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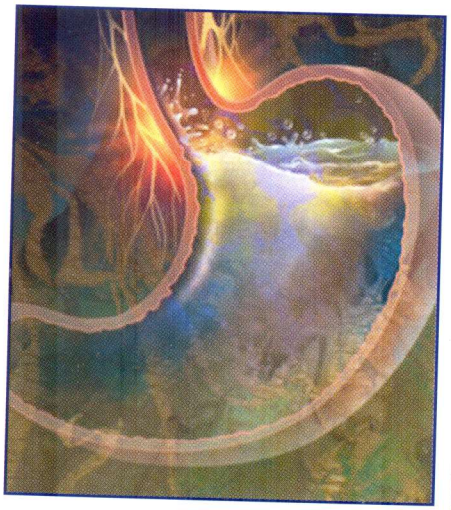

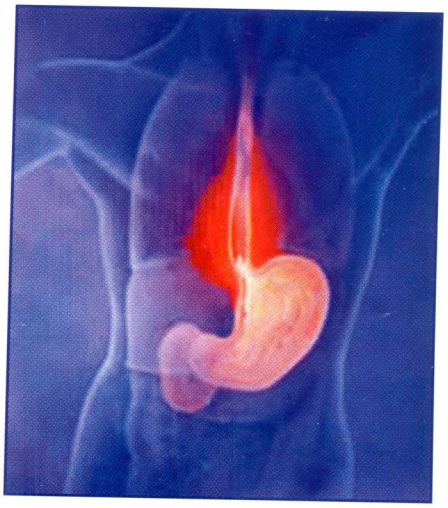

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"The ORION" medical journal is practicing ``Infrangible Aristocracy'' in every step. The ORION accomplishes the choice of millions readers in national and international arena. This volume compiles one special article, one original article, three review articles and three case reports.

The editorial,"Minimally invasive technologies for treating the small renal mass" focuses the uses of ethanol with Radio Frequency Ablation (RFA) in treating small renal mass. It envisages the use of tumor-specific therapies, auto antibodies and gene therapies in addition to tumor ablation technique in future (P-514).

The special article from Michigan State University, USA ``Update on endovascular repair of abdominal aortic aneurysm'' retrospects the epidemiological features, history & development of the endovascular surgery for abdominal aortic aneurysm and re-evaluates the complications of the procedure. The article emphasizes the distinctive advantages of endovascular procedure over the conventional open repair of the abdominal aortic aneurysm (P-515).

The original article on ``Effect of micronutrients on morbidity and duration of hospital stay in childhood pneumonia'' discloses the micronutrients deficiency among the children of Bangladesh especially children under-five in the northern zone of the country (P-519). The article reveals the beneficial effects like short hospital stay & the reduction of cost for pneumonic child by using micronutrients.

The first review article on ``Diabetes in pregnancy & its management'' narrates the most common management problem during pregnancy. It is also accentuating on the proper antenatal care, screening for GDM during 24-34 weeks and fetal surveillance test (P-524). The second review article, ``Stent thrombosis: Rethinking of drug eluting stents'' focuses on the inert-compound coated stents used for myocardial revascularization. The article also evokes the evolution of stent coated cytotoxic drugs, coating with Nitric Oxide-donors, biodegradable stents and newer anti-thrombotic therapy for the future prevention of stent thrombosis (P-528).

Last review article on ``Present advancement in the diagnosis and treatment of typhoid fever'' alarms the increasing resistance of typhoid fever pathogens to conventional antibiotics and evokes advanced diagnostics & alternative effective treatments along with the optimal treatments. The article also highlights concerted effort involving clean water supply, sanitary faeces disposal and prompt treatment of cases and carrier to control the disease (P-531).

First case report on ``A rare case of oral malignant fibrous histocytoma and short review of the literature'' exhibits the oral malignant fibrous histocytoma, a very rare case of oral malignancy diagnosed clinically and confirmed by histological feature. It was treated operatively with authentic reconstruction (P-535). The next case report ``Congenital absence of pulmonary valve'' evaluates a young lady of ventricular septal defect with pulmonary valve stenosis which was treated by replacement of homograft valve in pulmonary valve position (P-537). The last article ``Case history: A healthy pregnancy following chemotherapy for dysgerminoma'' evidences a pregnant lady with dyegerminoma delivered a healthy male baby with the help of accurate surgery and optimal chemotherapy (P-539).

Further opinion and suggestions are highly encouraged for development of `The ORION'. The journal makes freely available at www.orion-group.net/journal for contributing the advancement of public health and medical research. For reproducing multiple copies of any of `The ORION' articles, please e-mail: orionmsd@dhaka.net/ journal@orion-group.net/ orionjournal@yahoo.com & mention the article title, author's name, volume, page number, year of publication and mostly the purpose for reproducing.

May the Almighty bless all in the spirit of good health. `The ORION' wishes all a very colorful & Happy New Year 2008.

DR. MOHAMMAD ZAKIRUL KARIM
Chief Editor
The ORION medical journal

Minimally invasive technologies for treating the small renal mass

Salam MA[1]

The ORION 2008; 29: 514

Renal cancer is a very common problem in urological practice in this country. Each year, >200,000 new cases of kidney cancer are diagnosed and >100,000 deaths worldwide are attributed to this disease, with the highest incidences in North America, Europe and Australia[1]. The incidence of renal cancer is increasing in this country because of the fact that the average longevity of the people is improving and as such more renal cancer will be detected as the age advances. The detection rate of renal neoplasm continues to increase in part due to widespread use of cross sectional imaging techniques such as ultrasound scan, computed tomography (CT) and magnetic resonance imaging (MRI)[2].

The incidental finding of a renal mass 4 cm or less in size in an asymptomatic patient may pose a therapeutic dilemma depending on the clinical situation. These cases are different than conventional clinical picture of a classic, bulky renal cell carcinoma (RCC) and a more aggressive clinical course[1-3]. Incidentally detected renal tumors tend to be smaller in size, of lower clinical stage and often of lower histologic grade, and are associated with a decreased incidence of metastasis and better survival outcomes. It has been shown that the oncologic efficacy of nephron sparing surgery is equivalent to radical nephrectomy for renal cancers <4 cm[3].

In 2007, multiple options exist to treat small renal tumors in a minimally invasive fashion, ranging from laparoscopic nephrectomy and partial nephrectomy (extirpative) to ablative approaches, such as Radio Frequency Ablation (RFA), cryotherapy, or other investigational methods. In the recent past, laparoscopic nephrectomy was referred to as a ``minimally invasive'' procedure. However, with the advent of commercially available ablative needle technologies, the term ``minimally invasive'' now takes on new meaning and may be viewed more as a spectrum ranging from laparoscopy, needle technologies to transcutaneous therapies, such as high intensity focused ultrasound (HIFU) representing the least invasive method. Minimally invasive surgery (MIS) has therefore been developed in this context, to achieve two objectives: parenchyma preservation and low morbidity. Ablative therapy offers several benefits such as minimal, if any, change in renal function and minimal loss of normal parenchyma. Ablative therapy provides the least chance of ``over-treatment'' if the renal lesion is found to be nonmalignant at the time of surgical biopsy, which occurs with increasing frequency in the smaller the tumor. In addition, many of these ablative therapies cause minimal pain and may be performed on an outpatient basis or with a short hospital stay, if deemed medically necessary.

Modern ablative techniques including hyperthermal modalities, such as radiofrequency ablation (RFA), as well as hypothermal techniques, such as cryoablation, may be useful treatment options for patients who are unfit for or those who simply prefer to avoid conventional surgical resection. In contrast to some studies using watchful waiting or active surveillance as an option, many surgeons and patients would prefer to remove or destroy these small tumors. The growing use of RFA to treat small renal neoplasm has shown promise both in short-term cancer control and complications[4]. When reading articles on RFA, it is important to first understand the particular device used in the study[5]. A number of devices are available on the market and each may function in a different way. In general, RF devices can use ``wet'' or ``dry'' electrodes. Conventional or ``dry'' RF is an active electrode that delivers RF energy into the tissue without the aid of a liquid coupler. Dry RF is limited by impedance, or resistance to energy flow, due to a charring effect built up around the electrode over time. ``Wet'' RF electrodes drip a liquid, such as hypertonic saline, during the course of RFA to decrease impedance adjacent to the active tines of the electrode.

The use of wet electrodes allows the current generated to be more easily dispersed into the tissues, thereby generating quite large lesions in a relatively shorter time than conventional ``dry'' RF devices. Fotiadis et al describe their experience combining ethanol injection and RF energy to ablate renal tumors in 27 patients followed for a mean of 18.6 months[6]. Thus far, the combined use of ethanol and RFA has been mainly used in the liver to treat hepatocellular carcinoma. In a randomized controlled trial of 232 patients with hepatocellular carcinoma <3 cm treated with either ethanol injection or RFA, the authors concluded that RFA was superior to ethanol injection as monotherapy[7]. In a separate study of 40 patients with hepatocellular carcinoma >4 cm, the authors concluded that the combination of ethanol injection and RFA was effective[8].

Using normal porcine renal parenchyma, Rehman et al found that ethanol gel lesions had skip areas and did not exhibit complete necrosis by 1 wk when used as a monotherapy[9]. The reader must judge the manuscript by Fotiadis et al[6] as a combined treatment modality because it is unclear what the contribution of each treatment alone represents since there are no comparative arms in the study. In this paper, the authors used an impedance-based electrode (Cool- Tip, Radionics, Burlington, MA, USA) and first injected a mean of 1.7 ml ethanol per session into the center of the tumor. It is not clear where and how far the ethanol dispersed, whether it remained in the interstitial space or entered the cells, or what effect it had on coagulation necrosis, the end effect of RFA.

Several questions about the use of ethanol with RFA remain: How does ethanol exert cell kill in this context? Is it working synergistically with RF energy ? What would be the effect of ethanol alone on the tumor ? If ethanol is effective, where should it be injected- in the center of the tumor or around its perimeter? How much should be injected based on tumor volume? Is there another agent that is better suited to be combined with RF energy? A prospective trial would need to be done to compare the combination of RFA and ethanol injection to either modality alone. We are at an age when ablative technologies used to treat small renal tumors may soon surpass operative, extirpative therapy. For the very small renal tumor <2 cm, clinicians or patients may elect to ablate it in a minimally invasive fashion rather than elect a watchful waiting approach. Researchers are now reporting on short and intermediate-term results using a variety of devices and techniques. As a discipline responsible for the health and welfare of patients with kidney cancer, urologists must better define the indications, safety and contraindications for ablative technologies.

It may be emphasized that strong consideration should be given to obtain an adequate biopsy to identify the tumor type prior to ablation because renal neoplasm exhibits different tumor biology[10]. In the future, tumor-specific drug therapies, use of auto antibodies, gene therapies etc. can be used in addition with tissue ablation technique. The procedures may have a significant role in locally advanced or metastatic in renal cell cancer.

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Continued from Vol. 28

Update on endovascular repair of abdominal aortic aneurysm

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The ORION 2008; 29: 515-518

Abstract

Endovascular repair of abdominal aortic aneurysm was first introduced by Parodi in 1990. There has been tremendous development of the device and the procedure since the investigational stage. Also it has been over a decade of clinical experience of endovascular repair of abdominal aortic aneurysm worldwide. The purpose of this article is to review the application of the procedure related complications and overall outcomes.

Introduction

Abdominal aortic aneurysm is a silent killer. Most people are not aware of its presence until the patient presents with acute symptoms. Early detection and treatment is the key to the prevention of major morbidity and mortality. The incidence of abdominal aortic aneurysm (AAA) in the world is rising because of significant prolongation of longevity of the population, awareness of the disease in the medical community, and the ease of detecting an abdominal aortic aneurysm with a duplex scan. It is estimated that 3-5% of the western population over the age of 50 years have abdominal aortic aneurysm. Thirty percent (30%) of all patients with an abdominal aortic aneurysm have strong family history and there is high predilection to the male gender at a ratio of 4:1. Hypertension and atherosclerotic disease are major contributing risk factors of abdominal aortic aneuryms.

Clinical presentation

The vast majority of patients with abdominal aortic aneurysms are asymptomatic. These are diagnosed during routine physical examinations, during other diagnostic procedures, or with screening duplex scans for patients with high risk factors. 25-30% of patients with abdominal aneurysms present with chronic or acute symptoms. Acute symptoms include severe abdominal or back pain secondary to acute expansion or contained leak of an abdominal aortic aneurysm. Patients will present with symptoms of hypotension when the aneurysm is leaking or ruptured. They also may present with acute ischemic symptoms of the lower extremities, either with major embolic occlusion or as blue-toe syndrome secondary to microembolization.

Patients with abdominal aortic aneurysms frequently present with chronic back pain or abdominal pain. These symptoms can easily be confused with pain secondary to chronic lumbar degenerative disease or gastrointestinal diseases. Occasionally, the patient also presents with obstructive ureteric or gastrointestinal symptoms. Obstructive symptoms are proportionate to the size of the abdominal aortic aneurysm. A large abdominal aortic aneurysm can cause extrinsic compression of either ureter or gastrointestinal tract resulting in chronic symptoms from the obstructing organ. An inflammatory abdominal aortic aneurysm may also present with obstructing symptoms regardless of the size of the aneurysm. In this scenario, the severity of symptoms would depend on the extent and intensity of the inflammatory process around the aneurysm.

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Epidemiology

It is estimated that 40-50% of all ruptured abdominal aneurysm patients succumb to the event before the patient is able to reach the emergency facility. Of those who survive, the morbidity and mortality amongst those even with surgical intervention approaches 40-50%. Mortality is directly related to the immediate availability of an operating room, the experience and skills of the operating surgeon, institutional experiences, and the availability of other supporting specialties in the facility.

History & development of surgery

In 1888, Matas introduced the procedure of epoch-making significance. Later in 1909, he designated it as endoaneurysmorrhaphy. This principle is still an applicable technique in certain situations. In 1952, Dubost first performed the successful resection of abdominal aneurysm with homo-grafting. Debakey and many others have developed and expanded the surgical procedure and radically improved the prognosis of the fatal condition. Although abdominal aneurysm resection is very effective, it nevertheless is quite invasive. The morbidity and mortality of the procedure remains between 5-10% and is significantly higher with co-morbidity of cardiac, pulmonary and renal diseases. In 1990, Parodi performed the first endovascular repair of abdominal aortic aneurysm with the goal of reducing the morbidity and mortality of abdominal aortic aneurysm repair, even in patients with significant co-morbidity.

Since the initial deployment of aneurysm endograft, there has been tremendous technological advancement of graft design, deployment technique and the understanding of application of the procedure. Many graft devices have been approved and are commercially available for the repair of abdominal aortic aneurysms. There are a multiple series of continued development and clinical investigations for treating complex aneurysms, including suprarenal aneurysms with a fenestrated endovascular graft.

Endografts

The approved devices could be categorized into two types:

A. Infra renal fixating devices
B. Supra renal fixating devices

A. Infra renal fixation devices: Infra renal fixation devices (Excluder, Aneurex, Endologix) are deployed distal to the lower most renal artery origin. All grafts have self expanding stents to a predetermined diameter that affixes the graft against vessel wall with the stent's radial force. Excluder has micro-hooks all around the proximal part of the graft to anchor the graft onto aortic wall and thus enhance the fixation of the device. Aneurex has no fixation device and solely depends on the radial force of the stent, however, with this device it is recommended to

extend graft deployment to the iliac bifurcation to prevent migration. Endologix is a unibody bifurcated graft initially deployed at the aortic bifurcation and the graft is extended proximally with aortic cuff upto the lower most renal artery origin. Since the graft sits over the aortic bifurcation, the risk of migration of the graft is practically eliminated.

B. Suprarenal fixation devices: Suprarenal fixation devices (Zenith, Talant) have hooks or stents extending proximally from the upper most part of the graft. The graft is deployed below the lower most renal artery origin but the hooks and stents are placed above the renal artery origins. Zenith has multiple hooks at the proximal end of the graft and Talant has multiple stents for suprarenal fixation of the graft, thus preventing graft migration. All of the graft devices have stents of various configurations along the body and limb of the graft to achieve stability and apposition against the aortic and iliac arteries, thus preventing migration as well as leak around the graft (endoleaks). All of the grafts are bifurcated modular except Endologix, which is a unibody bifurcated graft.

During clinical investigational phase, only approximately 30-40% of patients with abdominal aneurysms were suitable candidates for endograft repair. With downsizing the diameter of the deploying device, upgrading the graft diameter and better understanding of application of the procedure, more and more patients with abdominal aneurysms are treated with endograft. At present, perhaps as high as 70% of patients with abdominal aneurysms are candidates for endograft repair. Before a patient is offered the option of endograft repair of an abdominal aortic aneurysm, a few detail anatomic assessments of the aneurysm are mandatory, not only for feasibility of the procedure but for the selection of the graft device. Proper selection of the patients and the graft device will ensure the success of the procedure and minimize the risks and complications. A good quality CT scan with contrast (preferably 3 mm or less slices) with 3D reconstruction is adequate for preoperative detailed assessment of the aneurysm. Occasionally an angiogram is necessary, particularly for the patient with complicated aneurysm anatomy or with occlusive disease.

Assessment of aneurysm anatomy

A. Proximal aortic neck length, diameter and angulation:

i. Proximal aortic neck length: The aortic neck length needs to be at least 15 mm to avoid any major proximal endoleaks and migration. A 15 mm neck length is not an absolute requirement and many vascular surgeons have successfully treated AAA with a neck shorter than 15 mm in length. In the case of a neck shorter than 15 mm, the choice and sizing of the graft become critical.

ii. Proximal aortic neck diameter: Most of the graft devices are designed to treat the aneurysm with a neck diameter of 26-28 mm or less. At present, Zenith graft is approved to treat aneurysms with a neck up to 32-33 mm. Other commercially available grafts are also in process of up-sizing the graft to treat aneurysms with a larger diameter aortic neck.

iii. Angulation of aortic neck greater than 45 degrees: This is a relative contraindication of endograft repair of an abdominal aortic aneurysm. With the availability of choice graft devices and it's variable compliances, the angle of the aortic neck has become less problematic.

B. Characteristic of plaque at aortic neck: 40% or more of aortic neck diameter calcification or soft atheromatous plaque is a relative contraindication of endovascular repair of an abdominal aortic aneurysm because of increased risk of endoleaks or embolization. With the availability of a suprarenal fixating graft device or the graft placed at the aortic bifurcation, problems arising from partial circumference calcification or soft atheromatous plaque can be avoided. Patients with a significant amount soft atheromatous plaque at the aortic neck have a higher risk of embolization to the renal or mesenteric artery during deployment of the graft. However, patients with total circumferential calcification or soft plaque at the aortic neck are not candidates for endograft repair of an abdominal aortic aneurysm.

C. Evaluation of access artery: The larger the diameter of the femoral and external iliac arteries, the easier it is to advance the device. The smallest of all devices is 7 mm in diameter. Even with less than 7 mm in diameter, sometimes a non-calcified or minimally calcified artery can be dilated to an adequate lumen to advance the device. On the other hand, a heavily calcified artery, even with diameter larger than 7 mm, may result in intimal dissection or rupture of the artery during advancement of the sheath or the graft. It is critically important to assess the access artery before consideration of endograft repair of abdominal aneurysm. If access artery is too small for the graft device, an 8-10 mm graft can be anastomosed to the common iliac artery and brought down to the femoral artery, thus creating an adequate access conduit for the graft device.

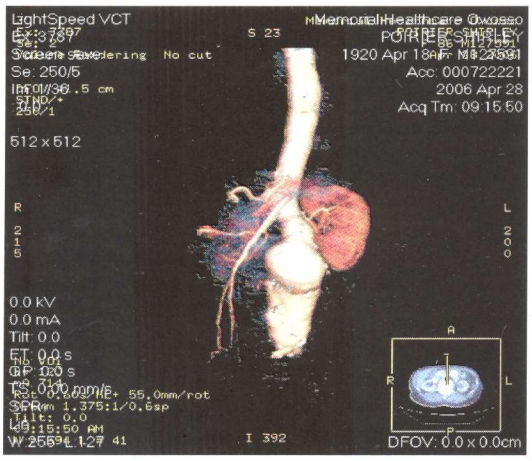

Figure: Pre-operative 3D CT reconstruction of AAA with diameter of 9cm

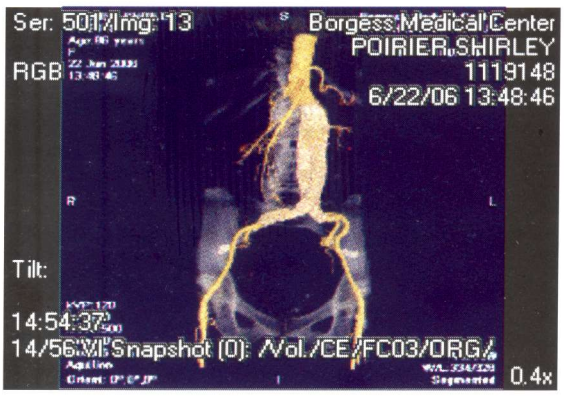

Figure: Post endograft repair 3d CT reconstruction of aorta

Overall, 97-98% of endovascular repair of abdominal aneurysm procedures are technically, as well as clinically, successful. However, the success of the procedure is directly linked to accurate anatomical assessment of the aneurysm, choice of the graft device, and technical skill of the operating surgeon. There are unique sets of complications in relation to endograft repair of aneurysms, in addition to overall complications related to anesthesia, blood loss, and the patient's co-morbidity.

Complications

A. Immediate and primarily technical during the placement of endografts

1. Tear or rupture of access artery (femoral, iliac) usually is because of poor preoperative assessment of access artery, unyielding attitude to an alternative approach or choice of the graft.

2. Rupture or penetration of the aneurysm sac is usually because of careless and unprotected manipulation of guide wire, sheath or graft device.

3. Occlusion of renal artery is due to the deployment of the graft across the renal artery origin. The graft can easily be misplaced because of poor visualization of the renal artery or the angle of the aortic neck is not taken into consideration during deployment. The aortic neck angle should be corrected by acquiring the image at the corrected angle prior to graft deployment. It is also of utmost importance to adequately visualize and map the origins of the renal artery prior to graft deployment. As long as the occlusion of the renal artery is recognized immediately, the deployed graft can be manipulated down to release the renal artery occlusion.

4. Embolic occlusion of renal, mesenteric, iliac and lower extremity arteries. A soft atheromatous plaque at the aortic neck, sac or at the iliac artery is usually visible on contrast preoperative CT scans. An atheromatous plaque can potentially be dislodged or squeezed out during advancement and inflation of the graft at the proximal or distal anchoring ends. These complications can be avoided with diligent advancement of the guide wire, sheath, deployment and inflation of the graft.

5. Acute occlusion or bleeding at the access site is self-explanatory.

B. Delayed and are related to graft device

1. Endoleaks are classified into four types:
   i. Type 1 endoleak is reported in 8-10% of the procedures. This happens during the deployment of the graft or delayed. Endoleaks during deployment of the graft is usually because of misplacement or under sizing of the graft. It also can be result of angulation, calcification or plaque of aortic neck. Delayed endoleaks are because of migration of the graft, enlargement of the aortic neck, and displacement of the graft secondary to remodeling of the aneurysm over a period of time. Most of the Type 1 endoleaks are amenable to placement of either a proximal or distal extender graft or stent larger than the graft size, depending on localization of the endoleak.
   ii. It is considered a Type 2 endoleak when the residual aneurysm sac fills through the inferior mesenteric or lumbar collaterals. The incidence of a Type 2 endoleak varies from 10-15%. Type 2 endoleaks are usually followed with serial CT scans, unless there is a rapid fill of the residual aneurysm sac or noted significant expansion of the residual aneurysm sac. Type 2 endoleaks can be difficult to localize and manage. When the endoleak is localized, the contributing feeding artery and its collaterals can be occluded by coiling, embolization or a combination of both. Other procedures such as injection of onyx or thrombin into the aneurysm sac and retroperitoneal laparoscopic clipping of inferior mesenteric or lumber artery been described with varying degree of success.
   iii. Type 3 endoleaks are due to failure of graft integrity or separation of the graft module, either because of primary failure of graft or secondary to aneurysm sac remodeling. The incidence of type 3 endoleaks depends on the graft device, and the true incidence of Type 3 has not been published. Management of a Type 3 endoleak would certainly depend on the extent of the leak and degree of graft failure. Patient may require surgical explantation of the graft and resection of the aneurysmal sac if leak can not be controlled with endovascular procedures.
   iv. Type 4 endoleaks are secondary to graft porosity. Type 4 endleak was noted in early stage of graft development. With the advancement of graft technology this complication is extremely rare.

2. Migration of the graft has been reported in 12-14% of the procedures in various series depending on the graft device. Aortic neck dilatation and aneurysm sac remodeling may contribute to the cause in migration of the graft and cause type 1 or type 3 endoleaks.

3. Thrombosis of the graft or limb has been reported in 14% of the cases and results from kink in the graft or outflow stenosis/occlusion. If detected early, occlusion of the graft can be managed by graft lysis with tissue plasminogen activator infusion. Post lysis of the graft, the patient may need placement of a stent graft or stent depending on the findings on follow-up angiogram. If the graft or limb occlusion is chronic, the patient would need the appropriate reconstructive procedure or extra-anatomic bypass graft.

4. Expansion of the aneurysm sac is believed to be either because of known or occult endoleak, thus resulting in increased tension in the residual sac. In general, expansion of aneurysm sac can be managed by endovascular placement of stented graft or stent when type 1 or type 3 endoleak is detected and localized, otherwise patient would require open surgical resection of the aneurysm depending on the size and rate of expansion. There also have been many reported cases of sac expansion because of seroma around the graft. The majority of these cases are followed carefully with serial CT scans in the absence of definite endoleaks.

Discussion

The annual rate of secondary procedures for open surgical

resection of an aneurysm has remained stable over the last several decades at 3%. The annual rate of secondary procedures for endovascular repair of an aneurysm is 9.6% in a cumulative experience. The first year rate of procedures is 6%, increases every year, and is reported at 14% on fourth year. The rupture-free rate is very similar to an open procedure at 99.5% at one year and 97.2% at four years.

Endovascular repair of abdominal aneurysms has certain distinct advantages. The procedure has significantly reduced blood loss, decreased complications even with multiple co-morbidities, and potentially can reduce the operating time depending on surgeon skill. The procedure has markedly shortened hospital stays and postoperative recovery time. The disadvantages of the procedure are that the device is expensive, long-term diagnostic follow up is required, and there is a significantly higher incidence of secondary procedures.

Endovascular repair of ruptured aneurysms is also feasible. Several series with small numbers of ruptured aneurysm patients treated with endograft have been reported. 50-60% of the patients in the series with ruptured abdominal aneurysms were suitable for endograft repair and 80-90% of those were technically successful. The complication rate with endograft repair of ruptured AAA is significantly lower at 24% compared to a complication rate of 40-50% in open surgical resection. A major percentage of morbidity and mortality in relation to endograft repair of ruptured AAA is contributed to blood loss, related coagulopathy and the unique complication of acute abdominal compartment syndrome.

The long-term follow up and outcome have not yet been established, especially since the development of endograft is still evolving. However, endovascular repair of abdominal aneurysm is a technically and clinically acceptable procedure and is significantly beneficial for patients with multiple co-morbidities.

Conclusion

Endovascular repair of abdominal aortic aneurysm is technically as well as clinically successful procedure. The procedure has advantage of reducing mortality and morbidity over conventional open repair of abdominal aneurysm, especially patient with significant cardiac, pulmonary and renal co-morbidity. Long term outcome yet to be determined since graft devices are still evolving, however there is no significant deference in rupture free and mortality rate in five years follow up between open and endovascular repair of abdominal aortic aneurysm.

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Effect of micronutrients on morbidity and duration of hospital stay in childhood pneumonia

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Abstract

A cross-sectional and controlled clinical trial was conducted in under-5 children to compare the effects of supplementation of five micronutrients (vitamin A, vitamin C, vitamin E, folic acid and zinc) on the morbidity and on the duration of hospital stay in pneumonia. Data were collected from 1150 children. Among them 8 children died, 100 children left the hospital on `Risk Bond', 190 children were discharged `On Request' of the parents before cure, 8 children developed various complications and 44 children had other factors to be excluded from the study. Finally data from 800 children were analyzed. Among these 800 children 59.00% were male and 41.00% were female. The mean ± SD age was 6.5 ± 5.6 months and 56.25% were infants. The children were divided into two groups - 400 in control group and 400 in intervention (case) group. In both the groups, specific treatment was given by Ampicillin and Gentamycin. In intervention group, five micronutrients were given in 200 children from the day of admission and continued up to discharge. Another 200 children were again divided into 5 sub-groups (40 in each sub-group) and a single micronutrient was given in the same way in each sub-group. All the samples were suffering clinically from severe pneumonia and radiologically from bronchopneumonia. Cases and controls were matched by parents' occupation (fathers were cultivators and mothers were housewives), education level (up to primary level), economic status (having no deficit or surplus of products) and family members (five in number). All the children were fully vaccinated as per existing EPI schedule of the country, partially fed by breastmilk and infant formula up to six months and after six months weaned by carbohydrate rich diet. All the children were in mild (grade I) PEM according to Gomez's classification. Venous blood was collected for estimation of serum level of vitamin A (retinol), vitamin C, vitamin E, folic acid and zinc from all the samples before starting treatment by standard procedures. The individual values of level of micronutrients in the samples were either low or marginally normal but the average level of all the values were low. The average duration of hospital staying was 6.75 days in intervention group and 7.75 days in control group. Chest indrawing and fast breathing disappeared earlier in the intervention group suggesting that supplementation of micronutrients decrease the morbidity and duration of hospital stay of children suffering from pneumonia.

Keywords

Micronutrient supplementation, morbidity from pneumonia, hospital stay.

Introduction

At present situation, Acute Respiratory Infection (ARI) is the most common cause of morbidity of under-five children in Bangladesh and a great public health concern[1,2]. Among all the ARI's, pneumonia occupies special attention because of a significant proportion of childhood mortality occurring due to this ailment[3,4]. On average, children have 4-6 ARI episodes each year; 5-8 episodes per child per year in urban areas and 3-5 in rural areas[4-6]. One third of all admissions in hospitals of children are sufferers from ARI and there are 85,000 deaths due to pneumonia each year in Bangladesh[7-9].

On the other hand, many children suffer from deficiency of micronutrients and more than 2 billion children are sick or disabled as a result of micronutrient deficiency in the world and a major portion remains the South-East Asia including Bangladesh[10]. Vitamin A deficiency causes epithelial defects, impairs the immune system and reduces children's resistance to diarrhoea, measles and increases the incidence and severity of pneumonia[11,12]. Zinc acts as an immunomodulant and its deficiency is associated with increased prevalence and delayed recovery from pneumonia. In a trial in our country on children aged 6-12 months of age, simultaneous weekly administration of zinc and iron was associated with 40% lower risk of severe pneumonia[13,14]. Supplementation of zinc has also been found to reduce risk of pneumonia by 45% and duration of hospital staying by 41%[15-17]. Folic acid, Vitamin C and Vitamin E play roles as antioxidant and decrease the severity of pneumonia by protecting the damage of cells and tissues from oxidants. A study conducted on infants and young children with vitamin C at a dose of 500mg IM six to twelve hours interval showed that 3-7 injections gave complete clinical and x-ray response in case of various pneumonia[18].

So, it is obvious that there is relationship between incidence and severity of pneumonia and micronutrient deficiency. Moreover, micronutrient deficient children require more admission in the hospital and more costly drugs are needed and they also require longer time in hospital[5,7,8]. This causes loss of resources from the parents because Government hospitals usually run short of costly drugs and maximum numbers of these drugs are usually bought by the parents from outside shops[19]. In Bangladesh, only few studies were conducted to assess the micronutrient supplementation on morbidity of pneumonia in under-five children. For this reason, the study was conducted to compare the effects of supplementation of micronutrients on the severity of pneumonia and duration of hospital stay.

Materials and methods

The study was a cross-sectional, prospective and controlled micronutrient supplementation trial. The trial enrolled children admitted to the hospital with pneumonia. The selected place of study was the Paediatrics Department of Rangpur Medical College Hospital. The study was conducted for a period of three years from 1st July 2004 to 30th June 2007. All the children admitted with various types of pneumonia were the study population. Among these, children having the clinical diagnosis of severe pneumonia and radiological diagnosis of bronchopneumonia on admission were selected as samples.

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The duration of hospital stay was calculated in a quantitative form and it is a continuous variable and the statistical formula $4\sigma^2/L^2$ was applied to determine the number of samples. Here σ was the standard deviation of average stay in hospital, 4.8 in this study and L was acceptable variation, 0.5 day in this study at 95% confidence interval[20-22]. In this way, the optimum number of samples became 384. This was rounded to 400. Since there were two independent groups, double the optimum number (400 x 2 = 800) was selected as samples. The sampling method was systematic sampling and every 1st patient was given the intervention and 2nd patient was treated as control from a prepared register.

A standard questionnaire was developed in accordance with the study objectives to obtain relevant information. The questionnaire contained some independent variables such as age of the child, educational status of the parents, monthly family income of the parents, breast feeding pattern, time and type of weaning foods offered to the child, immunization status of the child, vitamin A supplementation, vitamin C supplementation, vitamin E supplementation, supplementation of folic acid, supplementation of zinc etc. Anthropometric index such as weight was included in the questionnaire to obtain nutritional status. The dependent (outcome) variables were morbidity from pneumonia and duration of hospital stay in days. Few months before starting the formal study, the questionnaire was pre-tested among children of the ward. During pre-testing, all the variables were considered except collection of the blood. Then it was modified as required and finalized for collection of data from the selected study population. The questionnaire was in English language.

History of illness of the child was collected from the mother or guardian who attended the child in hospital. Clinical examination was carried out on the child on the day of admission and everyday up to discharge. Age was recorded from the memory of the mothers or from the birth certificates or immunization cards. Educational status of the parents was determined by direct question to the mother or attendant. Only those who had formal schooling were considered literate and those parents who had only education up to primary level were included. Occupation of the parents and amount of the monthly income was also determined by direct question to the mother. Only those fathers who were cultivators and mothers who were housewives and who had no deficit or no savings of products were under consideration. Status of breast feeding and daily food intake was collected from the memory of the mother. The children who were partially breastfed (taking breastmilk as well as other milks up to six months) and taking carbohydrate rich weaning foods after six months were included. During examination `the Bar Scale' designed by National Nutritional Council of Bangladesh was used to record the body weight. The balance was checked everyday before use and weight was recorded on bare foot and with light clothes. The children who received all the vaccines according to the existing EPI schedule was regarded fully vaccinated. All the questionnaires were filled by the investigator himself.

The children who left the hospital on `risk bond' or were `absconded' form the ward after admission or `expired' during treatment were excluded from the analysis. Also those who developed a complication such as effusion, collapse, pneumothorax etc. and who were suffering from bronchial asthma and other severe systemic diseases with pneumonia were excluded from the study. The children who required antibiotics other than the ampicillin and gentamycin for cure were also excluded from the study. The children whose parents did not give consent for drawing blood were also excluded from the study. The children who were in a convalescent stage from another disease and were taking or took any of the micronutrients within last one week also excluded from the study. Data were collected from 1150 children. Among them 8 children died, 100 children left the hospital on `Risk Bond', 190 children were discharged `On Request' of the parents before cure, 8 children developed various complications and 44 children had other factors to be excluded from the study. Finally data from 800 children were analyzed.

Answers of the mothers and findings of clinical examinations were recorded in the pre-tested and prepared "Interview Schedule". The nutritional status was assessed according to Gomez' classification. In all children, venous blood was taken before starting treatment. Then the blood was sent to the laboratory for centrifugation and separation of serum for the estimation of serum level of vitamin A (retinol), vitamin C (ascorbic acid), vitamin E, folic acid and zinc. The method of analysis was High Performance Liquid Chromatography (HPLC)[23-28] for vitamin A, vitamin C, vitamin E, colorimetric method for zinc[29,30] and ELISA[31] for folic acid. The selected laboratories were Padma Diagnostic Center, Dhaka and Apollo Diagnostic Center, Rangpur. Tests were performed by skilled laboratory technologists trained in that field and checked by the consultants experienced in the respective fields.

The children were followed daily up to discharge from the hospital. The criteria of discharge were free from the clinical features of severe pneumonia two consecutive days. There were six groups of children- one was intervention group (N=400) and the other control group (N=400). Again the intervention group was broken into five groups (200 + 40 + 40 + 40 + 40 + 40). In intervention group, specific treatment was given by Ampicillin (50-100 mg/kg/day) and Gentamycin (5-7mg/kg/day) in injection for six days.

Micronutrients were also given to the intervention group. The brands were selected from the products of reputed pharmaceutical companies. The doses of (a) vitamin A was 50,000 or 100,000 IU (age under 1 year) and 100,000-200,000 IU (age over 1 year), (b) vitamin C 125 mg daily, (c) vitamin E 40 IU daily, (d) folic acid 2.5 mg daily and (e) zinc 10.0 mg daily. In 200 children, all the 5 micronutrients were given and another 200 children were divided into 5 sub-groups (40 in each sub-group) and in each sub-group only one micronutrient was prescribed along with specific treatment. In control group, only specific treatment was given without micronutrients. Compliance was checked by Assistant Registrar every day during ward rounds. The drugs were administered by mothers and nurses.

There is no formal ethical committee in the hospital. Written permission was taken from the Director of the hospital and from the head of the department of Paediatrics to conduct the study in the ward. Then purpose of the study was explained to the parents. Then after having the consent, each child was included in the study maintaining the principles of Helsinki Declaration[32,33].

After completion of collection of data, all filled up `Interview Schedules' were checked for missing values and outliers. The data were then entered into a computer. The analysis was performed by SPSS + PC programme according to objectives. Descriptive statistical tests were applied to age, monthly

income and biochemical variables. Univariate, multivariate and ANOVA were also performed as necessary. Data were presented in simple and compound tables. The data were arranged according to the age group, micronutrient group and control group. The micronutrient group was also rearranged into single micronutrient group and all micronutrient groups.

Results

Among 800 children studied 56.25% (450) were infants (up to 1 year), 23.75% (190) were within 1-2 years, 11.25% (90) were within 2-3 years age group, 6.25% (50) were 3-4 years age group and 2.50% (20) were 4-5 years age group. Children of the infancy period were most sufferers from pneumonia. Among the above children 59.00% (475) were male and 41.00% (325) were female. The mean ± SD age was 6.5 ± 5.6 months (Table 1). The average serum level of vitamin A (retinol) was 0.60 µmol/l, vitamin C (ascorbic acid) was 32.50 µmol/l, vitamin E was 6.50 µmol/l, folic acid was 3.50 nmol/l and the average serum level of zinc was 9.70 µmol/l. The average serum level of all the micronutrients considered was lower than the normal level (Table 2).

Table 1: Distribution of children according to age and sex (N=800)

Age group	Sex of the children		Total (%)
	Male (%)	Female (%)	
Birth-1year	255 (31.88)	195 (24.37)	450 (56.25)
1-2 years	105 (13.12)	85 (10.62)	190 (23.75)
2-3 years	65 (8.12)	25 (3.12)	90 (11.25)
3-4 years	35 (4.37)	15 (1.88)	50 (6.25)
4-5 years	15 (1.88)	05 (0.63)	20 (2.50)
Total	**475 (59.00)**	**325 (41.00)**	**800 (100.00)**

(Mean age ± SD = 6.5 ± 5.6 months)

The average duration of hospital stay of children in control group was 7.75 days and that of children in intervention group was 6.75 days. Again the neonates in both the groups took more time in hospital than the older children.

Table 2: Average baseline serum concentrations of micronutrients in the samples (n=800)

Item	Average (serum) level ± SD	Normal value	Difference from lowest mean
Vitamin A	0.60 ± 0.05 µmol/l	0.70-1.50 µmol/l	0.10 µmol/l
Vitamin C	32.50 ± 0.15 µmol/l	34.00-113.00 µmol/l	1.50 µmol/l
Vitamin E	6.50 ± 0.45 µmol/l	7.00-21.00 µmol/l	0.50 µmol/l
Folic acid	3.50 ± 0.04 nmol/l	4.10-20.40 nmol/l	0.60 nmol/l
Zinc	9.70 ± 0.74 µmol/l	9.8-18.1 µmol/l	0.10 µmol/l

(ANOVA p< 0.10)

The average difference was 12.90% (1.0 day) in the groups (Table 3). The duration of hospital stay of children who got all the 5 micronutrients, vitamin A and zinc was shorter than those children who got vitamin C, vitamin E and folic acid (Table 4). There was no difference in time of disappearance of fever and feeding difficulty. But fast breathing and chest indrawing disappeared earlier in micronutrient group than control group (Table 5).

Table 3: Duration of hospital stay of control and intervention group (N=800)

Age group	Duration (Days)				Difference (%)
	Control group		Intervention group		
	No	Duration	No	Duration	
Birth-1year	229	7.78	221	7.23	0.55 (6.55)
1-2 years	94	7.75	96	6.75	1.0 (12.90)
2-3 years	42	7.75	48	6.75	1.0 (12.90)
3-4 years	23	7.75	27	6.75	1.0 (12.90)
4-5 years	12	7.74	8	6.25	1.49 (19.25)
Total	400	7.75	400	6.75	1.0 (12.90)

Table 4: Duration of hospital stay of intervention group (N=400)

Number	Average duration (Days)
Who got 5 micronutrients (200)	6.05
Who got vitamin A (40)	6.50
Who got vitamin C (40)	7.00
Who got vitamin E (40)	7.00
Who got folic acid (40)	7.00
Who got zinc (40)	6.75

Table 5: Effect of micronutrients on selected clinical signs

Signs	Duration of disappearance	
	Control group (Days)	Micronutrient group (Days)
Fever	2	2
Feeding difficulty	2	2
Fast breathing	4.5	4.0
Chest indrawing	3.5	3.0

Discussion

Among the children studied, 59.00% (475) were male and 41.0% (325) were females. The male female ratio was 1.4:1. A study conducted on children suffering from pneumonia in Dhaka Shishu (children) Hospital showed male and female ratio as 2:1[34]. Two other studies[35,36] conducted abroad showed male and female ratio as 61:39 and 69:31 respectively in hospitalized children suffering from pneumonia. This may be due to the fact that male children in our society are given more care than female ones due to various reasons or male children actually suffer more from diseases than female ones. The study shows that 56.25% (450) children were infants and the mean ± SD age was 6.5± 5.6 months. One study conducted in our country[37] has shown that ARI most commonly (84%) occurs

in infancy followed by 1-4 years of age, which is consistent with the present study.

The individual values of the levels of micronutrients in the samples were either marginally normal or below the normal level but the average serum level of all the micronutrients considered were lower than the normal level. There may be several reasons behind this. Bangladesh is a country of widespread micronutrient deficiency. The mothers and children are number one victim of micronutrient deficiency. WHO estimates that about 2.70% pregnant women suffer from frank vitamin A deficiency with a vast number suffering from borderline deficiency in developing countries[38]. As a result, the fetuses get less nutrients in utero and are born with deficit of micronutrients. The rate of exclusive breast feeding is also low. So, the breastfed children get less micronutrients. The non-breastfed children are also not properly weaned. Those weaned, the foods contain low amount of micronutrients. They also suffer from micronutrient deficiency[39]. Widespread micronutrient deficiency in preschool children and mothers has also been demonstrated in studies conducted in other places. In Nigeria, 40.00% of the boys had vitamin A deficiency and 47.00% had vitamin C deficiency[40]. In Nepal, there is widespread multiple micronutrient deficiency in pregnant women and 12.00-18.00% of the mothers suffer from night blindness during pregnancy[41,42]. There may be other factors for the lower values of micronutrients in this study. Fever or physical stress associated with acute infection can deplete the body stores of vitamin A or can increase the urinary loss of vitamin A[43,44]. Oxidative stress in infection can also decrease the level of anti-oxidant micronutrients[45,46]. But in these cases, the major clinical features were respiratory distress and many of the children did not require oxygen therapy which may be suggestive that the deficiencies were mainly due to dietary causes.

The average duration of hospital stay of children in control group was 7.75 days and that of children in intervention group was 6.75 days. The difference is statistically not very significant but the cumulative difference of 1.0 day for 400 cases (addition of differences) over the year is very important for a hospital. One study conducted in Brazil on children aged 6 months to 4 years has shown the duration of an episode in hospital as 6 days which is almost similar to the duration of this study[47]. Another case-control study in Brazil on efficacy of vitamin A treatment in non-measles pneumonia has shown the average duration of an episode as 7.60 days in cases and 7.50 days in the control group which was not statistically very much significant but the cumulative difference of 0.10 day for a hospital was significant[48]. Micronutrients enhance immune status and prevent tissue damage by antioxidant activity. They also exert enhanced regeneration of epithelium. As a result, morbidity is reduced and there is early recovery from the disease. But micronutrients take time to initiate full physiological function. Because, after administration of any micronutrient, at first, there is accumulation in the storage site, then there is increase in the serum level, then tissue binding through specific receptors and the exertion of physiological activity. So, immediately after administration of a micronutrient, there may no much difference in the period of morbidity as was in this study[49].

The duration of hospital stay of children who got all the 5 micronutrients was shorter than those children who got one micronutrient. As most of the children studied were malnourished and there were deficiencies of multiple micronutrients in these children, their immune status was probably very low. So, the children who got all the micronutrients, their immune status were probably improved to enhance the cure of the diseases than the children who got a single micronutrient. One study in Vietnam on 163 children of aged 6-24 months there was simultaneous low concentration of several micronutrients (haemoglobin, retinol and zinc) and after supplementation of micronutrients in these subjects, their micronutrient status were improved and took less time to be cured from acute infection which goes in favour of this study[50]. One review study has also described that micronutrient such as vitamin A and zinc given as a therapy may benefit the clinical course of childhood pneumonia[51]. Another study in Indonesia has shown that micronutrient supplementation in children improves the micronutrient status[52]. In the hospital, there was no difference in the mean number of days of disappearance of fever and feeding difficulty. But fast breathing and chest indrawing disappeared a bit earlier in micronutrient group. One study in Tanzania has shown that the average duration of hospital stay was 4.2 days and there was no difference of disappearance in the mean duration of fever in children suffering from pneumonia[53].

Conclusion

Every study has some weaknesses and constraints which is not an exception in this study. Micronutrient levels were done only before starting of treatment. They were not done at the end of the treatment due to economic constraints, which could be helpful to see the difference between the serum levels of micronutrients. Vacutainer testtubes were not used to draw blood which is ideal to prevent the contamination with air. After centrifugation and separation, the serum was kept in the refrigerator. Occasionally there was interference of supply of electricity. This may have some effect in the biochemical values of the micronutrients. There was difficulty in taking dietary history. It was very difficult to explore the monthly income of the parents, because there was no record of the income in the families. In some cases, there was tendency of by-passing to disclose the actual income. Blinding of the samples has not been done which could increase the quality of the study. If tissue levels of micronutrients could be done, it could reflect the actual micronutrient status in the samples. In spite of these constraints, this study documents the effectiveness of micronutrient supplementation as an adjunct to specific antimicrobial therapy among hospitalized children suffering from pneumonia. It may be concluded that micronutrient deficiency is abundant among children of Bangladesh especially among under-five children in the northern zone of country. The economic status of the people of this zone is poor which may contribute the situation. Micronutrients should be given routinely to all children suffering from pneumonia to reduce both public and private cost by reducing the duration of hospital stay.

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Information for Authors

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

The MANUSCRIPT should be prepared according 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. A major revision is scheduled for 2001. 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, and telephone number of the corresponding author, who is responsible for communicating with the other authors about revisions and final approval of the proofs. The letter should give any additional information that may be helpful to the editor.

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Diabetes in pregnancy & its management

Begum R[1]

The ORION 2008; 29: 524-527

Introduction

Diabetes mellitus is the most common medical complication of pregnancy and it carries a significant risk to the fetus and the mother. Congenital malformations and perinatal morbidity remain common compared with the offspring of non diabetic pregnancies. Diabetic mothers are at risk of progression of micro-vascular diabetic complications as well as early pregnancy loss, pre-eclampsia, polyhydramnios and premature labor. Glycemic control before and during pregnancy is critical and the benefit may result in a viable, healthy offspring. Gestational diabetes mellitus (GDM) which manifests for the first time during pregnancy is common and on the increase, its proper management will reduce the risk of neonatal macrosomia and hypoglycemia. Post-partum evaluation of glucose tolerance and appropriate counseling in women with GDM may help decrease the high risk of subsequent type 2 diabetes in the long-term. The article will briefly review the changes in the carbohydrate metabolism that characterise normal pregnancy and will focus on a practical approach to the care of patients with pre-existing diabetes as well as GDM.

Prevalence

Gestational diabetes mellitus (GDM) represents approximately 90% of these cases and affects 2-5% of all pregnancies and varies in direct proportion to type 2 diabetes mellitus in the background population[1]. Pre-existing diabetes mellitus complicates 0.2% to 0.3% of pregnancies[2]. The importance of diabetes in pregnancy stems from the fact that it carries a significant risk to both the fetus and the mother. Despite major advances in clinical management, there is still facing a higher incidence of malformations and perinatal morbidity compared to the non-diabetic population. Over the past 30 years, great strides have been made in improving the outcomes of women with type 1 diabetes who become pregnant. However, during the past decade, type 2 diabetes in pregnancy has emerged and is certain to become a prominent concern[3]. The overall prevalence of diabetes is 6.8% and 8.2% according to FBG and 2hBG, respectively[4]. The prevalence of type 2 diabetes is 8.1% and the prevalence for men and women is 7.7% and 8.5% respectively[5]. The prevalence of gestational diabetes is strongly related to the patient's race and culture. Typically, only 1.5-2% of white persons from the midwestern United States develop GDM, while American Indians from the southwestern United States may have rates as high as 15%. In Hispanic, African American, and Asian populations, the rate is 5-8%.

Normal glucose regulation during pregnancy: Metabolic changes occur in normal pregnancy in response to the increase in nutrient needs of the fetus and the mother. There are two main changes which are seen during pregnancy, progressive insulin resistance that begins near mid-pregnancy and progresses through the third trimester to the level that approximates the insulin resistance seen in individuals with type 2 diabetes mellitus. The insulin resistance appears to result from a combination of increased maternal adiposity and the placental secretion of hormones (progesterone, cortisol, placental lactogen, prolactin and growth hormone). The fact that insulin resistance rapidly abates following delivery suggests that the major contributors to this state of resistance are placental hormones. The second change is the compensatory increase in insulin secretion by the pancreatic beta-cells to overcome the insulin resistance of pregnancy. As a result, circulating glucose levels are kept within normal. If there is maternal defect in insulin secretion and in glucose utilization, then GDM will occur as the diabetogenic hormones rise to their peak levels.

During a healthy pregnancy, mean fasting blood sugar levels decline progressively to a remarkably low value of 74 ± 2.7 (standard deviation) mg/dL. On the other hand, peak postprandial blood sugar values rarely exceed 120 mg/dL. Meticulous replication of the normal glycemic profile during pregnancy has been demonstrated to reduce the rate of macrosomia. Specifically, when 2-hour postprandial glucose levels are maintained at less than 120 mg/dL, approximately 20% of fetuses demonstrate macrosomia. Conversely, if postprandial levels range up to 160 mg/dL, macrosomia rates rise to 35%.

Pathophysiology

1) Metabolic disorder characterized by hyperglycemia due to:

- Relative pancreatic insulin production
- Limited insulin release
- Impaired effect of insulin at the cellular level

2) Incidence : 1-3% of all pregnant women 0.5% overt DM
Cause: - Multifactorial includes genetic & environmental factor.

3) Carbohydrate metabolism during pregnancy:
Diabetogenic effects of pregnancy

A. Insulin resistance:
- Production of placental somatomammotropin
- Increased production of estriol & progesterone
- Increased insulin destruction by kidney & placenta

B. Increased lipolysis:
The mother uses fat for her calorie needs & saves glucose for fetal needs.

C. Changes in gluconeogenesis:
The fetus uses preferentially alanine & other amino acids & deprives the mother of major gluconeogenic source.

4) Effects of DM on pregnancy:

A. On mother:
1. 1st trimester abortion
2. ↑ Pre-eclampsia 15-25%
3. ↑ Polyhydramnious
4. ↑ Infections ⟶ ↑Chorioamnitis
   ↑Endometritis
5. ↑ Post partum haemorrhage
6. ↑ LUCS

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Table 1: Risks to the mother[6]

Maternal complications in diabetic pregnancy	
◆ Diabetic keto-acidosis	◆ Hypoglycemia
◆ Visual deterioration/retinopathy	◆ Miscarriage
◆ Deterioration of nephropathy	◆ Pre-eclampsia
◆ Polyhydramnios	◆ Premature delivery

B. On the fetus:
1. Abortion in 1st trimester
2. Congenital abnormalities
3. Macrosomia
4. Hypoglycemia
5. Hyperviscosity syndrome
6. Hyaline membrane disease
7. Hypocalcemia
8. Apnea & bradycardia
9. Traumatic delivery
10. IUFD

Table 2: Risks to the fetus

Fetal complications in diabetic pregnancy
◆ Congenital anomalies: cardio-vascular, central nervous system, skeletal (sacral agenesis) & genito-urinary
◆ Excessive fetal growth (macrosomia)
◆ Fetal growth retardation (in diabetic pregnancy complicated by nephropathy)

Table 3: Risks to the neonate [8-10]

Neonatal complications in diabetic pregnancy	
◆ Traumatic delivery	◆ Hypoglycemia
◆ Polycythemia	◆ Hypocalcemia
◆ Hypomagnesemia	◆ Hyperbilirubinemia
◆ Pulmonary surfactant deficiency	

5) Effects of pregnancy on DM:
1. More insulin required to achieve metabolic control
2. Progressive of diabetic retinopathy
3. Worsening of DM nephropathy
4. Risk of death for patient with DM cardiomyopathy

6) Preconception counseling on the diabetic patient:
- ◆ Pregnancy should be planned.
- ◆ Importance of blood glucose control patient should be informed about the outcome of pregnancy in a uncontrolled blood sugar level.
- ◆ Importance of self-monitoring & frequent test to detect early complication & therefore management.
- ◆ Importance of fetal surveillance during the diabetic pregnancy.

a) The problem affecting the fetus should be explained-
- ⁎ HBA1C
- ⁎ Sr fetoprotein at 16 wk
- ⁎ Fetal anomaly scan at 20 wk
- ⁎ Fetal echocardiogram at 24 wk
- ⁎ Serial USG to detect macrosomia or IUGR

b) Fetal well being should be monitored in last trimester by-
- ⁎ CST (Contraction Stress Test)
- ⁎ NST
- ⁎ Modified BPP (Biophysical profile)

7) Financial cost of the diabetic pregnancy:
- ◆ Needs frequent laboratory test
- ◆ Frequent visit to the doctor
- ◆ May need hospitalization for control of DM
- ◆ May need to terminate the pregnancy earlier
- ◆ Maximum will be ended with LUCS
- ◆ Baby may need NICU care, which cost lot.

Diagnosis

Screening for diabetes before the discovery of insulin in 1921, pregnancy in the diabetic women was uncommon & accompanied by high maternal & fetal mortality rates. But after the discovery of insulin & better understanding of the disease the mortality rate comes down from 65% to 2-5% if blood glucose controlled meticulously. So it is necessary to diagnose DM in pregnancy properly. So necessity for screening is very important[11].

Why screening is important
1) Risk of developing NIDDM/ IDDM at later age (off spring 1.5% at 25 yrs of age).
2) GDM is seldom symptomatic.
3) Impact of GDM on pregnancy similar to progestational diabetes mellitus though complications are fewer less severe.
4) To improve perinatal outcome.
5) To decrease the maternal morbidity & mortality.
6) To intervene in proper time.

When to screen
1. All pregnancies should be screened for GDM between 24-28 wks.

2. High risk group-
   - ⁎ On first visit
   - ⁎ If not on 28 wks
   - ⁎ If not on 32 wks

Blood flow may be the factor involved with IUGR and fetal death. They suggested that there is a relationship between maternal hyperglycemia and reduced uteroplacental blood flow. This is seen in cases of ketoacidosis and pre-eclampsia, two conditions associated with IUD. Alterations in fetal carbohydrate metabolism and fetal hyperinsulinemia leading to hypoxia and fetal death.

Goals to antepartum fetal surveillance
1. Avoidance of intrauterine death
2. Early detection of fetal compromise
3. Prevention of unnecessary premature delivery

Fetal surveillance test
1. Contraction Stress Test (CST)
2. Non- Stress test
3. fetal Biophysical Profile (FBP)
4. Maternal assessment of fetal activity (or kick count)
5. Doppler study

Prevention of respiratory distress syndrome: In diabetic pregnancies there are a delayed production of surfactant and lung maturity.

Education of the patient with newly diagnosed diabetes: Patient who newly detected has little idea about diet and blood glucose monitoring. Nutritionist will give the idea-

a) Calorie
b) Meal time
c) Balanced diet
d) Value of diet

So patient needs- 3D

a) Education about diet.
b) Discipline life.
c) Drug if needed - insulin education about self administration of insulin.
d) If possible home monitoring of blood glucose & to educate when to see the advice of doctor what is the level of blood glucose to be maintained.
e) The patient must be able to recognize & treat hypoglycemia instructions to be given to carry candy or sugar with them to combat hypoglycemia.
f) Instruction to be given if any infection immediately reports to the physician.
g) In last trimester patient asked for maintaining KICK count.

Management

The role of ultrasonography in the management of diabetic pregnancy:

1. Estimation of gestational age.
2. Assessment of altered growth- IUGR of macrosomia.
3. Dynamic assessment of fetal status- fetal biophysical profile.
4. Diagnosis of congenital anomalies.

Insulin therapy during pregnancy[12]

a) The American Diabetes Association recommends the use of human insulin for pregnant women with diabetes & diabetes considering pregnancy. Insulin in available in 3 different forms which may be mixed in one syringe or injected separately. Short acting insulin (regular & semi lente) have peak action at 2 to 4 hours post injection. Intermediate acting insulins (Lente & NPH) have peak action at 5 to 12 hours. Long acting insulins (Protanine Zinc & Ultra Lente) have peak action of 12 to 24 hours.

b) Insulin requirements increased throughout pragnancy
   - 6-18 weeks : 0.7 U/kg body wt
   - 18-26 weeks : 0.8 U/kg body wt
   - 26-36 weeks : 0.9 U/kg body wt
   - 36-41 weeks : 1.0 U/kg body wt

c) Regimens: Recommended regimens should be considered starting places & must be adjusted to each patients' specific needs. Generally for a patient who is familiar with here diabetes, it is best to maintain the form of administration that she used before pregnancy, if possible.
   - 2- injection regimen
   - 3- injection regimen
   - 4- injection regimen

Continuous subcutaneous insulin infusion

1) Two- injection regimen: Two- thirds of the total daily dose is given in the morning (2:1 ratio of NPH to regular insulin) & one- third in the evening (1:1 ratio of NPH to regular).
2) Three- injection regimen: Administration of NPH or lente insulin at bedtime, rather than with dinner, has been found to prevent nocturnal hypoglycemia & result in improved control of fasting morning glucose levels.
3) Four- injection regimen: 50% to 60% of the total daily insulin requirement is given as ultralente, together with regular insulin pre meal times.
4) Continuous subcutaneous insulin infusion: A pump system, which is usually attached to the patients abdominal wall, delivery regular insulin continuously to maintain basal blood glucose levels, with additional bolus administered at mealtimes. The some total insulin dose that would be administered in multiple injection therapy is administered as the basal rate infusion, with the remainder administered as boluses before meals. Breakfast usually require a larger bolus than other meals.

Insulin adjustment by neutralizing dose

Blood sugar mmol/ Lit	Insulin in drip 500cc 5% DA or DNS
6-9	6 unit Actrapid
9-11	8
11-13	10
13-17	12
17-21	12+4 unit s.c
> 21	12+8 unit s.c (consult the concern person)

Timing of delivery in diabetic pregnancy: Obstetric management has undergone tremendous changes in managing a diabetic pregnancy. Till 1960, all patients were induced at or before 36 weeks to avoid IUD. Later on inductions were carried out at 37-38 weeks to reduce RDS in the newborn.

However, now a days with the availability of sophisticated methods for antenatal fetal surveillance, and with a policy of intensive insulin administration and strict metabolic control using frequent glucose estimations, pregnancy is continued up to term and onset of spontaneous labour is awaited in all cases, provided the patient's diabetes is well controlled and the fetus is not a risk. Patients with vascular disease are delivered early if hypertension worsens or if there is IUGR. When antepartum testing suggests fetal compromise, immediate delivery is indicated, if pulmonary maturity is confirmed.

Factors influencing timing of delivery in diabetic pregnancy

A. Maternal factors:
   - Vascular disease complications
   - Control of diabetes
   - Condition of cervix
   - Previous obstetric history
   - Early elderly patient

B. Fetal factors:
   - Fetal weight
   - Fetal distress

Route of delivery: Primary ceasarean section (LSCS) rate in diabetes pregnancies is as high as 30-40%.

Indication for LSCS in diabetic pregnancy

1. Pregnancy complicated by PIH
2. Malpresentations
3. Previous LSCS
4. Macrosomia
5. Proliferative retinopathy
6. Fetal distress prior to or during labor

Conclusion

Abnormalities of glucose tolerance during pregnancy are a potential threat to the mother and the growing fetus. Not only that it is already established that mothers who developed GDM many of them develop frank DM/IGT later on. Therefore epidemiological studies are important to predict nature of distribution, progression of this particular disease. High risk group of patient can deliver healthy baby if screened for GDM with good glycemic control with proper antenatal care. It is evident that international comparison of the prevalence of GDM is not possible accurately due to-

a) Wide differences in screening protocol
b) Different cut off points of diagnostic criteria.

So, our recommendation is, population or community based studies are to be undertaken by unified-screening and diagnostic criteria.

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MSD NEWS

Rajshahi

Mohonpur UHC, Rajshahi: Mohonpur UHC arranged a round table meeting on "Role of ceftriaxone to treat various infections" on 14th December 2007 at the conference room. Dr. Md. Abul Fazal, UH & FPO chaired the meeting. About 15 doctors attended the meeting.

Khulna

Gynae ward, KMCH: Gynae ward of KMCH arranged a round table meeting on "A case presentation on ectopic pregnancy" on 7th August 2007 at the seminar room of KMCH. Dr. Shamsun Nahar, Associate Professor and head of the department, chaired the session. Dr. Rowshan Ara Begum, Associate Professor was the chief guest and Dr. Zinat Gulshan Ara was the keynote speaker. About 40 doctors attended the seminar.

Nowapara UHC: On 19th September 2007 a round table meeting was arranged by Nowapara UHC on "Role of ceftriaxone to treat various infections" at the training room. Dr. Poritosh Kumar Kundu, UH & FPO was the chairperson. About 15 doctors enjoyed the meeting.

Diabetic Hospital: A round table meeting was arranged by Khulna Diabetic Hospital on "First step antihypertensive with sustained efficacy" on 8th October 2007 at the hospital seminar room. Dr. Md. A. Sabur was present as the chairperson. About 10 doctors attended the meeting.

Dumuria UHC: Dumuria UHC arranged a round table meeting on "Role of ceftriaxone to treat various infections" on 2nd December 2007 at the room of UH & FPO. Dr. Dilip Kumar, UH & FPO chaired the meeting and Dr. Atiar Rahman was present as the chief guest. About 15 doctors attended the meeting.

Faridpur

Alamdanga UHC, Kushtia: On 10th August 2007 a round table meeting was arranged by Alamdanga UHC on "Role of ceftriaxone to treat various infections" at the room of UH & FPO. Dr. Liakot Ali, UH & FPO was the chirperson. About 20 doctors attended the session.

Kot-Chadpur UHC, Jhenaidah: A round table meeting was arranged by Kot-Chadpur UHC on 12th August 2007 on "Role of ceftriaxone to treat various infections" at the seminar room of the complex. Dr. Fazle Akbar, UH & FPO was the chairperson. About 20 doctors enjoyed the session.

Kaliganj UHC, Jhenaidah: Kaliganj UHC arranged a round table meeting on "Role of ceftriaxone to treat various infections" on 9th August 2007 at the room of UH & FPO. Dr. Gurudash Sikder, UH & FPO was the chairperson. About 20 doctors attended the meeting.

Shailkupa UHC, Jhenaidah: On 8th August 2007 Shailkupa UHC arranged a round table meeting on "Role of ceftriaxone to treat various infections" at the room of UH & FPO. Dr. Dulal Kumar Chokroboti, UH & FPO chaired the meeting and Dr. Hasanuzzaman was present as the chief guest. About 20 doctors enjoyed the meeting.

Dinajpur

Boda UHC, Panchagar: A round table meeting was arranged by Boda UHC, Panchagar on 14th July 2007 on "Role of ceftriaxone to treat various infection" at the conference room. Dr. Md. Amzad Hossain, UH & FPO was the chairperson. About 20 doctors attended the session.

Ranisankail UHC, Thakurgaon: On 15th July 2007 a round table meeting was arranged by Ranisankail UHC, Thakurgaon on "Role of ceftriaxone to treat various infections" at the conference room. Dr. Kamala Kanta Barman, Consultant Gynae was the chairperson and Dr. Jahangir Alam, RMO was the chief guest. About 15 doctors enjoyed the session.

Baliadangi UHC, Thakurgaon: A round table meeting was arranged by Baliadangi UHC, Thakurgaon on 3rd December 2007 on "Role of ceftriaxone to treat various infections" at the conference room. Dr. Md. Aminul Islam Mondol, UH & FPO chaired the meeting. About 15 doctors attended the meeting.

Debigonj UHC, Panchagar: On 1st December 2007 a round table meeting was arranged by Debigonj UHC, Panchagar on "Role of ceftriaxone to treat various infections" at the conference room. Dr. Nurul Alam Mondol, UH & FPO on charge chaired the meeting. About 15 doctors attended the meeting.

Sylhet

BMA Sreemongal, Moulvibazar: On 15th December 2007 a round table meeting was arranged by BMA Sreemongal branch on "Review on cephalosporins" at Agra Continental Chinese Restaurant. Dr. Rama Ranjan Deb, President BMA chaired the meeting and Dr. Haripada Roy, UH & FPO, Sreemongal UHC and General Secretary, BMA was present as the chief guest. About 40 doctors attended the session.

Brahmanbazar Christian Hospital, Kulaura, Moulvibazar: A round table meeting was arranged by Brahmanbazar Christian Hospital, Kulaura on 15th December 2007 on "Role of ceftriaxone to treat various infections" at the library room. Dr. Andrew, Hospital Incharge was present as the chairperson. About 15 doctors attended the meeting.

The rest of the MSD news at page - 541

Stent thrombosis : Rethinking of drug eluting stents

Rahman MT[1], Haque SA[2], Chowdhury AW[3], Aziz M[4]

The ORION 2008; 29: 528- 530

Introduction

Percutaneous transluminal coronary angioplasty has become the most frequently used method for myocardial revascularization[1]. The use of uncoated coronary-artery stents during percutaneous intervention has decreased the incidence of acute complications and improved the outcome of patients[2], but restenosis within the stent compromises the long-term results. As a consequence, the prevention and treatment of in-stent restenosis have become priorities in interventional cardiology.

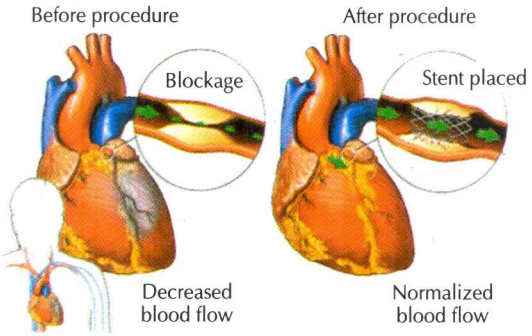

Figure: Placing of Stent

Drug-eluting stents, which markedly reduce in-stent restenosis[3], have relegated all other therapeutic approaches to the background. However, it is gradually emerging that rates of late restenosis after the use of drug-eluting stents are higher than initial experience suggested, particularly in patients who have complex lesions or are at high risk for complications (e.g. those with multivessel disease or diabetes). In such cases, rates of binary in-segment restenosis are 8.9 to 18.9%[4,5]. Recently, the problem of late thrombosis (>1 month after the procedure) has further dampened initial enthusiasm and has reduced the indiscriminate use of first-generation drug-eluting stents. As a result, interventional cardiologists have tended to revert to more predictable devices (e.g. uncoated stents or ones that are coated with so-called inert compounds, such as silicon carbide and titanium-nitride-oxide), which are designed to decrease acute surface thrombogenicity. Thus, in-stent restenosis is likely to remain an important clinical issue.

Catheter-based drug delivery was originally developed by Harvey Wolinsky to prevent restenosis after balloon angioplasty[6]. In the 1990s, extensive research was carried out to improve catheter-based, site-specific (or local) intra-arterial delivery of drugs[7]. However, studies in animals and humans showed marked variability of site-specific uptake in the arterial wall and a quick washout of the compound that were being studied[8,9], so clinically convincing results could not be demonstrated. These difficulties favored the development of stent-based drug delivery.

For several years restenosis was the Achilles' heel of coronary artery stenting by limiting long-term efficacy. Introduction of drug eluting stents (DES) reduced this problem dramatically[3,4].

Recently, studies have indicated that this reduction in restenosis might have been obtained at the expence of a higher incidence of stent thrombosis, particularly late stent thrombosis. This supposition has reignited a debate about the mechanisms of stent thrombosis especially in relation to DES.

Epidemiology

The incidence of stent thrombosis has been reported in a number of studies most of which have found an incidence of 0.5-2%, but despite being a quantitatively minor problem, stent thrombosis has a major clinical impact owing to high risk of myocardial infarction and death. Thus, mortality due to stent thrombosis has been reported to be as high as 45%[10].

Definition and classification

A new standard definition of stent thrombosis was recently proposed by an Academic Research Consortium (ARC) in order to make it possible to compare the true rates of stent thrombosis across different trials and registries[11]. The ARC is composed of clinical investigators, industry representatives and regulators including the Food and Drug Administration, and the definition categorizes stent thrombosis according to the level of documentation and timing.

- Definite or confirmed event (symptoms suggestive of an acute coronary syndrome and angiographic or pathologic confirmation of stent thrombosis).
- Probable event (unexplained death within 30 days or target vessel myocardial infarction without angiographic confirmation of stent thrombosis).
- Possible event (any unexplained death after 30 days).

Based on the elapsed time since stent implantation stent thrombosis can be classified as:

- Early (0-30 days post stent implantation)
- Late (>30 days)
- Very late (>12 months)

Often, early stent thrombosis is further subdivided into acute (<24 hours) and subacute (1-30 days) events.

Mechanisms: vascular response to stenting and the importance of platelets and coagulation

Both bare metal stents (BMS) and DES induce platelet adhesion, activation and thrombus formation and, therefore, effective anti-platelet therapy is mandatory for some time after

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stent implantation. Gradually, stents are covered with endothelial cells that do not induce thrombus formation, and the need for platelet inhibition decreases.

Cytotoxic drugs used in DES in order to reduce smooth muscle cell growth after coronary intervention also inhibit this endothelialisation[12].

Furthermore, sirolimus and paclitaxel induce expression of tissue factor in the stented lesion causing activation of the coagulation system.

The polymers used to load these drugs may cause inflammation in the coronary artery characterized by infiltration of eosinophilic cells in the vessel wall suggestive of hypersensitivity reaction and this might also contribute to a prothrombotic environment[12].

Mechanisms

Clinical factors:

Procedure and lesion-related parameters:

* Use of multiple stents
* Small vessel diameter
* Coronary dissection
* Geographic miss
* Slow flow
* Long lesions
* Stent malapposition
* Underexpansion of the stent
* Stent design (strut thickness and polymer type)
* Bifurcation lesions

Patient characteristics:

* Diabetes
* Acute Coronary Syndromes (especially STEMI)
* Left ventricular dysfunction
* Renal failure
* Advanced age
* High platelet reactivity

Anti-platelet therapy:

* Inadequate intensity of therapy (i.e. non-dual platelet inhibition or insufficient dose)
* Non-compliance
* Premature cessation of anti-platelet therapy

Platelets and anti-thrombotic therapy

Platelets have a pivotal role in thrombus formation including stent thrombosis and thus, an optimal anti-platelet therapy is of crucial importance in the prevention of stent thrombosis. High platelet reactivity is a risk factor for thrombotic events.

Relative low-responsiveness to anti-platelet therapy (often referred to as drug resistance) is associated with ischemic cardiovascular events such as unstable angina, myocardial infarction and cardiac death.

Furthermore, it has been shown that high post-interventional platelet reactivity and incomplete inhibition of the P2Y12 platelet receptors are risk factors for subacute stent thrombosis[13,14]. An impaired response to anti-platelet therapy with aspirin has been reported in patients suffering stent thrombosis[15].

Thus, measuring the effect of anti-platelet therapy might prove valuable in determining the optimal treatment for the individual patient. However, currently no golden standard or guidelines on such measurements exist.

Dual anti-platelet therapy with aspirin and clopidogrel must be continued for a longer time period after implantation of DES than after BMS implantation and treatment for 12 months are usually recommended.

Aspirin should be continued life-long. Clinically, there is a temporal link between cessation of dual anti-platelet therapy and occurrence of stent thrombosis[16], and recently presented registry data indicate that some patients might benefit from prolonged dual anti-platelet therapy[17,18].

However, dual anti-platelet therapy for more than 12 months has not been tested in clinical trials and is, therefore, currently not recommended, because long-term dual anti-platelet therapy is associated with an increased risk of bleeding complications[19]. The challenge is to find the optimal balance in order to achieve the lowest possible risk of stent thrombosis without subjecting patients to an unnecessary risk of bleeding complications.

Perspectives: Future prevention of stent thrombosis

Stents coated with new cytotoxic drugs and polymers may have different properties in terms of affecting endothelialisation, vascular inflammation and indication of tissue factor activity.

Coating with NO-donors may decrease platelet adhesion and aggregation. Stents coated with CD34-antibodies may capture circulating endothelial progenitor cells and may be able to prevent thrombosis by increasing and accelerating endothelial coverage.

Furthermore, development of biodegradable stents also be a way to decrease the incidence of late and very late stent thrombosis.

Anti-thrombotic therapy is likely to be optimized with the development of new more efficient anticoagulants and anti-platelet drugs with a lower risk of bleeding complications. Patients and health personnel should be informed about the risk associated with premature cessation of therapy.

Development of new tests able to assess platelet inhibition may identify patients with a reduced benefit from aspirin or clopidogrel and may make it possible to further individualize and optimize anti-platelet therapy.

The risk of stent thrombosis has been a known complication after PCI for quite a long time and might be increased after implantation of DES. The issue of in-stent thrombus formation, therefore, has attracted great attention once again.

Though evidence remains inconclusive, some studies indicate that the incidence of late and very late stent thrombosis is increased after DES implantation.

Importantly, it is unknown whether very late stent thrombosis is a time limited phenomenon and thus, the problem might increase, if events continue to accrue over time.

As a consequence, large-scale clinical trials with long-term follow-up as well as mechanistic studies are highly warranted.

Currently, it is not known whether very late stent thrombosis is prevented with an extended course of dual anti-platelet therapy.

Certainly, the issue of stent thrombosis emphasizes the importance of careful patient selection and individualized therapy, which, in future, might partly be based on measurement of the intensity of platelet inhibition.

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Present advancement in the diagnosis and treatment of typhoid fever

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Introduction

Although advances in public health and hygiene have led to the virtual disappearance of enteric fever (more commonly termed typhoid fever) from much of the developed world, the disease remains endemic in many developing countries. Typhoid fever is caused by *Salmonella enterica serovar typhi* (S. typhi), a gram negative bacterium. A similar but often less severe disease is caused by S. paratyphi A and less commonly, by S. paratyphi B (Schotmulleri) and S. paratyphi C (Hirschfeldil). The common mode of infection is by ingestion of an infecting dose of the organism, usually through contaminated water or food. Although the source of infection may vary, person to person transmission through poor hygiene and sewage contamination of water supply are the most important[1].

Epidemioloy

Worldwide, 15 to 30 million cases of typhoid occur each year with half a million deaths. In affluent countries, typhoid is seen in travellers or when food or water safety measures fail, with antibiotic treatment death is rare[2].

Few established surveillance systems for typhoid exist in the developing world, especially in community settings, so the true burden is difficult to estimate. This is shown by recent revisions in the global estimates of the true burden of typhoid. In contrast to previous estimates, which were 60% higher, investigators estimate that there are average 21.6 million typhoid cases annually, with the annual incidence varying from 100 to 1000 cases per 100000 population[3,4]. Preliminary results form recent studies conducted in Bangladesh by ICDDR,B show an incidence of approximately 2000 per 100000 per year. Typhoid fever also has a very high social and economic impact because of the hospitalization of patients with acute disease and the complications and loss of income attributable to the duration of the clinical illness. It is important to note that reports form some provinces in China and Pakistan have indicated more cases of paratyphoid fever caused by S. paratyphi A than by S. typhi[5-7]. The global mortality estimates from typhoid have also been revised downwards from 600000 to 200000, largely on the basis of regional extrapolations[4]. Recent population based studies from South Asia suggest that the incidence is highest in children aged less than 5 years, with higher rates of complications and hospitalization, and may indicate risk of early exposure to relatively large infecting doses of the organisms in these populations[8-10]. These findings contrast with previous studies from Latin America and Africa[3], which suggested that S. typhi infection caused a mild disease in infancy and childhood.

There are may be other factors that affect the changing epidemiology of typhoid. Although the overall ratio of disease caused by S. typhi to that caused by S. paratyphi is about 10 to 1, the proportion of S. paratyphi infections are increasing in some parts of the world[11].

Also, in contrast to the Asian situation, the HIV and AIDS epidemic in Africa has been associated with a concomitant increase in community acquired bacteraemia due to nontyphoidal Salmonella such as S. typhimurium, an illness that may be clinically indistinguishable from typhoid[12,13]. The exact reasons for these differences in the epidemiology and spectrum of Salmonella infections between Asia and Africa remain unclear.

Antibiotics resistance, particularly emergence of multidrug, resistant (MDR) strains among Salmonella is also a rising concern and has recently been linked to antibiotic using livestock. After sporadic outbreaks of Chloramphenicol resistant typhoid between 1970 and 1985, many strains of S. typhi developed plasmid mediated multidrug resistance (PMMDR) to the three primary antimicrobials used (Ampicillin, Chloramphenicol, and Co-trimoxazole)[14]. This was encountered by the advent of oral Quinolones. Resistance to Ciprofloxacin also called Nalidixic Acid-resistant S. typhi (NARST) strain either chromosomally or plasmids encoded has been observed in Asia. A significant number of strains from Africa and the Indian subcontinent are MDR type. A small percentage of strains from Vietnam and the Indian subcontinent are NARST strains[4].

Diagnosis of typhoid fever

Typhoid fever is among the most common febrile illness encountered by practitioners in developing countries. The advent of antibiotic treatment has led to a change in the presentation of typhoid, and the classic mode of presentation with a slow and ``Stepladder'' rise in fever and toxicity is rarely seen. However, rising antimicrobial resistance has been associated with increased severity of illness and related complications.

Many other factors influence the severity and overall clinical outcome of the infection. They include the duration of illness before the start of appropriate treatment, the choice of antimicrobial, the patient's age and exposure or vaccination history, the virulence of the bacterial strain, the quantity of inoculum ingested and several host factors affecting immune status. Recent data from South Asia indicate that the presentation of typhoid may be more dramatic in children younger than 5 years, with higher rates of complications and hospitalization[8-10]. So typhoid is predominantly an infection of children and young adults, affecting both sexes equally. Diarrhoea, toxicity and complications such as disseminated intravascular coagulation are also more common in infancy, with higher mortality.

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The presentation of typhoid fever may be altered by co-existing morbidities and early administration of antibiotics. In areas where malaria is endemic and where schistosomiasis is common the presentation of typhoid may be atypical[15,16]. Multidrug resistant typhoid and paratyphoid infections are more severe with higher rates of toxicity, complications and mortality than infections with sensitive strains[7]. This may be related to the increased virulence of multidurg resistant S. typhi as well as higher number of circulating bacteria[17].

The predominant symptom is the fever which rises gradually to a high plateau of 39 to 40°C, and shows little diurnal variation. Rigors are uncommon, except in late or complicated typhoid or in patients treated with antipyretics. Most patients will experience diarrhoea and typhoid can present as an acute gastroenteritis. Severe diarrhoea or colitis has been reported in HIV infected patients and bloody diarrhoea may be seen.

The abdominal pain is usually diffuse and poorly localized but occassionally sufficiently intense in the right iliac fossa to suggest appendicitis. Nausea and vomiting are infrequent in uncomplicated typhoid but are seen with abdominal distension in severe cases. Other early symptoms include cough, sore throat and epistaxis. In developing countries, patients with typhoid in its second to fourth weeks present with accelerating weight loss, weakness, altered mental state, intestinal hemorrhage and perforation, refractory hypotension, pneumonia, nephritis and acute psychosis. Those infected with multidrug resistant S. typhi may suffer more severe disease. Physical examination is often unremarkable apart from fever. Careful examination may reveal splenomegaly, hepatomegaly or rose spots. Tachycardia is common although temperature pulse dissociation (relative bradycardia) is considered characteristic. Hypotension has important implications. A coated tongue is often observed. The lenticular rose spots, appear at the end of the first week. They form a sparse collection of maculopapular lesion on the abdominal skin, which blanch with pressure and fade after 2 or 3 days. The rash may extend on to the trunk and arms[2].

The challenge of appropriate diagnostics in typhoid

Although the main stay of diagnosing typhoid fever is a positive blood culture, the test is positive in only 40-60% of cases. Usually early in the course of the disease. Stool & urine cultures become positive after the first week of infection, but their sensitivity is much lower. In much of the developing world, widespread antibiotic availability and prescribing are another reason for the low sensitivity of blood cultures. Although bone marrow cultures are more sensitive, they are difficult to obtain, relatively invasive and of little use in public health settings.

Other hematological investigations are non-specific. Blood leukocyte counts are often low in relation to the fever and toxicity, but the range is wide, in younger children leukocytosis is a common association and may reach 20000-25000/mm3[3]. Thrombocytopenia may be marker of servere illness and accompany disseminated intravascular coagulation. Liver function test results may be deranged, but significant hepatic dysfunction is rare.

The classic Widal test measures agglutinating antibody levels against O and H antigens of S. typhi and is more than 100 years old[3].

The levels are measured by using doubling dilutions of sera in large test tubes. Usually, O antibodies appear on days 6-8 and H antibodies on days 10-12 after the onset of the disease.

Although robust and simple to perform, this test lacks sensitivity and specificity and reliance on it alone in areas where typhoid is endemic may lead to overdiagnosis.

It may be negetive in up to 30% of culture proven cases of typhoid ever. This may be because of prior antibiotic therapy that has blunted the antibody response. On the other hand S. typhi shares O and H antigens with other Salmonella serotypes and has cross-reacting epitopes with other Enterobacteriacae and this can lead to false positive results. Such results may also occur in other clinical conditions, eg. malaria, typhus, bacteraemia caused by other organisms and cirrhosis. In areas of endemicity there is often a low background level of antibodies in the normal population. Determining an appropriate cut off value for a positive result can be difficult since it varies between areas and between times in given areas[18].

Despite these limitations the test may be useful, particularly in areas that cannot afford the more expensive diagnostic methods[19]. The test is unnecessary if the diagnosis has already been confirmed by this isolation of S. typhi from a sterile site[3].

Newer diagnostic tests have been developed such as the Thyphidot or Tubex[3], which directly detect IgM antibodies against a host of specific S. typhi antigens but these have not proved to be sufficiently robust in large scale evaluation in community settings. A nested polymerase chain reaction using H1d primers has been used to amplify specific genes of S. typhi in the blood of patients and is a promising means of making a rapid diagnosis. Table-1 compares the performance of the various tests for typhoid[3].

Despite these new developments, the diagnosis of typhoid in much of the developing world is made on clinical criteria. This poses problems since typhoid fever may mimic many common febrile illnesses without localizing signs. In children with multi system features, the every stages of enteric fever may be confused with conditions such as acute gastroenteritis, bronchitis and bronchopneumonia.

Subsequently, the differential diagnosis includes malaria, sepsis with other bacterial pathogens, infections caused by intracellular organisms such as tuberculosis, brucellosis and infectious mononucleosis. There is thus an urgent need to develop a multipurpose ``fever stick'' that may allow the rapid and specific diagnosis of common febrile illnesses, especially malaria, dengue fever and typhoid[3].

Definitive diagnosis of enteric fever requires the isolation of S. typhi or S. paratyphi. Cultures of blood, stool, urine, rose spots, the blood mononuclear cell platelet fraction, bone marrow and gastric or intestinal secretions may each be useful in establishing the diagnosis. The duodenal string test is especially useful as a noninvasive technique to sample duodenal secretion. A positive culture for a S. typhi or S. paratyphi is obtained in more than 90% of patients; if blood, bone marrow and intestinal secretions are all performed. The sensitivity of blood culture alone is only 50 to 70% probably because small quantity of S. typhi (i.e.<15organisms/ml) are typically present

Table 1: Laboratory diagnosis of typhoid

Diagnostic test	Sensitivity range (%)	Specificity range (%)	Comments
Microbiological tests			
Blood culture	40-80	NA	Widely regarded as the gold standard, but sensitivity may be low in endemic areas with high rates of antibiotic use-hence true specificity is difficult to estimate
Bone Marrow culture	55-67	30	Greater sensitivity but invasive and thus of limited clinical value, especially in ambulatory management
Urine culture	0-58	NA	Variable sensitivity
Stool culture	30	NA	Sensitivity lower in developing countries and not used routinely for follow-up
Molecular diagnostics			
Polymerase chain reaction	100	100	Promising, but initial reports indicated similar sensitivity to blood cultures and lower specificity
Nested polymerase chain reaction	100	100	Promising and may replace blood culture as the new "gold standard"
Serological diagnosis			
Widal test (tube dilution and slide agglutination)	47-77	50-92	Classic and inexpensive. Despite mixed results in endemic areas, still performs well for screening large volumes. May need standardization and quality assurance of reagents
Typhidot	66-88	75-91	Lower sensitivity than Typhidot-M
Typhidot-M	73-95	68-95	Higher sensitivity and specificity than classic Typhidot in some series, but other evaluations suggest that the performance may not be as robust in community settings as hospital.
Tubex	65-88	63-89	Promising initial results but has yet to be evaluated in larger trials in community settings.
Other			
Urine antigen detection	65-95	NA	Preliminary date only

in the blood of patients with typhoid fever[20,21]. The sensitivity of bone marrow culture is 90% and unlike blood culture is not reduced by up to 5 days of prior antimicrobial therapy[20,21]. In some patients with negetive results on bone marrow cultures, the duodenal string cultures have been positive.

One study found that in children the combination of blood and duodenal string culture was as sensitive as bone marrow culture[22]. Children also have a higher incidence of positive stool cultures than adults do (60% versus 27%). Therefore, ideally in adults and children blood, bone marrow, stool, and duodenal string cultures should all be performed. DNA probes for S. typhi and other Salmonellae have been developed, but these tests are not commercially available.

Treatment of typhoid fever

Azithromycin, a new macrolide antibiotic administered in a dose of 1 gm. once daily for 5 days is also useful for the treatment of typhoid fever, although the disease takes longer peroid to defervesce[23,24]. The main advantage of Aztreonam and Azithromycin is that they can be used in children and in pregnant or nursing females.

These drugs should be reserved for Quinolone resistant cases. It is recommended to treat with Ceftriaxone for 10-14 days. Several small studies have reported successful treatment of typhoid fever with Aztreonam, a Monobactam antibiotic[25]. This antibiotic has been shown to be more effective than Chloramphenicol in clearing the organism from the blood and was associated with fewer adverse reactions. However a prospective clinical trial in children in Malaysia was discontinued because of a high failure rate with Aztreonam[26].

Appropriate antibiotic treatment (the right drug, dose and duration) is critical to curing typhoid with minimal complications[27]. Standard treatment with Chloramphenicol or Amoxicillin is associated with a relapse rate of 5-15% or 4-8% respectively, where as the newer Quinolones and third generation Cephalosporins are associated with higher cure rates[5]. The emergence of multidrug resistant typhoid in the 1990s led to widespread use of Floroquinolones as the treatment of choice for suspected typhoid especially in South Asia and South East Asia where the disease was endemic. In recent years however, the emergence of resistance to Quinolones has placed tremendous pressure on public health systems in developing countries as treatment options are limited[28,29].

Table 2 shows the World Health Organization's recommendations for treating uncomplicated and severe cases of typhoid fever. Studies of short course antibiotic treatment for multidrug resistant typhoid have shown that Fluroquinolones can achieve satisfactory cure rates[3], but parenteral Ceftriaxone was associated with higher rates of relapse. A recent review of antimicrobial treatment of typhoid fever concludes that there is little evidence to support administration of Fluoroquinolones to all cases of typhoid and that satisfactory cure rates can be achieved in drug sensitive cases with first line agents such as Chloramphenicol. Although some open studies have suggested that cure rates may be better with oral Fluroquinolones compared with Chloramphenicol. These case series also included multidrug resistant cases.

Table 2: Recommended antibiotic treatment for typhoid fever (adapted from WHO[17] and Bhutta[20])

Susceptibility	Optimal treatment: Drug	Daily dose (mg/kg)	Course (days)	Alternative effective treatment: Drug	Daily dose (mg/kg)	Course (days)
Uncomplicated typhoid fever						
Fully sensitive	Fluoroquinolone (such as Ofloxacin or Ciprofloxacin)	15	5-7	Chloramphenicol	50-75	14-21
				Amoxicillin	75-100	14
				TMP-SMX	8-40	14
Multidrug resistance	Fluoroquinolone or	15	5-7	Azithromycin	8-10	7
	Cefixime	15-20	7-14	Cefixime	15-20	7-14
Quinolone resistance†	Azithromycin	8-10	7	Cefixime	20	7-14
	Ceftriaxone	75	10-14			
Severe typhoid fever requiring parenteral treatment						
Fully sensitive	Fluoroquinolone (such as Ofloxacin)	15	10-10	Chloramphenicol	100	14-21
				Ampicillin	100	14
				TMP-SMX	8/40	14
Multidrug resistant	Fluoroquinolone	15	10-14	Ceftriaxone or	60	
				Cefotaxime	80	10-14
Quinolone resistant	Ceftriaxone or	60	10-14	Fluoroquinolone	20	14
	Cefotaxime	80				

* Three days course also effective, particularly so in epidemic containment.
† Optimum treatment for Quinolone resistant typhoid fever has not been determined. Azithromycin, third genration Cephalosporins, or a 10-14 day course of high dose Fluoroquinolone is effective. Combinations of these are now being evaluated.

The use of glucocorticoid has been advocated for the treatment of severe typhoid fever based on a randomized, double blind, placebo controlled trial carried out in Indonesia. This study showed a significant reduction in mortality in patients with severe typhoid fever (ie. associated delirium, obtundation, stupor, coma, or shock) treated with Chloramphenicol and Dexamethasone as compared with Chloramphenicol treated control patients (case fatality rate 10% versus 56%)[30]. Although the case fatality rate in the control group was high and the study has never been repeated on the basis of this study Dexamethasone, 3 mg/kg. intravenously, followed by eight doses of 1 mg/kg every 6 hours for 48 hours, should be considered for the treatment of severe typhoid with altered mental status or shock. This must be done only under strictly controlled conditions and supervision, and signs of abdominal complications may be masked. Steroid treatment beyond 48 hours may increase the relapse rate[31].

Despite appropriate treatment, some 2-4% of infected patients relapse after initial clinical response to treatment. Individuals who excrete S. typhi for more than three months after infection are regarded as chronic carriers. However, the risk of becoming a carrier is low in children and increases with age but in general it occurs in less than 2% of all infected children[6].

Conclusion

In summary, management of typhoid fever remains a challenge, even one hundred years after the micro organism was first isolated by Gaffkey a German in 1884. Although these include establishing rapid clinical diagnosis and confirmation, the fact that both S. typhi and S. paratyphi are rapidly becoming resistant to commonly used antibiotics is of great concern. A concerted effort involving clean water supply, sanitary faeces disposal, effective vaccination and early diagnosis and prompt treatment of cases and carriers will be required to control the disease. Therapeutic strategies will have to take in to account the local antibiotic sensitivity patterns of S. typhi while defining treatment.

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A rare case of oral malignant fibrous histocytoma and short review of the literature

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Abstract

Malignant fibrous histocytoma (MFH) is the most common soft tissue sarcoma of late adult life, usually develops in the lower extremity and retro-peritoneum. They are very rare in head-neck region particularly in young life. A young adult present with a malignant fibrous histocytoma of Pleomorhpic-storiform type in the right molar region of maxilla and short review of the literature on malignant fibrous histocytoma of the oral cavity is presented.

Introduction

Malignant fibrous histocytoma is a controversial soft tissue malignancy whose pathogenesis continues to be re-defined. The most often used term soft tissue sarcoma, is a high grade aggressive sarcoma consist of fibroblastic and histocytic cells. This is usually soft tissue sarcoma of late adult life[1]. Man is affected more than women and it is rare in children. The extremities, especially lower extremities and retro-peritoneum are favored sites and rare in head and neck.

Case report

Raju Das, a 18 years old male patient was referred to the Department of Oral and Maxillofacial Surgery, Bangabandu Sheikh Mujib Medical University (BSMMU) on 13th June, 2007 with measuring 5x6 cm in diameter mass on the right molar region of maxilla. This mass is bi-lobuleted extended from buccal vestibule to hard palate, where it cross the midline and anterio-posteriorly from canine region to maxillary tuberosity. This mass was firm in consistency, pinkish colour, mildly tender on palpation and there is no sign of ulceration but growing rapidly. No sign of paraesthesia or anaesthesia on skin or mucous membrane and no palpable cervical lymphnode.

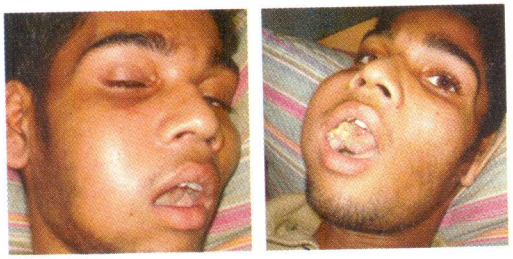

Figure1& 2: Pre-operative condition

Past history of the histopathology after excisional biopsy of a smaller lesion done outside BSMMU on 23rd April, 2007 revealed the tumour was benign type composed of oval to elongated cells and polygonal cells arranged in storiform pattern in some places and in intersecting bundles, finding on biopsy was benign fibrous histocytoma but after 1 month recurrence occur aggressively on the primary site and admitted to BSMMU on 13th June 2007.

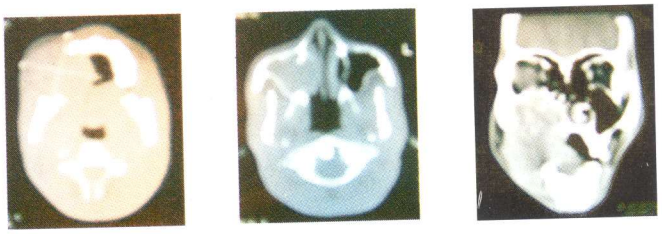

Figure 3, 4 & 5: Pre-operative CT

Pre-operatively computed tomography (CT) revealed a fairly large lobulated enhancing soft tissue mass in the right maxillary antrum. The lesion extended medially into the nasal cavity and oral cavity, laterally into the right side of the lower cheek superiorly it invade the floor of orbit with underlying bone destruction. Visible portion of brain parenchyma appear normal.

Operation procedure

The patient underwent excision of lesion and immediate reconstruction by temporalis muscle and local buccal fat on 27th June, 2007. Elective tracheostomy was done preoperatively for the administration of general anaesthesia. During operation, standard right submandibular incision was given for ligation of right external carotid artery to control per operative bleeding because the patient had the history of traumatic bleeding form lesion and reduced Hb% level.

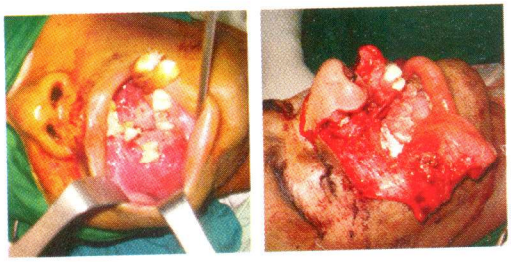

Figure 6 & 7 : Operation Procedure

Then a conventional Weber- Farguson incision was given to expose tumour. Total tumour mass removed from maxillary antrum, right lateral wall of the nose, beneath the floor of the orbit, frontal sinus in a capsulated mass. The right maxilla was partially resorbed. Unsupported and sharp bony spicules were trimmed. Right maxillary defect was reconstructed by right sided temporalis muscle and local buccal fat.

Drug history

24 hour before operation, following drugs was started upto postoperative 7 days- Injection form Ceftriaxone, Methylprednisolon, Ketorolac, Ranitidine and Infusion form Hartman solution, 5% DNS, Normal saline and 5% DA. The patient was discharged as without any significant problem. Later, the patient was referred to Oncology Department, BSMMU on 11th July, 2007 for postoperative management.

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Five (5) cycle chemotherapy schedule was made and 1st cycle started on 21st July, 2007 with Hologen 2 gm and Doxorubicin 30 mg per day. At present patient has no evidence of recurrence at the primary surgical site.

Pathological findings of excision of mass

Histopathologycal report of the resected mass revealed spindle cell neoplasm. The cells had spindle shaped hyperchromatic nucleus with blunted ends. The cells were arranged in interlacing fascicles. Mitosis was not infrequent. In some areas, it revealed myxiod back-ground. The tumour was seen up to the resection margin. The histological appearance was that of soft tissue sarcoma, low-grade compatible with malignant fibrous histocytoma.

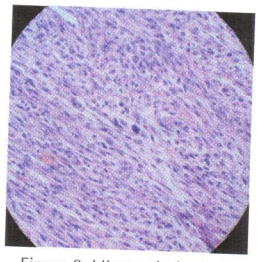

Figure 8: Histopathological slide of histocytoma

Discussion

Since the first recognition by O' Brien and stout, in 1464, Malignant Fibrous Histocytoma (MFH) has continually been reported in the world literature and is considered the most common kind of adult soft tissue sarcoma[2]. MFH is more common in the extremities and trunk than in the head and neck. In the head and neck region it is found only 1% to 7.2%, among them in oral cavity it accounts 5% to 15%. But the patient was young having the lesions in maxilla. The intrinsic features of MFH arising from different parts of the body might be directly related the different prognosis.

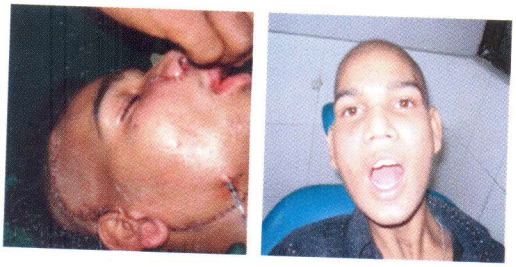

Figure 9 & 10 : Post-operative condition

Based on cellularity, pleomorphism, necrosis and mitotic activity, MFH is classified as low grade for well differentiated, intermediate grade for moderate differentiated and high grade for poorly differentiated and undifferentiated. Based on histology MFH is classified into 5 types- storiform-pleomorphic, giant cell, inflammatory, myxoid (myxofibrosarcoma) and angiomatoid.

Among them the case was histologically diagnosed as low grade for well differentiated and storiform-pleomorphic. The giant cell type MFH is believed to have the worst prognosis[3]. The site of origin included the paranasal sinuses, the nasal passages, mandible, supraglottic larynges and trachea[4]. In this case, the site of origin was right maxilla. Blitger et al reported 29 cases of MFH of deep structure of head and neck with a metastatic potential of 22%[5]. In another study, review of the sites of metastasis indicated that the lung is the most frequent initial site, either solitary or multiple, occurring in 61.5% of case[6]. In our case there was no evidence of metastasis.

WU xuexi et al reported that the extend of surgery may be defined as radical, wide or local resection[7]. In the treatment protocol, radical surgery with a minimum margin of 3 cm is the choice of treatment followed by the combination with radiotherapy and / or chemotherapy is advocated by most of the authors. In case of this patient, surgery was done followed by chemotherapy due to anatomical limitation and as the patient was young. WU xuexi reported 40.9% of head and neck patients with local recurrence survived by repeated operation and they suggested that initial resection for a pathologically proven MFH in head and neck should be as radical as possible[7]. Recurrence of MFH in head and neck will cause difficulty for secondary surgery. Though radiotherapy is indicated but few researchers reported that the efficacy of radio therapy could not be established in MFH. Few also suggested that radiotherapy may be used for recurrent, unresectable or extremely aggressive lesions[8].

Head and neck MFH tends to be more aggressive than MFH of extremity. This is probably responsible for the poor prognosis in head neck MFH. Factors of prognostic importance of MFH are histological grade, size and site of primary tumor. Lymphnode involvement is rare for MFH[7]. Neck dissection should be done in the presence of clinically positive nodes but in this case there was no positive neck node[5]. Five years survival was around 50% for MFH[9]. Inadequate initial resection, high incidence of local recurrence and limited anatomical allowance for additional surgery are factors related with treatment failure in head and neck MFH. Being a locally aggressive tumor, MFH penetrates the surrounding tissues in a multidimensional fashion.

Leite C et al reported that recent study of MFH-chemotherapy shows a significant response and adjuvant chemotherapy against MFHs demonstrated increase in both survival and disease free survival rate in these patients involving the jaw bone[10]. After development of metastasis, however chemotherapy has not been a helpful adjunct. But in another Chinese report suggested that they did not find any significant change for their patients with adjuvant radiotherapy and/or chemotherpy[7].

Conclusion

Head neck MFH is rare but aggressive with poor prognosis. Radical resection with adjuvant chemotherapy is the treatment of choice. Local radical resection was done along with primary reconstruction by temporalis muscle and local buccal fat, followed by adjuvant chemotherapy. There was no evidence of recurrence within first 8 months.

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Congenital absence of pulmonary valve

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Introduction

Congenital absence of pulmonary valve presents a characteristic clinical, physiologic and pathologic syndrome[1].

Absent Pulmonary Valve (APV) is defined as total or subtotal absence of pulmonary valve leaflets.

Ruttenberg and co-workers commented on 25 cases from 1908 to 1964 and Felix Wyler and co-workers presented 15 observations from 1964 to 1969[2].

APV can be associated with simple or complex cardiovascular malformation. It occurs as an isolated anomaly in non-syndromic patient or as a part of a genetic syndrome in syndromic patient. The most common association is APV and Fallot's tetralogy with absence of ductus arteriosus, Fallot type APV. APV with intact ventricular septum or muscular VSD with persistent Ductus Arteriosus is less common[4]. Non Fallot type APV/ADA.

The main symptoms of APV are pulmonary insufficiency and bronchial obstruction. The overall frequency of APV is not known. But the Fallot type APV/ADA may be estimated to occur in 6:3000 live born infants with congenital heart disease[4].

William Osler said there should be no teaching without a patient for a text. This can focus attention on the condition itself as well as what we should do to help the patient[3].

Aneurysmal dilatation of the pulmonary artery may result either from a congenital weakness at the base of the pulmonary artery or from the hemodynamic effect of a ventricular septal defect and infundibular stenosis in the presence of pulmonary regurgitation[1].

Case history

An 11 year-old young lady noted exertional dyspnea from her early childhood and was treated with bronchodilators. On examination of the chest, a parasternal heave was palpable, auscultation revealed a single second heart sound, a grade 3/6 harsh systolic murmur, and heart beat at the left sternal angle. The extremities were cool and cyanosed.

A chest radiograph demonstrated cardiomegaly, a grossly enlarged left pulmonary artery, a right aortic arch and narrowing of the distal trachea (Fig 1).

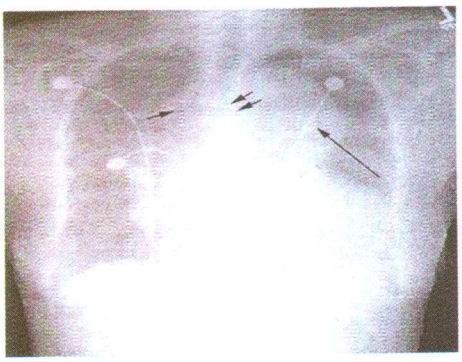

Figure 1: Chest X-Ray showing grossly enlarged left pulmonary artery (long arrow). Narrowing of the trachea is evident just above the carina (paired arrows). The aortic knob can be seen arising to the right of the trachea (short arrow).

An electrocardiogram showed sinus tachycardia with signs of right atrial abnormality and right ventricular hypertrophy (Fig 2).

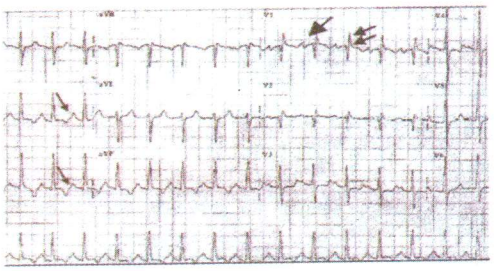

Figure 2: ECG showing peaked P-waves in inferior and lateral leads (narrow arrows) and a bi-phasic P-wave in lead V1 (wide arrow) indicating right atrial abnormality. There is prominent R-wave in V1 (paired arrows) consistent with right ventricular hypertrophy.

Two dimensional and Doppler Echocardiogram disclosed normal LV systolic function with a large ventricular septal defect, dilated right ventricle with thickned right ventricular wall and narrowing of right ventricular outflow tract [RVOT] (Fig 3).

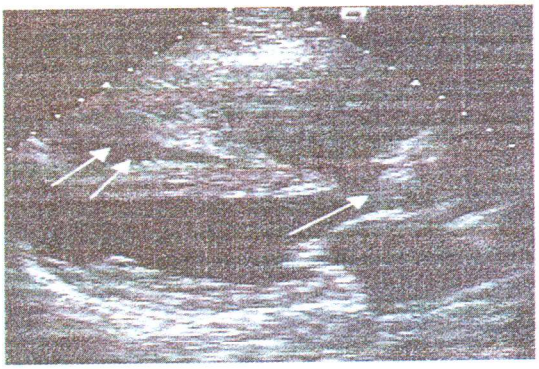

Figure 3: Two-dimensional echocardiogram (parasternal long axis view) demonstrating a large ventricular septal defect and over-riding aorta (single arrow), and a dilated RV with a thickened RV wall (paired arrows)

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Cardiac catheterization done in 2006 had documented on elevated right ventricular pressure (RV) of 135/20, a pulmonary artery pressure of 24/12 and a left ventricular pressure of 135/20. Oxymetry confirmed a R>L ventricle shunt with a pulmonary to systemic flow ratio 2.2:1. A left ventriculogram demonstrated overall normal LV function with a ventricular septal defect (VSD) in membranous septum. A right ventriculogram showed RV outflow tract (RVOT) narrowing and marked dilatation of the left pulmonary artery. Ventricular septal defect with pulmonary valve stenosis was diagnosed.

The VSD was closed with a PTFE patch and the RVOT was reconstructed with placement of a 22 mm homograft valve in the pulmonary valve position.

The patient had dramatic improvement postoperatively, with immediate resolution of symptoms and signs of RV failure and reduction of the heart rate from 120-130 to 70-80 beats per minute by postoperative day 2 (Two).

Discussion

Congenital APV was first described by Chever in 1847[4]. It is defined as total or subtotal absence of the pulmonary valve leaflets. This may be the result of error of complete failure in valve development[5].

Mild stenosis of the pulmonary artery orifice and aneurysmal dilatation of the main pulmonary artery as well as of the right and left or both pulmonary artery branches co-exist.

Compression of the major bronchi at the hilum is a secondary phenomenon and is assumed to develop in fetal life[6]. In addition, compression of the intrapulmonary bronchi by abnormally branching pulmonary arteries may represent a serious complication[7].

The definite confirmation of an absent pulmonary valve can only be obtained by surgery or necropsy. The diagnosis, however, based on the presented data can be presented to correct since full correlation between auscultatory, angiocardiographic findings was established[4].

In our patient, the diagnosis was made by surgery and the present postoperative good clinical condition seemed not to warrant any surgical intervention. The surgical outcome of APV was closely related to preoperative ventricular dependency. Martin et al (2006) named 36 patients underwent surgical correction from 1979-2004, 28% were ventricular dependent, while 72% were underwent repair electively[11].

The spectrum of malformations to which APV may be associated can be categorized into two types of APV with or without VSD[8].

APV with VSD

The most common form with VSD is the association with TOF. The similarities with TOF include:

* Anterior deviation of the infundibular septum in relation to the muscular septal crest
* Malaligned VSD
* Overriding of the Aorta

The distinguishing features are:

* Unobstructed right ventricular infundibulum
* Aneurysmal dilated pulmonary arteries.

Typically absent Ductus Arteriosus is reported. It is an uncommon condition comparing 2-6% of all cases of TOF[9].

APV without VSD

In this less frequent form without VSD, muscular VSD may be rarely observed. The association of PDA is reported[4].

Differential diagnosis of an aneurysmal dilatation of the pulmonary trunk include APV, agenesis of the ductus arteriosus, truncus arteriosus, ventricular aneurysm and ventricular diverticula[10].

Conclusion

Surgical correction of this severe pathology has a high mortality rate (20-35%)[12]. The success of corrective heart surgery is infact determined in more severe cases by progressively resolving respiratory failure preoperatively and therefore the reliance on mechanical ventilation[12].

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Case history : A healthy pregnancy following chemotherapy for dysgerminoma

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Abstract

Dysgerminoma, a malignant germ cell tumour of the ovary develops in females, girls and young women in 2nd to 3rd decade. Usually diagnosed in early stage (Stage Ia), 90% cases unilateral, so conservative surgery followed by chemotherapy is the treatment of choice, specially in young patients who are desirous for children[1]. Response to multiagent chemotherapy is excellent but careful and critical follow up is mandatory. The 5 years survival rate is > 90%. Even it is curable when diagnosed & treated in early stage[2]. A case is documented here who had normal pregnancy and normal delivery after dysgerminoma treated by chemotherapy.

Introduction

Ovarian cancer is the 5th leading cause of cancer related death in women. Though documented to occur in all age groups, it is usually a disease of postmenopausal and pre-pubertal girls[2]. According to FIGO and WHO, germ cell tumour of the ovary constitutes 5-10% of all ovarian cancers and dysgerminoma constitutes 50% of all germ cell tumour and many of them produce biological markers like AFP, HCG, LH which is monitored to assess the response to therapy.

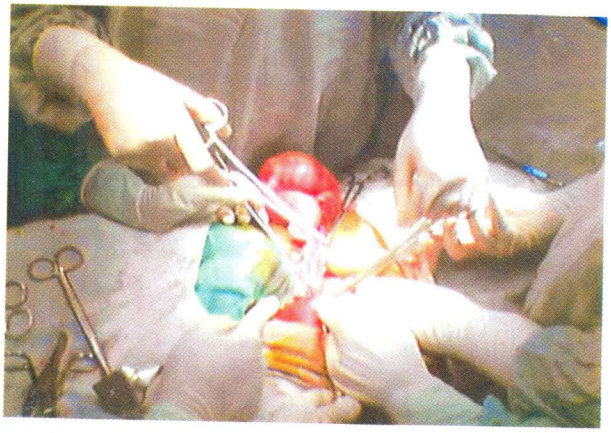

Figure: Operation of Dysgerminoma

Seventy five percent (75%) of ovarian cancer patients present in advanced stages III and IV, but a few presents in early stage along with other pathology[3]. Typically it develops as an insidious disease with few warning sings and symptoms. A history of nonspecific gastrointestinal complaints as nausea, vomiting, dyspepsia, altered bowel habit, early satiety are the early features. Abdominal distension due to ascites & urinary disturbance, rectal discomfort, bowel obstruction are features of late and advanced disease.

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Macroscopically solid tumour, rubbery consistency, cut surface shows homogenous appearance[5,11].

Microscopically mimic that of primitive gonad i-e. most of the germ cells are arranged in bundles or alveoli with central nuclei surrounded by undifferentiated stroma. Lymphocytes may invade the stroma and its presence favour a favorable prognosis[5].

The treatment of choice includes removal of tumour with thorough exploration of intraabdominal organs, FNAC of opposite ovary if facilities available[4]. Though sensitive to both radio and chemotherapy, radiotherapy is not given because of extensive destruction of soft structures like kidneys, intestine and bladder.

Combination chemotherapy used are[2,9]:

1. Platinum based drugs: Cisplatin & its newer analogue Carboplatin.
2. Anthracycline antibiotics: Bleomycin.
3. Plant Alkaloid: Podophylotoxin such as Taxol or Paclitaxel used. Often 6 cycles of such therapy are used, prognosis is excellent.

Case history

Mrs. Romana, 21 years, P=1 (NVD) housewife, was attended to gynecologist with the history of lump in lower abdomen and amenorrhoea for 4 months, she had nausea, vomiting, abdominal discomfort after meal. She was a normally menstruating woman with average flow and duration, she had no family history of breast, ovary or colon cancer or cancer related deaths. She was examined and found uterus 16 weeks size and another palpable lump about 12X12 cm firm, non-tender with well-defined margin and overlying skin was free. There was no ascites and no enlarged lymph nodes. Per vaginal examination revealed same features and a cleavage was found between uterus and palpable lump, so our clinical diagnosis was 16 weeks pregnancy with left sided ovarian tumour. Routine investigation including USG done which showed 16 weeks pregnancy with loculatted hypoechoic solid mass in left adnexae. After proper counseling laparatomy was done which showed right ovary completely healthy, so left sided salphingo-oophorectomy done preserving right ovary and intrauterine pregnancy as it was already 17+ weeks pregnancy. Histopathology revealed it is a case of dysgerminoma. So, she was advised to attend Mohakhali Cancer Hospital where she received 6(six) cycles of combination chemotherapy immediately after termination of pregnancy by prostaglandin gel.

Except for alopecia, diarrhoea, no other serious side effects occurred. She was under regular follow up for six months. She conceived after this and had also regular careful antenatal check up. Anomaly scan was done at 20 weeks and was found everything normal. Seven (7) days before her E.D.D she was admitted with early labour pain. Labour progresses were recorded in partograph and after 6 hours she delivered a healthy male baby, weight 3 kg. Apgar score and other reflexes of the baby were normal.

She was discharged on next day and was advised to have USG and serum AFP after 6 weeks. She was then clinically evaluated 3 monthly for the 1st year, 6 monthly for next year. Now she is on yearly follow up and is found completely ok.

Discussion

Dysgerminoma is one of the commonest malignant germ cell tumour. It is the adult counterpart of seminoma in male. It is highly sensitive to both radio and chemotherapy, with the introduction of newer combination chemotherapy that has largely superceded the radiotherapy, it is now almost a curable condition[7,8].

With few exceptions, those who are fortunate enough usually present in this early stage of ovarian cancer. Our patient was lucky enough that she was symptomatic in early stage, got the benefit of modern treatment and showed excellent response.

Dysgerminoma, an undifferentiated germ cell tumour, needs further tests for pre-operative diagnosis as transvaginal colour and pulsed Doppler USG, CT scan, Karyotyping (acquired in dysgenetic gonad/turner's syndrome if the person has a chromosome in her genotype but not others). Dysgerminoma usually has chromatin negative pattern[2,12].

So, early stage of tumour, unilateral, early laparotomy and use of combination chemotherapy plus critical follow up had made her pregnancy a successful one.

Conclusion

Dysgerminoma locally malignant germ cells tumour, 90% unilateral, early stage diagnosis, early laparotomy and histopathology, early starting of combination chemotherapy and critical follow up can make the patient almost cure.

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Launching of New Products

Gold kiD

Multivitamin syrup with cod liver oil

The Golden formula for kids

Gold kiD syrup contains 8 essential vitamins with cod liver oil which helps the children to grow strongly and stay healthy. Each 5 ml Gold kiD syrup contains Vitamin A 2000 IU, Vitamin D 200 IU, Vitamin C 17.50 mg, Vitamin B_1 0.70 mg, Vitamin B_2 0.85 mg, Vitamin B_6 0.35 mg, Vitamin E 1.50 mg, Nicotinamide 9.00 mg, Cod liver oil 100 mg. Gold kiD syrup is used for the treatment and prevention of vitamin deficiencies associated with restricted diet, improper food intake and decreased absorption. Gold kiD syrup can be given ½ teaspoonful/day for infants (1-12 months), 1 teaspoonful/day for children (1-4 years), 1½ teaspoonful/day for children (over 4 years) and 2 teaspoonful/day for adults. Gold kiD is available in Amber glass bottle containing 100 ml syrup. MRP of Gold kiD syrup is Tk 80/ phial.

Orfenac-plus Injection

Diclofenac & Lidocaine

The quick relief analgesic for acute pain

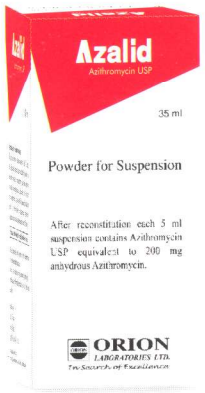
Orfenac-plus is one of the potent analgesic drugs having analgesic, anti-pyretic and local anesthetic properties. Each 2 ml Orfenac-plus ampoule contains Diclofenac Sodium BP 75 mg and Lidocaine HCl USP 20 mg. Orfenac-plus is indicated for Rheumatoid Arthritis, Osteoarthritis, Ankylosing Spondylitis, Acute Gout, Periarthritis, Bursitis, Tendonitis, Low Back Pain, Sprains, Strains, Dislocation, Orthopedic & Dental Surgery, Renal and Biliary colic. Orfenac-plus can be administered intramuscularly once daily, in severe cases twice daily in adult and 1-3 mg of Diclofenac/Kg body wt daily in Juvenile Chronic Arthritis. It is presented in box containing 2x5 ampoules in blister pack. MRP of each ampoule of Orfenac-plus inj is 9.00 Tk.

Azalid 35 ml Powder for suspension

Azithromycin USP 200 mg/ 5 ml

Powerful punch with bigger pack size

Orion has launched Azalid 35 ml suspension, which is the new pack size of Azithromycin. Azalid 35 ml will cover once daily 3 days, 5 days and 7 days course of Azithromycin for treating different types infections in children. Azalid is indicated for the treatment of infections like- 1. Upper respiratory tract infections, including pharyngitis, tonsillitis, sinusitis and otitis media; lower respiratory tract infections including bronchitis and pneumonia. 2. Skin and soft tissue infections including cellulites, pyoderma, wound infections etc. 3. Genital infections including chancroid, gonococcal and nongonococcal urethritis, cervicitis caused by *Chlamydia trachomatis* and uncomplicated gonococcal infections of the cervix, urethra and rectum caused by *N. gonorrhoea.* 4. Odontogenic infections including dental caries, pulpitis, periapical abscess, osteoperiostitis of the jaw, maxillary cysts and periodontal and deep facial space infections. Recommended dose of Azalid for children over 6 months is 10 mg/ kg once daily for 3 days to 7 days. Azalid 35 ml powder for suspension is presented in a bottle containing dry powder to prepare 35 ml suspension. MRP for 35 ml Tk. 130/-.



Iftar Party

Dhaka

Medi Aid Hospital, Dhaka: An Iftar Party was arranged on 27th September 2007 by Medi Aid Hospital at Suruchi Restaurant, Dhanmondi. Dr. Md. Jalilur Rahman was the chairperson. About 20 doctors attended the Iftar Party.

Cardiac Surgery unit, BSMMU: An Iftar Party was arranged by cardiac surgery unit, BSMMU on 29th Septamber 2007 at Star Kabab Restaurant, Dhanmondi. Professor Abtabuddin chaired the session. About 20 doctors attended the Iftar Party.

Hepatology Department, BSMMU: An Iftar Party was arranged by Hepatology department, BSMMU on 4th October 2007 at Star Kabab Restaurant, Dhanmondi. About 20 doctors attended the Iftar Party.

Neurosurgery Department, BSMMU: An Iftar Party was arranged by neurosurgery department, BSMMU on 8th October 2007 at Star Kabab Restaurant, Dhanmondi. Dr. Khairun Nabi Khan, Assistant Professor was present at the meeting. About 20 doctors attended the Iftar Party.

Sylhet

Adhunik Hospital: On 9th October 2007 an iftar party was arranged by Adhunik Hospital, Sylhet at the Crystal City Restaurant. Mr. M. A. Ques, Managing Director, Adhunik Hospital was present as the chief guest. About 25 doctors attended the iftar party.

Orthopaedic Department, SOMCH: An iftar party was arranged by Orthopaedic department, SOMCH on 4th October 2007 at the Crystal City Restaurant. Dr. Ahsan, CA, was present as the chief guest. About 30 doctors attended the iftar party.

Gynae Unit-II & III, SOMCH: On 7th October 2007 an iftar party was arranged by gynae unit-II & III, SOMCH at the class room. Dr. Shornali, CA, was present as the chief guest. About 55 doctors attended the iftar party.

Sylhet Metropoliton Hospital: An iftar party was arranged by Sylhet Metropoliton Hospital on 2nd October 2007 at the Taradin Restaurant. Dr. Awolad, SMO, was present as the chief guest. About 25 doctors attended the iftar party.

Rajshahi

Medi Heart Centre, Sathia, Pabna: An Iftar Party and round table meeting was arranged by Medi Heart Centre on 20th September 2007 on "Management of hypertension" at Sathia Bazar. Dr. Md. Monsurul Islam, UH & FPO, Sathia UHC was present as the chairperson. Dr. Md. Shamimur Rahman, Sr. Medical Officer, National Heart Foundation, Dhaka was the keynote speaker. About 70 doctors of Sathia, Pabna attended the meeting.

Faridpur

Diabetic Hospital, Faridpur: An Iftar Party was arranged by Diabetic Hospital, Faridpur on 3rd October 2007 at the seminar room. Mr. Abdus Samad, Secretary, Diabetic Society, Faridpur chaired the meeting. Dr. Sahidur Rahman Bhuia was the chief guest and Dr. Johirul Islam Mia was present as the special guest. About 50 doctors attended the Iftar Party.

Islami Bank Community Hospital, Faridpur: On 1st October 2007 an Iftar Party was arranged by Islami Bank Community Hospital at the seminar room. Md. Sahedur Rahman, Chairman, Islami Bank Hospital chaired the meeting and Md. Khaled, Secretary was the chief guest. Dr. Md. Bodrul Alam, Assistant Professor, Cardiology was present as the special guest. About 60 doctors attended the Iftar Party.

Doulotpur UHC, Kustia: An Iftar Party was arranged by Doulotpur UHC on 2nd October 2007 at the room of UH & FPO. Dr. Rajendra Nath Mehta, UH & FPO Chaired the meeting and Dr. Anabinda Paul, RMO was the chief guest. About 15 doctors attended the Iftar Party.

MSD NEWS

Medical Services Department (MSD) of ORION Laboratories Limited successfully arranged significant number of Round Table Meetings, Scientific Seminars in different venues of all over Bangladesh during July 2007 to December 2007.

Scientific Seminar

BMA Faridpur: On 7th September 2007 a scientific seminar was arranged by BMA Faridpur on "Low back pain" at the BMA Bhaban. Dr. Mostafizur Rahman Shamim, Associate Professor, FMCH was the chairperson. Dr. S. M. Jahangir Choudhury Tito and Dr. Golam Kabir were the keynote speakers. About 185 doctors attended the session.

ENT Department, DMCH: ENT department of DMCH arranged a scientific seminar on "Cholesteatoma" on 13th August 2007 at the seminar room. Professor Md. Abdul Quadir, Head of the dept. was the chairperson and Dr. M A Matin, Associate Professor was the keynote speaker. About 60 doctors enjoyed the session.

Round Table Meeting (RTM)

Dhaka

BIHS, Mirpur: On 5th August 2007 a round table meeting was arranged by BIHS, Mirpur on "Indapamide" at the seminar room. Dr. Aminur Rashid Minu, Consultant, Surgery was the chairperson. About 25 doctors attended the session.

Medicine unit, Shaheed Suhrawardi Hospital: A round table meeting was arranged by medicine unit, SSH on 7th August 2007 on "Acute pancreatitis" at the seminar room. Professor Dr. Md. Redwanur Rahman, Head of the Department of Medicine was the chairperson and Dr. Kazi Farhadul Huq, Assistant Registrar was the keynote speaker. About 40 doctors attended the session.

Green View Clinic, Green Road: Green View Clinic arranged a round table metingon "Role of ceftriaxone to treat various infections" at China Kitchen restaurant, Hatirpool on 16th August 2007. About 10 doctors attended the meeting.

Dohar UHC, Dhaka: Dohar UHC arranged a round table meeting on "Role of ceftriaxone to treat various infections" on 19th August 2007 at the seminar room. Dr. Md. Abdus Samad, UH & FPO chaired the session. About 25 doctors attended the meeting.

Yellow Unit-I, NITOR: On 8th Nobember 2007 a round table meeting was arranged by Yellow unit-I, NITOR on "Recent concept of flexor tendon injury management" at the room of head of the department. Professor R. R. Kairy chaired the meeting. Dr. A. S. M. Monirul Alam Rintoo was the keynote speaker. About 20 doctors attended the session.

HCDP, Uttara: On 17th November 2007 a round table meeting was arranged by HCDP, Uttara on "Lower abdominal findings in ultrasonogram" at the conference room. Professor Md. Sadequzzaman chaired the session and Dr. Fazle Nur, Consultant was present as the chief guest. Dr. Md. Maksudul Alam, Consultant was the keynote speaker. 11 doctors of Uttara HCDP attended the meeting.

NHN, Mirpur: A round table meeting was arranged by NHN, Mirpur-10, Dhaka on 5th December 2007 on "Role of indapamide in the management of hypertension" at the seminar room. Dr. Md. Ataur Rahman, Centre Director chaired the meeting. About 10 doctors attended the session.

ICU, Dhaka Shishu Hospital: A round table meeting was arranged by ICU, Dhaka Shishu Hospital on "Role of ceftriaxone to treat various infections" at the Cheer's Chinese Restaurant, Dhanmondi on 8th December 2007. Dr. Enayet Hossain, Registrar, ICU chaired the meeting. About 20 doctors attended the meeting.

CRP, Savar: On 29th November 2007 a round table meeting was arranged by CRP on "Role of ceftriaxone to treat various infections" at the Younk King Restaurant, Savar. About 20 doctors attended the session.

Chittagong

Fuad Al Khatib Hospital, Cox's Bazar: On 5th August 2007 a round table meeting was arranged by Fuad Al Khatib Hospital, Cox's Bazar on "Role of ceftriaxone to treat various infections" at Hotel Media International. Dr. G. M. Rahimullah, Managing Director, chaired the session. About 45 doctors attended the meeting.

Zam Zam Hospital, Chokoria, Cox's Bazar: Zam Zam Hospital, Chokoria arranged a round table meeting on "Role of ceftriaxone to treat various infections" on 6th August 2007. Dr. Faizur Rahman, CMO, was the chairperson. About 15 doctors enjoyed the session.

Centre Point Hospital, Jamalkhan, Chittagong: A round table meeting was arranged by Centre Point Hospital, Jamalkhan, Chittagong on 29th July, 2007 on "Role of ceftriaxone to treat various infections" at the seminar room. Dr. M. Abdus Salam, Hospital Director, chaired the session and Dr. Shaifuddin Khaled, Consultant, Anaesthesiology, was the chief guest. About 20 doctors attended the session.

Patiya UHC, Chittagong: Patiya UHC arranged a round table meeting on "Role of ceftriaxone to treat various infections" on 8th August at the seminar hall. Dr. Saroj Kumar Barua, UH & FPO chaired the meeting. About 30 doctors attended the session.

Padua UHC, Lohagara: A round table meeting was arranged by Padua UHC, Lohagara on 9th August 2007 on "Role of ceftriaxone to treat various infections" at the seminar room of the complex. Dr. Sarwar Jahan, UH & FPO was the chairperson. About 25 doctors attended the meeting.

Paediatric ward, USTC: Paediatric ward of USTC arranged a round table meeting on "Childhood diabetes mellitus" on 15th August 2007 at the seminar room. Professor Dr. Md. Sahadat Hossain, head of the department of Paediatric chaired the meeting and Dr. Md. Didarul Alam, Associate Profesor was the chief guest. Dr. Tarun Kumar Roy, Assistatnt Registrar was the keynote speaker. About 60 doctors attended the meeting.

National Hospital, Chittagong: On 21st August 2007 National Hospital, Chittagong arranged a round table meeting on "Basic concept of operative management" at the seminar hall. Dr. Md. Rafique, MD, National Hospital was the chairperson and Dr. Md. Ehtasamul Haque, Assistant Professor, Nephrology, USTC was present as the special guest. Dr. A. T. M. Rezaul Karim, Orthopaedic surgeon, was the keynote speaker. About 50 doctors attended the session.

Ichakhali UHC, Rangunia: A round table meeting was arranged by Ichakhali UHC on "Role of ceftriaxone to treat various infections" on 5th September 2007 at the seminar room. Dr. Bizon Kanti Biswas UH & FPO chaired the session and Dr. Md. Zahid Hossain, Consultant was the special guest. About 25 doctors enjoyed the session.

Skin & VD Hospital, Agrabad: On 3rd August 2007 Skin & VD Hospital, Agrabad arranged a round table meeting on "Azythromycin in treating skin infections" at Hotel Silver Spoon, Agrabad. Dr. Didarul Alam, Associate Professor chaired the meeting and Dr. Abul Kashem Chy, Assistant Professor was the Special Guest. About 15 doctors attended the meeting.

Sitakundu UHC: Sitakundu UHC arranged a round table meeting on 27th August 2007 on "Role of ceftriaxone to treat various infections" at the room of UH & FPO. Dr. Paresul Alam, UH & FPO chaired the session. About 25 doctors attended the meeting.

South Point Hospital, Agrabad: On 20th November 2007 a round table meeting was arranged by South Point Hospital, Agrabad on "Role of ceftriaxone to treat various infections" at the seminar room. Dr, Minhaz, Managing Director was the chairperson and Dr. Wajeda Safiullah, Consultant, Gynae was the special guest. About 25 doctors attended the meeting.

CCC Urban Maternity Hospital, Mohora: On 13th November 2007 a round table meeting was arranged by CCC urban Maternity Hospital on 'Role of ceftriaxone in pregnancy related infections" at the CCCUMH corridor. Dr. Ashish Mukherzee, Director chaired the meeting and Dr. Nibedita Chy, Consultant, Gynae was the keynote speaker. About 45 doctors attended the round table meeting.

Mymensingh

Pakundia UHC, Kishorgonj: A round table meeting was arranged by Pakundia UHC on "Role of ceftriaxone to treat various infections" at the seminar room of the complex on 15th August 2007. Dr. M. A. Hatem, UH & FPO was the chairperson and Dr. A. K. M. Shahidullah, RMO was the chief guest. About 15 doctors attended the meeting.

Rajshahi

Shibgonj UHC, Chapainawabgonj: On 4th August 2007 a round table meeting was arranged by Shibgonj UHC, Chapainawabgonj on "Role of ceftriaxone to treat various infections" at the conference room. Dr. Md. Sharifur Rahman, UH & FPO was the chairperson. About 20 doctors attended the session.

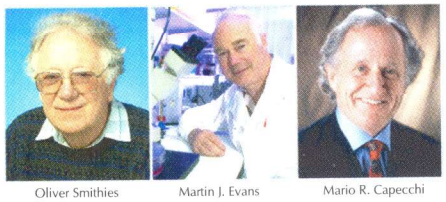
Gurudaspur UHC, Natore: Gurudaspur UHC, Natore arranged a round table meeting on "Role of ceftriaxone to treat various infections" at the seminar room on 18th July 2007. Dr. Abdur Rahman, UH & FPO chaired the meeting. Dr. Md. Selim Khan, RMO was the chief guest and Dr. Afroza Khan, MO was the special guest. About 20 doctors were present at the meeting.

The rest of the MSD news at page - 527

Medi News

Nobel prize in physiology or medicine 2007

Mario R. Capecchi, Martin J. Evans and Oliver Smithies won the 2007 Nobel Prize in medicine or their discoveries of "principles for introducing specific gene modifications in mice by the use of embryonic stem cells". This year's Nobel Laureates have made a series of ground-breaking discoveries concerning embryonic stem cells and DNA recombination in mammals. Their discoveries led to the creation of an immensely powerful technology referred to as gene targeting in mice. It is now being applied to virtually all areas of biomedicine - from basic research to the development of new therapies. Gene targeting is often used to inactivate single genes. Such gene "knockout" experiments have elucidated the roles of numerous genes in embryonic development, adult physiology, aging and disease. To date, more than ten thousand mouse genes (approximately half of the genes in the mammalian genome) have been knocked out. Ongoing international efforts will make "knockout mice" for all genes available within the near future. With gene targeting it is now possible to produce almost any type of DNA modification in the mouse genome, allowing scientists to establish the roles of individual genes in health and disease. Gene targeting has already produced more than five hundred different mouse models of human disorders, including cardiovascular and neuro-degenerative diseases, diabetes and cancer.



Oliver Smithies | Martin J. Evans | Mario R. Capecchi

nobelprize.org

Kidney-liver transplant patient goes back to work

A 47-year-old police officer in north China's Shanxi Province remains on the job five years after his lifesaving kidney-liver transplant, becoming Asia's longest survivor of the dual organ transplant operation in Asia. Jia huimin returned to his job two years ago, some three years after receiving a new liver and kidney. Suffering from cirrhosis of the liver and kidney failure, Jia entered the People's Hospital in Taiyuan, the provincial capital of Shanxi on Sep. 28, 2000 to undergo the dual organ transplant operation. "It is extremely difficult to transplant two organs simultaneously," said Feng Bianxi, the chief surgeon who performed the operation. He says there can be many complications and many favorable factors have to be in place for the operation to be successful. Currently, the patient's normal functions have been restored and he continues to work as a member of the local police department. The world's first liver kidney transplant operation was carried out in the United States in 1983 and only a few countries have conducted such surgeries successfully. The world's longest survival patient has lived 10 years.

china.org

Cleaning sprays and air fresheners may lead to asthma

Occasional use of cleaning sprays may increase the risk of developing asthma in adults. The same applies to the use of air fresheners. While it has already been established that cleaning professionals are at an increased risk of developing asthma, this particular study conducted by the Centre for Research in Environmental Epidemiology at the Municipal Institute of Medical Research in Barcelona, has focused on an occasional spray cleaner use by non-professionals. Scientists analyzed the data from one of the world's largest epidemiologic studies of airway disease, the European Community Respiratory Health Survey (ECRHS I) and the follow-up phase ECRHS II. The data included more than 3,500 subjects in 190 European countries. Subjects were evaluated for asthma, wheezing, physician-diagnosed asthma, allergies. All individuals were also asked about the frequency of cleaning spray use. Two-thirds of the groups studied were women doing majority of household cleaning. Asthma was found in 60% of them. Overall, the results have shown that the risk of developing asthma increases by 30-50% with more frequent cleaning activity. Cleaning sprays, air fresheners, furniture cleaners and glass cleaners have a particularly negative impact. It is estimated that 1 in 7 cases of adult asthma may be due to exposure to cleaning agents. "Our findings are consistent with occupational epidemiological studies in which increased asthma risk was related to professional use of sprays among both domestic and non-domestic cleaning women," wrote Dr. Jan-Paul Zock, Ph.D., the lead author of the report, "This indicates a relevant contribution of spray use to the burden of asthma in adults who do the cleaning in their homes."

American Thoracic Society

Fasting may lower risk of heart disease

Going without food for one day a month may help lower the risk of heart disease, according to a report presented at the American Heart Association's "Scientific Sessions 2007." This could be one of the many reasons why members of the Church of Jesus Christ of Latter-Day Saints have lower rates of heart disease than other Americans. The report concluded that fasting has a heart-protective benefit. The religious prohibition against tobacco use is usually credited with the low rates of heart disease in LDS members, but researchers wanted to find out if other religious teachings were also important in their overall health. The study was authored by Dr. Benjamin Horne, director of cardiovascular and genetic epidemiology at Intermountain Medical Center in Salt Lake City. "Fasting was the strongest predictor of lower heart disease risk in the people we surveyed," said Dr. Horne. "About 8 percent of the people who fasted did not express an LDS preference and they also had less coronary disease," he said. According to the report, fasting lowers the odds of being diagnosed with coronary artery disease by 39 percent. The study's authors caution that people with diabetes, who are not encouraged to skip meals, should not try this approach until more research is conducted.

American Heart Association

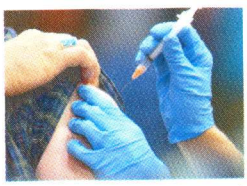
Cigarette smoking increases risk of erectile dysfunction

A study conducted by Tulane University School of Public Health and Tropical Medicine, found a significant link between cigarette smoking and erectile dysfunction. This indicates that men, who have a habit of smoking cigarettes, face a greater risk of erectile dysfunction than their non-smoking counterparts. This risk increases with the amount of cigarettes smoked. The study, which was conducted in China in 2000-2001 involved examining 7,684 men without vascular disease in the age group of 35-74 years. The researchers used questionnaires to measure the status of cigarette smoking and erectile dysfunction. The study revealed an important statistical association between the number of cigarettes smoked by men and the possibility having erectile dysfunction. This association was more evident in those with diabetes. It was further shown that nearly 22.7 percent of Chinese men experienced erectile dysfunction due to cigarette smoking.

American Journal of Epidemiology

Vaccine for hypertension

A research team in Switzerland is studying the viability of a vaccine that could boost compliance among patients who take blood pressure medications. Despite the fact that drugs are readily available, only about one out of four people with high blood pressure has their condition under control. "Many patients are either unable or unwilling to take pills every day for the rest of their lives," noted Dr. Juerg Nussberger, author of the study. "If we could add or substitute a vaccine that would need to be given just every few months, I think we could achieve better control of high blood pressure." The study is focused on a vaccine that targets angiotensin II, a molecule that constricts blood vessels and raises blood pressure. After injections at zero, four and 12 weeks from the start of the study, patients who received the vaccine had a strong antibody response against angiotensin II. Blood pressure changes were evaluated at week 14. The study team reported that antibodies produced by the vaccine seem to function "like a sponge." The sponge empties out during the night when little angiotensin is produced, so it is able to take up all the angiotensin produced early in the morning." The next step in developing the vaccine will be another trial to determine whether a different injection regimen will create a larger antibody response and a greater reduction in blood pressure.



American Heart Association

pep Corner

Low Zinc levels may raise pneumonia risk in the elderly

Low blood levels of zinc may be linked to an increased risk of pneumonia amongst the elderly, suggesting the benefits of supplements for this at risk population, says new research.

"Normal serum zinc concentrations in nursing home elderly are associated with a decreased incidence and duration of pneumonia, a decreased number of new antibiotic prescriptions, and a decrease in the days of antibiotic use," wrote lead author Simin Meydani in the American Journal of Clinical Nutrition.

"Zinc supplementation to maintain normal serum zinc concentrations in the elderly may help to reduce the incidence of pneumonia and associated morbidity."

Zinc is one of the most plentiful trace elements in the body, second only to iron. It mediates many physiological functions and is believed to be essential for maintaining a healthy immune system.

The researchers, from the US Department of Agriculture, Tufts University, and Boston University, investigated the effect of low serum zinc concentrations on the incidence of pneumonia in elderly men and women (average age 84.6) living in nursing homes. The study was part of study to evaluate the effect of vitamin E supplements on respiratory infections.

Over the course of 12 months, the subjects received vitamin E and a supplement containing half of the recommended dietary allowances (RDA) of other essential micronutrients, including zinc.

Meydani and co-workers report that participants with low zinc levels at the end of the study, defined as having levels less than 70 micrograms per decilitre, had increased incidence of pneumonia, longer pneumonia episodes, about 50 per cent more new antibiotic prescriptions, and more days of antibiotic use.

"Our finding of a significantly lower all-cause mortality rate (by 39 percent) in those with normal baseline serum zinc concentrations than in those with low baseline serum zinc concentrations suggests that zinc may play a crucial role in influencing mortality in the elderly," wrote Meydani.

Other studies have suggested that zinc deficiency may be a risk factor for immune deficiency and subsequent infection relapses in the elderly, based on zinc role in membrane integrity and DNA synthesis. The mineral also acts a cofactor to more than 300 enzymes.

"The results from our current study, in addition to these earlier findings, suggest that elderly with low serum zinc concentrations might benefit from zinc supplementation," stated the authors.

"Such a measure has the potential to reduce not only the number of episodes and duration of pneumonia and the number of new antibiotic prescriptions and days of antibiotic use due to pneumonia but also all-cause mortality in the elderly. An adequately powered randomized, double-blind, controlled trial seems to be the likely next step.

Such a study is needed to determine the efficacy of zinc supplementation as a potential low-cost intervention to reduce morbidity and mortality due to pneumonia in this vulnerable population," they concluded.

Reference:
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Role of Zinc in Pregnancy and infertility, Brain functions, Skin healing and protection

Pregnancy and infertility

- Because of zinc's role in generating cells, it is essential for the developing foetus where cells are rapidly dividing.
- Adequate zinc in the pregnant mother's diet also reduces the risk of premature birth and other complications and has been shown to improve neonatal survival.
- There is believed to be a link between zinc deficiency during pregnancy and learning difficulties.
- Research has been undertaken into the possibility of treating male infertility with zinc therapy to increase sperm count and motility.

Brain functions

- Zinc interacts with other chemicals to send messages to the sensory brain centre, enhancing memory and thinking skills.
  In the weeks following a head injury patients tend to have lower zinc levels which, when boosted by zinc supplements, are thought to give improved cognitive function.
- Zinc activates areas of the brain that receive and process information from taste and smell sensors.
  Insufficient zinc has been linked to anorexia, which responds well to zinc replacement treatment.
- Zinc deficiency is often found in mood disorder patients. Zinc sulphate, taken as a supplement, appears effective in reducing fatigue, mood swings and changes in appetite.

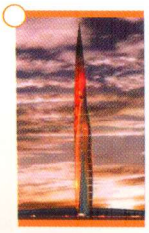
Skin healing and protection

Zinc and zinc compounds are of major importance in skin care. Some of its vital uses are:

- To soothe nappy rash and itching thanks to its astringent and drying properties.
- As a sun-block to protect the skin from the sun's harmful rays.
- As an effective treatment for acne.
- In the relief of cold sore symptoms.
- To aid the healing of wounds, like surgical incisions, burns and other skin irritations. Many adhesive plasters contain zinc oxide for this reason.
- As an anti-inflammatory to relieve the discomfort from sunburn, blisters and gum disease.
- As an insect repellent.
- Helping to protect body tissue from damage by stimulating the transport of Vitamin A from the liver to the skin.
- As bactericides in high quality cosmetics and toiletries.
- To help heal leg ulcers through addition to the diet.

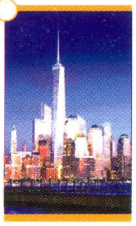
Reference : Galvanizers Association, December 10, 2007

SEVEN SKYSCRAPERS OF THE WORLD !


Shanghai, China (1228 m)


Dubai, UAE (705 m)


Tokyo, Japan (600 m)

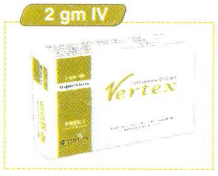

New York, USA (541 m)


Shanghai (514.8 m)


Shanghai (421 m)


Dubai, UAE (321 m)

& the Seven Strengths of



Ceftriaxone BP

Vertex

Unique & Unparalleled