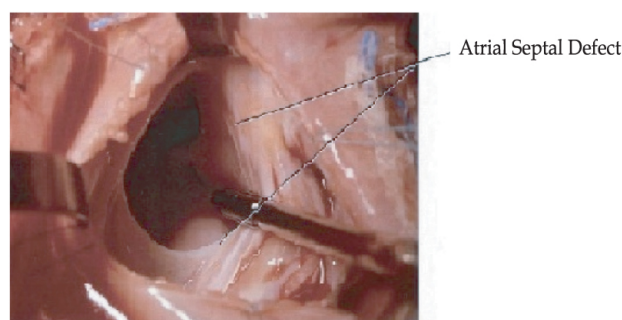


Figure 5. Peri Operative view of Secundum ASD

is a fenestration we kept), good LV systolic function with PASP 70 mm Hg. The pulmonary artery pressure significantly came down after ASD closure and patient clinically and symptomatically improved.

Discussion

Atrial septal defects are classified according to their location relative to the fossa ovalis and their proposed embryogenesis. Interatrial communications in the region of the fossa ovalis may represent either a true secundum ASD or a valvular incompetent patent foramen ovale. Defects anterior to the fossa ovalis (primum defects) often are associated with a cleft in the anterior leaflet of the mitral valve. Those posterior and superior to the fossa ovalis, the sinus venosus defects, usually occur in conjunction with anomalous connection of the right pulmonary veins. Finally, interatrial communications at the expected site of the coronary sinus ostium are often associated with an unroofed coronary sinus and left atrial connection of a persistent left superior vena cava.⁵

A secundum ASD allows blood to cross the atrial septum. The presentation of secundum ASD depends on the size of the shunt and the associated cardiac status. Amount of shunting is determined by the end-diastolic pressures of the ventricles, the size of the defect and the status of the atrioventricular valve.⁶

In large ASD, severe pulmonary hypertension may develop and seems to be inoperable. These cases may be made operable when treated with *Sildenafil*.

Same experiences with other centers have been proven effective in surgical closure of adult ASD with severe pulmonary hypertension.

A woman with atrial septal defect and severe pulmonary hypertension with 25.0 Wood unit/m² of indexed total pulmonary vascular resistance, underwent successful corrective repair of atrial septal defect after 2 years of treatment with sildenafil, and has been monitored for 4 years after repair. Their case suggests that sildenafil treatment in some selected patients with ASD and severe pulmonary hypertension can result in significant improvements in pulmonary hypertension, which may allow corrective repair of ASD.¹ The experience of

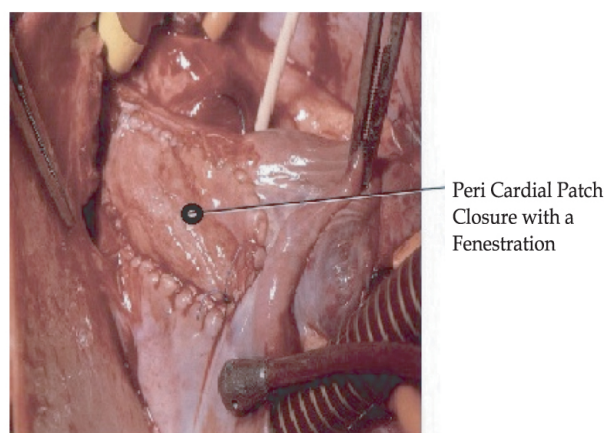


Figure 6. Peri cardiac Patch Closure of ASD

benefit of atrial septal defect closure in adults in another centre: The presence of arrhythmias, right ventricular (RV) remodelling, and pulmonary artery pressure (PAP) were studied in 236 consecutive patients undergoing ASD closure [164 females, mean age of 49±18 years, 78 younger than 40 years (Group A), 84 between 40 and 60 years (Group B) and 74 older than 60 years (Group C). Defect size [median 22 mm] and shunt ratio [Qp:Qs = 2:2] did not differ among age groups. Post-surgically, RV size and PAP decreased and patient improved symptomatically.⁷

At any age, ASD closure is followed by symptomatic improvement and regression of PAP and RV size.⁴ However, the best outcome is achieved in patients with less functional impairment and less elevated PAP. Considering the continuous increase in symptoms, RV remodeling, and PAP with age, ASD closure must be recommended irrespective of symptoms early after diagnosis even in adults of advanced age.⁸

In Conclusion it is evident that patient with moderate to severe pulmonary hypertension with any shunt (ASD, VSD) needs treatment with pulmonary vasodilator, Sildenafil what

we used here, for significant period of time pre and post operatively. It can certainly reduce complication and improve the outcome of operation significantly, and ameliorate the non operability of late presenting patient.

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Two captains with one mission

Systemic Lupus Erythematosus (SLE) with Pregnancy -A successful Outcome

Nahar N¹, Chaudhury S², Jessmin S³, Paul S⁴

The ORION Medical Journal 2012 July;15-1(38): p23-24

Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease that predominantly affects women of reproductive age. Pregnancy and its outcome is a major concern to most SLE patients. Queries regarding the risk of disease flares during pregnancy, chance of fetal loss, and the safety of various drugs are often raised. With the improvement in the understanding of the pathogenesis of SLE and the judicious use of immunosuppressive drugs, better disease control can now be achieved and SLE patients should not be deprived of the opportunity for bearing children. Pre-pregnancy counseling and close collaboration with other specialists such as the obstetricians and the perinatologist is essential in optimizing the fertility rate, optimal timing of conception, risk of disease flares during lupus pregnancy, pregnancy course, fetal outcome, safety of various drugs used for disease control during pregnancy and lactation, and contraceptive advice are discussed.

Introduction

SLE is an autoimmune disease of unknown cause, characterized by the production of multiple auto antibodies. It affects predominantly young women.

SLE is an autoimmune disease that is well recognized to affect women primarily, especially those of childbearing age. As a consequence, pregnancy and its outcome are of particular importance in this condition. Although advances in the treatment of obstetric complications and improvements in neonatal medicine have allowed women with SLE to have successful pregnancies, SLE remains a disease associated with significant fetal and maternal morbidity.¹

The impact of pregnancy on lupus disease has been investigated but remains controversial, especially with regard to the incidence of disease exacerbations during gestation.

Key words: SLE, Systemic Lupus Erythematosus

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Various studies have demonstrated that lupus activity may increase,²⁻⁵ decrease or remain unchanged throughout pregnancy.⁶⁻¹¹ Several reasons have been proposed to explain this disparity.

Differences in the composition of patient cohorts and the use of non-standardized definitions of lupus flare make comparison between studies difficult. Moreover, many complications common to pregnancy may be mistakenly attributed to SLE.^{9,12}

In contrast, the impact of SLE on pregnancy is more clearly understood. Women with lupus disease are not less fertile than unaffected women,¹³ but fetal outcome in lupus pregnancy is characterized by higher rates of fetal loss, preterm delivery and intrauterine growth restriction (IUGR).¹ Multiple factors have been identified in association with this less successful outcome, including lupus activity during pregnancy, previous nephropathy, maternal hypertension and positivity for antiphospholipid (aPL) antibodies.^{1,14}

Finally, SLE may affect the outcome of pregnancy through the development of neonatal lupus, a syndrome that is characterized by fetal and neonatal heart block and subacute cutaneous lupus lesions and is associated with the presence of antibodies to the cytoplasmic ribonucleoproteins SSA (Ro) and SSB (La).¹⁵

Case Report

Mrs. Nuri Nusrat, 23 years old, lady P-1+1 (abortion) house wife of middle class family hailing from Rajpara, Rajshahi, got herself admitted in RMCH on 11th March 2011 at her 37 weeks of pregnancy with known case of SLE for last 12 years with chronic HTN. She was in remission phase for last 5 years & became pregnant as per her doctors advice. She was under care of an obstetrician and medicine specialist at the same time. She was treated with antihypertensive drugs & low dose aspirin throughout her pregnancy period. Antenatally, she repeatedly developed anaemia without any visible blood loss & received 20 units of fresh blood. After admission, she noticed less fetal movement & on examination of the patient, there was fetal bradycardia. A medical board was formed by medicine specialist, anaesthetist, obstetrician, and neonatologist. As per decision of the board emergency caesarean section was done. A mildly asphyxiated female baby weighing about 2.5kg was delivered. The baby was managed by the neonatologist present. The post-operative period of the patient was uneventful. And after 8th postoperative day the patient was discharged with a healthy kid.

Discussion

Patients with SLE have normal fertility and should not be discouraged from having children. A thorough and detailed discussion with the couples regarding the risk of disease flares, optimal timing of conception, possible maternal and fetal complications during pregnancy and their consequences is essential in relieving anxiety from the patient and ensuring a satisfactory pregnancy outcome. Pregnancy is best undertaken when the general health of the patient is at its best and when the disease, especially lupus nephritis, is in clinical remission for at least six months. Appropriate counseling for the risk of neonatal lupus syndrome should also be given to those patients with positive anti-Ro or anti-La antibodies. Aspirin and / or subcutaneous heparin should be considered for those who have recurrent miscarriages and positive antiphospholipid antibodies. Pregnancy in women SLE is a high risk and judicious monitoring for disease flares and thrombo-embolic phenomena during the pregnancy course and the puerperal period is mandatory. Blood pressure, urine protein, creatinine clearance, complement concentrations, anti-DNA titres, and blood counts should be obtained at each antenatal visit and close collaboration with obstetricians and perinatologists is essential.

Regular surveillance for the well being of the fetus can be achieved by methods such as the non-stress test and biophysical profile. Fetal ultrasonography and echocardiography is useful in picking up CHB (Congenital Heart Block) during the second trimester of pregnancy and monitoring for progress.

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Information for Authors

The followings are the minimum requirements for manuscripts submitted for publication-

The MANUSCRIPT should be prepared according to the modified Vancouver style as proposed by the International Committee of Medical Journal Editors (ICMJE). The entire uniform requirements document was revised in 1997 which is available in the Journal of American Medical Association (JAMA. 1997;277:927-934) and is also available at the JAMA website. Sections were updated in May 1999 and May 2000. The following section is based mostly on May 2000 update.

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, telephone number and email address 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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Acute Inversion of Uterus

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The ORION Medical Journal 2012 July;15-1(38): p25

Abstract

Inversion is an extremely rare but a life threatening complication in third stage in which the uterus is turned inside out partially or completely. Acute inversion usually occurs during or immediately after child birth-causing shock. Obstetric inversion is almost always and acute and usually complete. Non puerperal inversion is rare and it is usually associated with an underlying benign or malignant uterine mass.

Case Report

Mrs. Lata, 25 years old (Parous women) referred from Harirampur Health Complex to Manikgang Islami Bank Hospital on 7th June, 2011 with the diagnosis of PPH (Post Partum Haemorrhage). She had vaginal delivery conducted by untrained birth attendant two hours prior to admission followed by heavy vaginal bleeding, which was continuing till admission. Patient was exhausted, dehydrated and hypotension with tachycardia.

On abdominal examination - Uterine fundus could not be palpated but cupping could be appreciated.

On vaginal examination - A pear shaped mass protruded outside the vulva with the broad base pointed downwards and looked reddish purple in color.

Bimanual examination was done not only to confirm the diagnosis but also to note its degree. In such a way a clinical diagnosis of acute inversion of uterus was made.

Management

1. General condition was improved by blood transfusion.
2. Broad spectrum antibiotics were given to control sepsis.
3. Manual reposition of the uterus was done under general anaesthesia and hand remained inside the uterus till the uterus becomes contracted by parenteral oxytocin. Patient tolerated the surgery well.

Discussion

Inversion of uterus may be classified into two groups- puerperal and non puerperal. Puerperal uterine inversion is one of the most serious complications in obstetrics. Degree of uterine inversion- incomplete (first & second degree) and complete (third degree). Common risk factor for acute inversion of uterus is mismanagement of third stage of labour.

Key words: Acute Inversion of Uterus

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Imaging procedures such as ultrasound and Magnetic Resonance Imaging (MRI) facilitated diagnosis of uterine inversion. MRI is too expensive and not available everywhere in our country.

Treatment of uterine inversion depends on preoperative diagnosis. As it is commonly met in unfavourable surroundings - prognosis is extremely gloomy. Patient usually present with shock, but even if the patient survives - infection, sloughing of the uterus, chronic inversion with ill health may occur.

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Freedom from visceral pain

Rhabdomyosarcoma of the uterus

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The ORION Medical Journal 2012 July;15-1(38): p26-27

Abstract

Rhabdomyosarcoma of uterus is an uncommon malignant soft tissue tumor rarely found in female genital tract and carries a very poor prognosis especially in adult. A 72 years old postmenopausal widow was evaluated for a lower abdominal mass, intermittent and unprovoked vaginal bleeding, weight loss and anemia. Examination showed a huge abdomino-pelvic mass and also irregular cauliflower mass protruding through the cervix & foul smelling profuse vaginal discharge with pruritus vulvae. Exploratory laparotomy showed the uterus was enlarged about 24 weeks pregnancy size, firm in consistency, but without involvement of the surrounding structures. All the fornices were found free but left lateral fornix was slightly involved. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was done. And the specimen was sent for histopathological examination. Histopathology report revealed rhabdomyosarcoma of the uterus. The post operative period of the patient was uneventful & removal of stitches was done on the 8th post operative day. And then she was referred to radio-oncology department for further management.

Introduction

Rhabdomyosarcoma is a soft tissue neoplasm arising from the primitive embryonal mesenchyme. Embryonal rhabdomyosarcoma is the most common subtype. It is generally regarded as a neoplasm occurring during childhood, although there have been a few reports of these neoplasm in adults.¹

It is a very rare tumour, and till now only 60 cases have been reported.² Middle aged women are most often affected and usually have irregular vaginal bleeding, lower abdominal pain and enlarged uterus on physical examination.³ Prognosis is usually poor, with reported 5 year survival of 8.8%-20%^{4,5,6}

Key words: Rhabdomyosarcoma, uterus

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In patients with distant metastasis survival is usually short (mean 15.7 months).⁷ In uterine rhabdomyosarcoma metastasis is confined to the pelvis. Metastasis outside the pelvis typically involving the lung parenchyma producing pulmonary nodules.

Case report

Mrs. Momena, 72 years old widow from Kanaikhale, Natore was admitted in Gynae department of Rajshahi Medical College Hospital, Rajshahi with the complaints of mass in the lower abdomen with foul smelling per vaginal discharge, and for the last one year she had post menopausal bleeding also. She also gave the H/O polypoidal fleshy mass coming out through the vagina with foul smelling vaginal discharge. She was para 7, all delivered at home by vaginal delivery. Age of her last child was 25 years. And she was post-menopausal for 22 years. Her family history was unremarkable. Examination revealed, the patient was severely anemic, normotensive with debilitating general condition. Per abdominal examination showed a 24 weeks size firm mass in the lower abdomen, mobile and mildly tender. Pelvic examination showed a polypoid fleshy mass protruding through the cervix, with foul smelling, profuse, vaginal discharge. All fornices were free but the left lateral fornix was slightly involved. USG report stated that, it was a pelvic mass. Anemia was corrected by blood transfusion. Regular hip bath was advised. After one week of her admission, total abdominal hysterectomy with bilateral salpingo-oophorectomy was done & the specimen was sent for histopathological examination. Report showed rhabdomyosarcoma of the uterus. The post operative period was uneventful except mild bloody P/V discharge for a few days which was controlled with conservative management. After removal of the stitches she was referred to the Radio-oncology Department for further management.

Discussion

Uterine rhabdomyosarcoma is an uncommon tumour that usually occurs in post menopausal woman. Histologically round, polygonal or spindle shaped cells grow in a diffuse, haphazard pattern mixed with aggregates of rhabdomyoblasts. Necrosis and hemorrhages are frequently found in the tumour mass. Mitotic figures range from 1-20 mitosis per HPF.⁸ Though the cytological and architectural features of our tumor were consistent with the above features, we found that, it was necessary to confirm our diagnosis with immunohistochemistry and FISH. (Fluorescence in-situ hybridization).

The immunohistochemical stains of this tumor are positive for myoglobin, desmin and muscle specific actin. The tumor primarily metastasizes locally in the pelvis and to the legs,⁹ and autopsy studies by Rose et al¹⁰ showed lung metastasis in 52% of patients, with all pathologic types of uterine sarcoma being represented.

The treatment of uterine rhabdomyosarcoma is hysterectomy. Adjuvant chemotherapy & radiotherapy have been ineffective in prolonging survival in most series¹¹. Due to rarity of tumor variety there is no standard treatment established in the literature for adult patient and optimal management remains unknown.^{12,13,14} Though there is limited recommendation for the definite management of rare tumor variety, due to its rapid progression only recognition and diagnosis and a prompt multimodality treatment approach comprising surgery, chemotherapy & radiotherapy offers the best chance of cure.

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Orion Pharma Ltd. has launched Cefditoren INN 200 mg tablet under the brand name of Cefditor 200. Cefditor 200 (Cefditoren) is a third generation broad spectrum cephalosporin with the lowest MIC against the most common RTI pathogens among the available cephalosporins. Therefore, Cefditor ensures maximum benefits with minimum concentration in RTI. Cefditor is approved by the USFDA for acute exacerbation of chronic bronchitis (AECB), pharyngotonsillitis and uncomplicated skin and skin structure infections (USSSIs). Moreover, the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) has recommended Cefditoren as a treatment option in CAP. The dosage for Community-Acquired Pneumonia is 400 mg BID for 14 days, Acute Bacterial Exacerbation of Chronic Bronchitis - 400 mg BID for 10 days, Pharyngitis/Tonsillitis 200 mg BID for 10 days, Uncomplicated Skin and Skin Structure Infections - 200 mg BID for 10 days. Cefditor 200 is available in 2x4's tablets in blister strips at TK. 1200 per box.



Novoxen

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Naproxen which effectively relief pain decreasing the risk of GI complication as well. Novoxen is approved by the USFDA. It is indicated for the relief of signs and symptoms of Osteoarthritis, Rheumatoid arthritis and ankylosing spondylitis. Novoxen 375 is available as 5X4's Tablets in blister strips at Tk 160/box. Novoxen 500 is available as 5X4's Tablets in blister strips at Tk 200/box.

Nuvace

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To reduce various cardiovascular events beyond hypertension Orion Pharma Ltd. introduces Nuvace-2.5 Tablet (Ramipril BP 2.5 mg) & Nuvace-5 Tablet (Ramipril BP 5 mg). Nuvace is an Angiotensin converting enzyme (ACE) inhibitor. It is indicated in mild to severe hypertension, congestive heart failure, patients with a history of cardiovascular disease with the risk of stroke, myocardial infarction and death from cardiovascular events, proteinuric non-diabetic nephropathy. The usual initial dose of Nuvace in hypertension is 1.25 - 2.5 mg once daily. For Congestive heart failure after myocardial infarction, the initial dose initial dose of Nuvace is 2.5 mg twice daily but if hypotension occurs, dose should be reduced to 1.25 mg twice daily. For prevention of major cardiovascular events, the recommended dose is 2.5 mg once daily for the first week of therapy and 5 mg once daily for the following 3 weeks. The initial dose in renal impairment is 1.25 mg Nuvace once daily. For the patients with heart failure and renal impairment, the recommended dose is 1.25 mg once daily. Nuvace-2.5 is available in 3X10's blister strips of at Tk. 131.95/box and Nuvace-5 is available in 3X10's blister strips of at Tk. 211.13 /box.



Onium

Freedom from short-term visceral spasm of children

To get freedom from short-term visceral spasm of children Orion Pharma Ltd has introduced Onium 50 ml (Tiemonium Methylsulphate INN 10 mg/5ml) syrup. Onium is indicated for pain in Gastroenteritis, Diarrhoea, Dysentery, Biliary Colic, Enterocolitis, Cholecystitis, Colonopathies, Mild Cystitis and Spasmodic Dysmenorrhoea. Dosage of Onium includes : Tablet In adults the usual oral dosage is 2 to 6 tablets (100-300 mg) daily in divided doses as required and Onium Syrup: Children: 1.5 - 3.0 ml (3-6 mg)/kg body weight daily in divided doses. Adult: 15 - 45 ml (30-90 mg) three times daily. Onium 50 ml syrup is available in a PET bottle with a dropper at MRP Tk. 50.00/Bottle.



Launching of New Products

Oranex

A non-hormonal antifibrinolytic agent

Reducing blood loss in Menorrhagia or after dental surgery is a great concern. Orion Pharma Ltd introduces ORANEX Capsule (Tranexamic Acid BP 500 mg) to reduce the blood loss. Oranex is a non-hormonal antifibrinolytic agent with greater superiority over Norethesteron. It is indicated for Fibrinolysis conditions like Prostatectomy and bladder surgery, Menorrhagia, Epistaxis, Haematuria, Conisation of the cervix, Management of dental extraction in patients with coagulopathies, Ulcerative colitis, Gastrointestinal haemorrhage, Hereditary angioneurotic oedema. The usual dosage of Oranex for the patients who are above 15 years, is 500 mg, 2 to 3 times daily for 7 to 10 days. It is available as 2 x 10's capsules in Alu-PVDC pack at MRP Tk. 300/box.



Ambrotil-Drops

Only recommended expectorant for infants and children (≤2 years)

To ensure expectoration of infants and children (≤2 years) Orion Pharma Ltd. has introduced Ambrotil-Drops (Ambroxol HCl BP). It is indicated in Productive cough, Acute and chronic inflammatory disorders of upper and lower respiratory tracts associated with viscid mucus including acute and chronic bronchitis, Inflammatory disease of rhinopharyngeal tract (laryngitis, Pharyngitis, sinusitis and rhinitis) associated with viscid mucus, Asthmatic bronchitis, bronchial asthma with thick expectoration, Bronchiectasis, Chronic pneumonia. Dosage and administration of Ambrotil Pediatric Drops are: 0 - 6 months old: 0.5 ml, 2 times a day, 6 - 12 months old: 1 ml, 2 times a day, 1 - 2 years old: 1.25 ml, 2 times a day. Ambrotil Pediatric Drops is available in Amber color glass bottle containing 15 ml pediatric drops with a calibrated dropper at MRP Tk. 25/Bottle



Novodol

Judicious combination in justified price

To ensure rapid onset of action with longer duration of analgesia Orion Pharma Ltd. has launched an unique combination of Tramadol HCl BP 37.5 mg & Paracetamol BP 325 mg Tablet under the brand name of NOVODOL, a Judicious combination in justified price. Novodol is indicated for the symptomatic treatment of moderate to severe pain, such as post surgical pain, acute and chronic low back pain, osteoarthritic pain, dental pain, muscle pain etc. It has excellent efficacy for long-term pain management with splendid tolerability profile in patients with acute & chronic pain. The dosage for the management of pain,



the recommended dose is 1 or 2 tablets every 4 to 6 hours as needed for pain relief up to a maximum of 8 tablets per day. Novodol is not recommended in patients under 18 years of age. Novodol is available as 5x10 tablets in blister strips at MRP Tk. 250.00

Xil-50

Start at low & go slow

Orion Pharma Ltd. has introduced Xil-50 (Pregabalin INN 50 mg) Capsule to ensure effective treatment with low dose. It is indicated for: Neuropathic pain, Fibromyalgia, Seizures/epilepsy, GAD. The Dosage & Administration of Xil capsule are:



1. Neuropathic pain, initially 150 mg daily in 2-3 divided doses, increased if necessary after 3-7 days to 300 mg daily in 2-3 divided doses, increased further if necessary after 7 days to max. 600 mg daily in 2-3 divided doses. Child and adolescent under 18 years not recommended.
2. Fibromyalgia, the recommended dose is 300 to 450 mg daily. Dosing should be begin at 150 mg daily in two divided doses and may be increased to 300 mg daily in two divided doses within 1 week based on efficacy and tolerability. Patients who do not experience sufficient benefit with 300 mg daily may be further increased 450 mg daily in two divided doses.
3. Epilepsy, initially 150 mg daily in 2-3 divided doses, increased if necessary after 7 days to 300 mg daily in 2-3 divided doses, increased further if necessary after 7 days to max. 600 mg daily in 2-3 divided doses. Child and adolescent under 18 years not recommended.
4. Generalized anxiety disorder, initially 150 mg daily in 2-3 divided doses, increased if necessary at 7 days intervals in steps of 150 mg daily; max. 600 mg daily in 2-3 divided doses. Child and adolescent under 18 years not recommended.

Xil-50 is available as 3x10's capsules in blister strips at Tk.240/box

Eroflam

A rapid pain killer

For rapid relief of pain Orion Pharma Ltd has launched Eroflam (Etoricoxib INN) 60 mg and 90 mg tablet. Eroflam is indicated for relief of pain and inflammation in osteoarthritis, rheumatoid arthritis, other chronic musculoskeletal disorders, acute gout, dysmenorrhoea & following dental surgery. Dosage and administration in Adult and adolescent over 16 years are: Osteoarthritis, Chronic musculoskeletal disorders & Dysmenorrhoea: 60 mg once daily, Rheumatoid arthritis: 90 mg once daily, Acute gout & Pain following dental surgery: 120 mg once daily. Eroflam 60 tablet is supplied as 3x10's tablets/box in blister strips at Tk.240 and Eroflam 90 3x10's tablets / box in blister strips at Tk.360.



Chili peppers 'help to burn fat'

"A sprinkling of red chili peppers on your dinner keeps hunger pangs at bay," reports the Daily Mail. It said that spicing up a daily diet with chopped chili peppers could help curb your appetite. The effects of capsaicin, the chemical that makes peppers and chilies hot, have been studied again in a small trial investigating what effects hot red (cayenne) pepper has on energy expenditure, body temperature and appetite. It used doses that people would normally eat and found that 1g of pepper reduced cravings for salty, sweet and fatty foods and increased energy expenditure. It noted that this effect was greater among the 12 trial participants who did not normally eat spicy peppers compared with the 13 who reported being regular users. This study tested the effects of eating hot red pepper at mealtimes on post-meal energy expenditure, body temperature and appetite. It found that, compared with eating no cayenne pepper with the meal, 1g of pepper reduced salty, sweet and fatty food cravings and also increased energy expenditure. The effect was greater in people who did not normally eat spicy peppers compared with those who reported being regular users. In general, the press accurately represent the reporting of this study. However, as the study was conducted in people of normal healthy weight, the suggestion that chilies may be of benefit to people trying to lose weight is an assumption that should not be made on the basis of the current study alone.



Source: NHS, UK, Daily Mail, April 27 2011

Chemicals in nail polish, hair spray may increase diabetes risk

A group of chemicals found in personal care products may raise the risk of diabetes, a new study suggests. Women in the study with highest concentrations of these chemicals, called phthalates, in their bodies were more likely to have diabetes than women with lowest concentrations, the researchers said. Phthalates are found in a variety of products, including nail polish, hair sprays, soaps and shampoos. There was also a link between high concentrations of phthalates and insulin resistance among women who did not have diabetes. The findings suggest that phthalates could disrupt blood sugar metabolism, said study researcher Tamarra James-Todd, of Brigham and Women's Hospital's Division of Women's Health. James-Todd and colleagues analyzed information from 2,350 women ages 20 to 80 who took part in the National Health and Nutrition Examination Survey, conducted by the Centers for Disease Control and Prevention, between 2001 and 2008. As part of the survey, participants underwent physical exams and provided urine samples. Of the participants, 217 reported having diabetes. Women who had the highest levels of two chemicals



mono-benzyl phthalate and mono-isobutyl phthalate in their urine samples were nearly twice as likely to have diabetes as women with the lowest levels of those chemicals, the study found. Women with moderately high levels of the chemicals mono-n-butyl phthalate and di-2-ethylhexyl phthalate had approximately a 70 percent increased risk of diabetes. It's possible that phthalates indirectly increase the risk of diabetes by interfering with the metabolism of fat tissue, which can lead to insulin resistance, the researchers said.

Source: Fox Health News

Fighting Malaria by modifying friendly bacteria in Mosquito gut

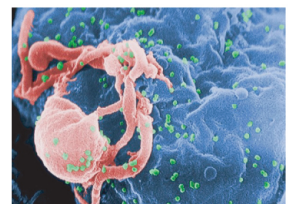
By genetically modifying gut bacteria in the malaria mosquito, US researchers have found a potentially powerful way to fight malaria. The modified "friendly" bacteria, which live in the midgut of the mosquito alongside the malaria parasite, produce toxins that are deadly to the parasite but do not harm humans or mosquitoes. The researchers suggest their findings provide a "foundation for the use of genetically modified symbiotic bacteria as a powerful tool to combat malaria". They already knew that the most vulnerable stage of development of Plasmodium, the mosquito parasite that causes malaria, occurs in the lumen of the midgut in the mosquito, an environment shared with symbiotic or "friendly" bacteria. Also, from previous work, Jacobs-Lorena had already established that one of the symbiotic bacteria, Pantoea agglomerans, can be genetically modified to secrete "antimalaria effector molecules" that are toxic to the malaria parasite. The battle against malaria has to be fought on a number of fronts: insect repellent and bed nets can help prevent transmission from mosquitoes to humans, but work like that of Jacobs-Lorena and colleagues helps to find ways to control malaria one step earlier by eliminating infection within the mosquito itself.



Source: Medical News Today

US FDA approves first drug shown to reduce risk of HIV infection

A daily pill to protect people at risk of HIV from infection has been approved by the US Food and Drug Administration (FDA), potentially offering a new and powerful weapon in the battle against AIDS. The pill, Truvada, will be available in the US to people at extreme risk of HIV because their partners are infected. But at \$14,000 (£9,000) a year, it will be expensive - even though far cheaper than a lifetime of treatment after infection - and those without health insurance are unlikely to get it. The Aids Healthcare Foundation (AHF) said evidence published recently showed the

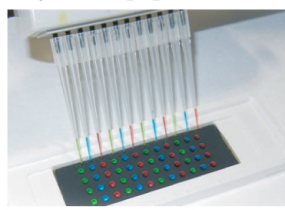


drug could possibly cause kidney damage. It also argued Truvada should not be given without an HIV test to ensure the person taking the pills is not already infected - otherwise the virus could become resistant to the drug. Trials of the drug were run both in the US and in Africa. The University of Washington's international clinical research centre recruited more than 4,700 discordant couples - in which one partner had HIV but the other did not - in Kenya and Uganda starting in 2008. The Partners PrEP (pre-exposure prophylaxis) study, as it was called, was one of the largest-ever HIV prevention trials. General side effects of Truvada include diarrhoea, pain and weight loss, but the FDA considered that they were outweighed by the benefit to people who were at high risk of HIV infection. The study, recently published in the New England Journal of Medicine, found a 75% protection rate in the couples where the uninfected partner took Truvada.

Source: The Guardian

IBN develops biochip for investigating the effect of drugs on cancer stem cells

Researchers at the Institute of Bioengineering and Nanotechnology (IBN), the world's first bioengineering and nanotechnology research institute, have developed a miniaturized biochip for investigating the effect of drugs on cancer stem cells (CSCs). Published recently in Nano Today, this new technology could boost the development of more effective cancer drugs. In a tumor, CSCs form a small and distinct class of cancer cells that are more resistant to chemotherapy. Similar to stem cells found in human tissues, CSCs can produce and differentiate into different cell types. If CSCs are not eradicated, they can repopulate the tumor and lead to cancer recurrence.



Hence, it is important for researchers to understand the efficacy of anti-cancer drugs against CSCs. However, since CSCs are so scarce - they make up approximately 1% of cancer cells - their study has been hampered by

conventional drug screening methods, which require large sample volumes and are slow and expensive. A team of researchers led by IBN Executive Director, Professor Jackie Y. Ying, has developed a miniaturized biological assay called the Droplet Array to perform cheaper, faster and more convenient drug screening using limited samples. In traditional biological assays, microplates - a flat plate with multiple wells in which samples are placed - are commonly used, and each well requires at least 2,500 or 5,000 cells, to be present for viable analysis. By comparison, IBN's Droplet Array is a flat, rectangular glass plate on which a series of spots, each 2 millimeters in diameter, are arranged. The samples are pipetted into these tiny spots, making them appear like droplets. The plate is then coated with a layer of proprietary oil to prevent evaporation and cross contamination between the sample droplets during the rinsing process. An accompanying bench-top device to automate the rinsing process of the plate has also been developed. Being one-

fifth the size of a well in a standard microplate, each spot on IBN's Droplet Array requires only 500 cells for screening. This massive reduction in sample volume not only saves money, but is also particularly advantageous for studying scarce quantities of target cells, such as CSCs. Using the Droplet Array, the IBN researchers investigated the drug responses of CSCs extracted from breast, liver and colon cancer cells. It was found that chemotherapeutic drugs such as doxorubicin, which usually induce cell death in liver cancer cells, demonstrated poor efficacy in liver CSCs. The CSCs from the breast and colon tumors also showed much greater ability to survive the effects of anti-cancer drugs. Animal studies were conducted to validate the findings of the Droplet Array. CSCs and non-CSCs from liver tumors were implanted into two different sets of mice at the same time. After 6 weeks, tumors were formed in the mice implanted with CSCs, whereas the mice without CSCs did not develop any tumors. Tumors extracted from the mice with CSCs also showed blood vessel formation, which confirmed the self-renewal property of these cells. The drug resistance properties of CSCs have been widely discussed in recent years but until now, it has been challenging to quantify this correlation. Using the Droplet Array, IBN researchers have successfully demonstrated that CSCs can survive chemotherapy and drive metastasis.

Source: Nano Today

Breast cancer risk lower in migraine sufferers

For women there may be one good thing about having migraines: a reduced risk of breast cancer. In a study of more than 9,000 people, Dr. Christopher I. Li of Fred Hutchinson Cancer Research Center in Seattle and his colleagues found that those with a history of migraines were 26% less likely to develop breast cancer. The findings back up an earlier study, also by Li and his team, which included about 2,000 women and found a 33% lower breast cancer risk among women with migraines. Low estrogen levels appear to increase the severity and frequency of migraines in women, the researchers note in their report, while increased levels of the hormone are known to boost breast cancer risk, so it's "biologically plausible" that migraine sufferers would be less prone to breast cancer. In the current study, Li and his team compared 4,568 women with breast cancer, ranging in age from 34 to 64, to 4,678 healthy controls. They accounted for the effects of migraine triggers such as alcohol, smoking or hormone use, which hadn't been done in the previous study. The researchers found a 26% lower risk of breast cancer in the women with migraines, which didn't change when they took migraine triggers or whether or not a woman was menopausal into account. Similarly, use of prescription drugs for migraine did not change the risk. Migraine patients' greater use of non-steroidal anti-inflammatory drugs (NSAIDs), painkillers including ibuprofen and naproxen, could explain some, but probably not all, of their lower breast cancer risk, Li and his colleagues say.

Source: Cancer Epidemiology, Biomarkers & Prevention.



Medical Services Department of Orion Pharma Ltd. successfully arranged significant number of Scientific Seminar, Round Table Meeting and Clinical Meeting in different venues of Bangladesh.

Scientific Seminar (SS)

Faridpur

Bangladesh Medical Association, Faridpur Branch

On 28th March 2012 a Scientific Seminar on "Perioperative fluid management" was arranged by the Bangladesh Medical Association (BMA), Faridpur Branch at the Ambika Memorial Hall, Faridpur. The seminar was presided over by the renowned physician Dr. ASM Jahangir Chowdhury, Honorable president of BMA, Faridpur. About 400 doctors were welcomed by Dr. SM Khairul Islam, secretary, BMA, Faridpur. A prominent anesthesiologist Dr. Jahangir Alam, Assistant Professor and Head of the Department of Anesthesiology, FMCH was the core speaker of the seminar. In his speech he established the 'Fluid Management' as an integral and important function for anesthesia providers in perioperative management. Dr. Ananta Kumar Biswas, Medical Officer, Department of Anesthesiology, FMCH also spoke on fluid loss and significant fluid shift of the patients during perioperative period. The program was concluded with an attractive raffle draw sponsored by the Orion Pharma Ltd.



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Department of Pediatrics, KMCH

A Scientific Seminar on "Child Health Problem: Neonatal Convulsion" was arranged by the Department of Paediatrics, Khulna Medical College & Hospital on 18th June 2012 at Hotel Western Inn International Ltd. Khulna. Dr. Kazi Hafizur Rahman, a famous consultant of paediatrics of Khulna took the chair of the seminar. Dr. AKM Mamunur Rashid, Associate Professor, Department of Paediatrics, KMCH also present as Co-Chairperson. The main discussion on the topic has been made by Dr. MA Hassan, Assistant Professor, Department of Paediatrics, KMCH. Dr. Upananda Roy also took part and presents his paper. Around 100 doctors were participated the seminar.

Round Table Meeting

Department of Medicine, DNMCH

"Side Effect of Mobile Phone" an interesting discussion has been taken by the department of Medicine, Dhaka National Medical College & Hospital, on 22nd May, 2012 at the college building. The meeting was presided over by Dr. AKM Morshed, Associate Professor, Unit-II, Department of Medicine. Dr. MAZ Khan Galib, Registrar, Medicine Unit-II and Dr. Kalimullah, Assistant Registrar, Medicine Unit-II Spoke on the clinical effects of daily exposure to mobile phones in general populations and also addressed the impact on developing head and brain tumours, other morbidity-related outcomes.

Department of Physical Medicine and Rehabilitation, DMCH
round Table Meeting was arranged on 26th May, 2012 by the Department of Physical Medicine and Rehabilitation, Dhaka Medical College & Hospital, Dhaka. At the department a discussion on "Management of gouty arthritis" took part.

Dr. Ruhul Amin elaborately discussed on the topic. The meeting was chaired by the head of the department, Professor Dr. Soheli Rahman. All members of the department were present at the program. It was concluded with a product discussion on 'Fostat' by Mr. AfjalusSiraj, Product Executive, Product Management Department of the sponsoring company Orion Pharma Ltd.



CRP, Savar

On 14th June 2012 a round table meeting was arranged by the Centre for the rehabilitation of the Paralyzed (CRP), Savar. A discussion was held on "New Horizon in Pain Management" in the meeting. Dr. MA Kader, Principal, Bangladesh Health Professionals Institute was adorned the seat of chairperson. On behalf of Orion Pharma Ltd. Dr. Md. Shafiqur Rahman spoke on the topic and he designated the "Tendonil" as the new opportunity in the pain management. The program was concluded by a closing speech given by Dr. A Razzak, CMO, CRP, Savar.



Department of Medicine, KMCH

A round Table Meeting on "Headache and its management" was arranged by the Department of Medicine, Khulna Medical College & Hospital at KMCH auditorium, Khulna. Dr. Md. Abu Bakkar, Associate Professor, Department of Medicine, adorned the seat of the chairperson.

MMCH

On 26th April 2012, A round table meeting was organized by ward-15 of Mymensingh Medical College & Hospital at Young King Chinese Restaurant. Dr. Chittaranjan Debnath adorned the seat of the chairperson. Dr. Md. Shafiqur Rahman, Manager MSD, Orion Pharma Ltd. spoke on "Hyperacidity and its Management" in the meeting. All renowned doctors were present at the program.



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