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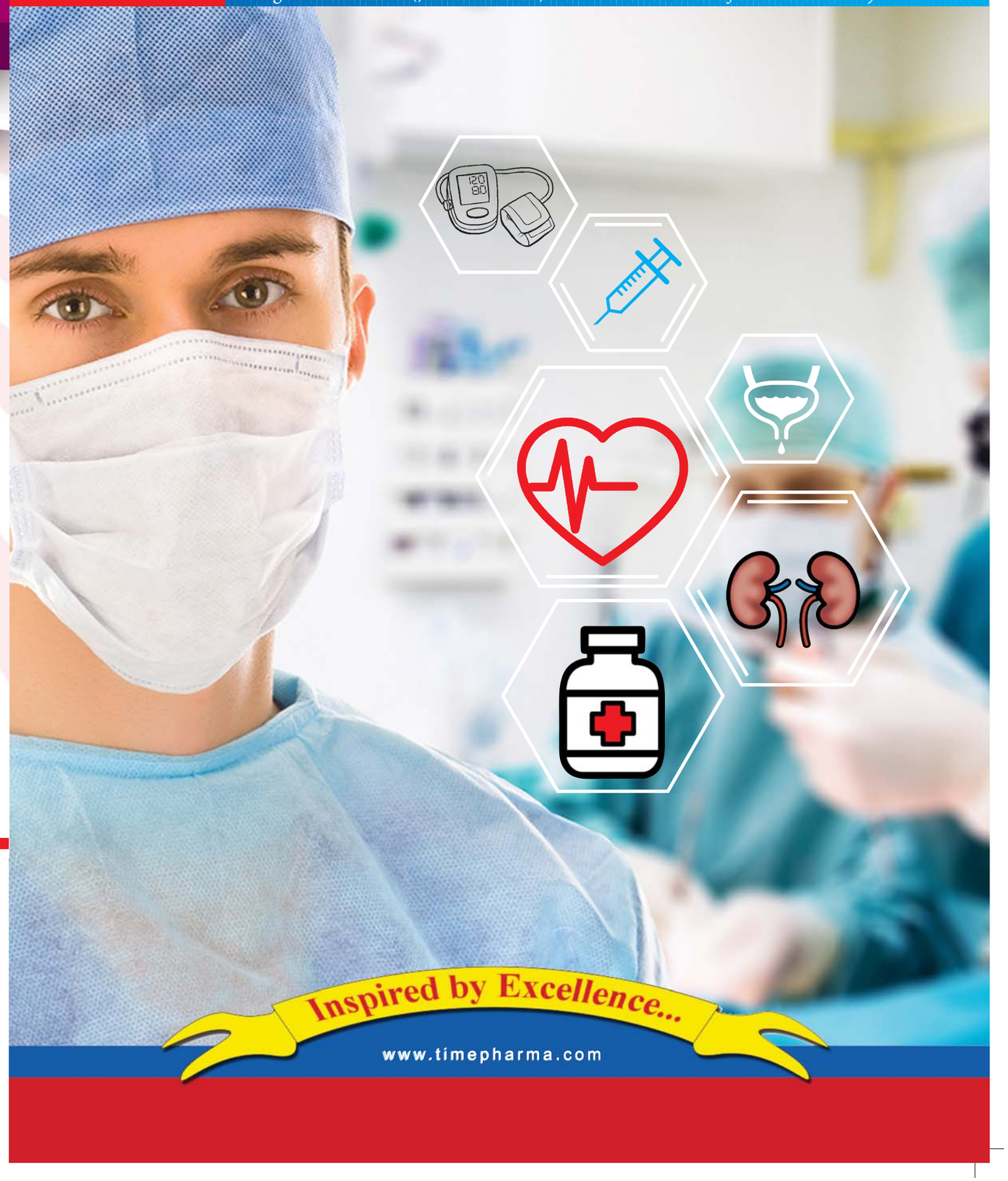

MEDITIME

A Medical Bulletin from TIME Pharmaceuticals (P.) Ltd.

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Message from Patron

19 years of persistent and satisfying services to the national health by delivering best in its class products, **TIME** Pharmaceutical envision to strengthen its infrastructure to cater the advanced technology based products to bear the new challenges in health delivery.

G. Narayan B. Chhetri
Patron/CMD

Message from Editor in Chief

On behalf of whole editorial team, I feel very happy to serve the 20th issue of MEDITIME with celebration of 20th Anniversary of **TIME** Pharmaceuticals. I take this opportunity to thank our valued writers, editors, anonymous reviewers, all of whom have volunteered to contribute to the success of the 20th journey of this quarterly magazine. It is with profound pleasure, humility and anticipation; I hope the upcoming quarterly magazines also provide the ideal forum for exchange of information and new learning between medical fraternities all over Nepal. As a New Year resolution of 2017, editorial team works with best effort to provide the health sector with new findings in medical field, sharing information from expertise in this field.

January 2017 had already knocked on the door along with cold weather. For some, the winter season can bring lots of enjoyment as they can play with snow but for geriatric patients, it can be curse. Mainly the immune system, skin and heart may be at risk. The flu virus is more contagious in winter season as people spend more time inside and in close contact with each other. Dry skin is another common condition which worsens in winter; possiblely low humidity in air causes skin to lose moisture rapidly. People aged 65 and above and with long term diseases like diabetes and kidney diseases are more prone to the flu. Asthma and painful joints are other diseases that affect elderly. Though it is not clear, it is believed that fall in barometric pressure in atmosphere and lack of physical activity might be the cause of joint pain. Beside this, cold weather also raises the risk of heart attack. Cold weather acts as vasoconstrictor, which means it narrows the blood vessel and puts more strains in the heart. So, in winter season we need to be more alert to prevent complications in the geriatric patients.

Lastly, thanking all medical fraternities and supporters, I wish to have continuous support in upcoming issue as well.

And Happy New Year 2017.

Sudarshan Lal Shrestha
Editor in Chief/DMD

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Moments in TIME

Dr. Pukar Thapa
Internal Medicine, Alka Hosp.

Dr. Kalyan Sapkota
Internal Medicine, Bharatpur Hosp.

Dr. Tulika Dube
ENT Specialist, Pokhara

Dr. Rupak Bhandari
MDGP & ENT, BPKISH

Participation in CPHI/PMEC 2016, Mumbai

Participating in Surgery conference 2016

Participating in Cardiac Conference 2016

Celebrating Diabetic Day

Participating in ANMECON 2016

Participating in GASTRO Conference 2016

For stress, superfoods are better than comfort foods

By Jacqueline Howard, CNN

When times get stressful, many of us find solace in traditional "comfort foods," from savory macaroni and cheese to a big bowl of ice cream. Though research suggests that, it's actually not the high-fat and high-sugar comfort foods that do the trick. Rather, it's superfoods.

What to eat to fight stress

Superfoods are items that are found to provide health benefits beyond your basic nutrients, according to the National Institute of Health. "Many of these 'superfoods' also work to boost glutathione in the body: an amino acid in charge of detoxification. So superfoods nourish and detoxify, and in this way, they combat stress," said stress expert Pete Sulack, author of "Unhealthy Anonymous," a book about stress management and overall wellness.

The top superfoods that are recommended to munch on when feeling anxious are kale, broccoli, leafy greens, celery, nuts, oily fish like salmon, fermented foods like kimchi, herbs and spices, and organic berries high in vitamin C. In animal studies, vitamin C fed to rats who were undergoing stress both prevented an increase in cortisol levels and known signs of physical and/or emotional stress like losing body weight. "Animals that didn't receive the vitamin C had three times the level of cortisol in their bodies," Sulack said. Stress can increase levels of the hormone cortisol, which manages stress in the body. "Human studies have been done as well," he said. A small study published in the journal in 2001 suggests that ascorbic acid, or vitamin C, can help in humans.

How do these foods influence our mood?

That's an active topic of research, said Kate Brookie, a PhD candidate studying nutritional psychology at the University of Otago in New Zealand.

"While there are biologically plausible ways that diet can influence our state of mental health, the exact mechanisms of action are still being investigated," she said.

"Whole foods, especially fruit and vegetables, provide your brain with the nutrients necessary for key processes involved in mood and well-being," she said.

For instance, vitamin C is involved in the production of dopamine, a feel-good hormone associated with motivation and drive, Brookie said, adding that B vitamins and carbohydrates are associated with the synthesis of serotonin, a neurotransmitter that plays a role in our daily moods.

"It could be that eating a high-quality, whole-food diet, rich in fruits and vegetables, provides the nutrients for these systems to function more optimally, leading to better mental health," Brookie said.

Meanwhile, there are some other foods that might do the opposite.

Food to avoid when Stressed

Innately as humans, we know that food can relieve stress. That's why we refer to 'comfort foods,' " Sulack said. "The only problem is that most 'comfort foods' like french fries, ice cream macaroni and cheese offer some release of brain chemicals that make us feel good for the moment but in the long run cause the body more stress and the brain more distress."

Foods that may stress the body, he said, are processed foods such as deli meat and foods high in sugar and caffeine, like some energy drinks or sugary sodas. "One of the biggest causes of stress is your blood sugar. When blood sugar is between the glucose levels of 75 to 95 nanograms per deciliter, the body functions well. The more time you spend outside that range, the more your body feels stressed," Sulack said. Excessive caffeine consumption can induce heart palpitations, shaking and difficulty sleeping, all a recipe for triggering the stress response," he added. "It's not just enough to look at the foods you eat but also the ingredients in those foods." Ingredients to limit include sugar, saturated fats and trans fats, refined carbohydrates, casein-containing items, such as processed foods, and the artificial sweetener aspartame, Sulack said.

Reaching Nepal's mothers in time

Women's chances of survival during pregnancy and childbirth have greatly improved in Nepal, Sophie Cousins reports. Standing at a community health post and looking around the valley, Laxmi Tamang, a nurse and public health expert from the Midwifery Society of Nepal, points to the other side of the mountain. "See that, all the way over there? That's all the same district. If a woman is in labour, how on earth will she get here?" The Midwifery Society of Nepal is running an outreach health camp in Nuwakot, 75 km from Nepal's capital of Kathmandu, after much of the district's infrastructure was damaged by the April 25 earthquake last year. But for expectant mothers living in remote parts of the district – where there are few if any roads – accessing this midwifery care, especially in emergencies, is difficult – if not impossible. Between 1990 and 2015, the country reduced its maternal mortality ratio by 71% from 901 deaths per 100000 live births to 258 – just four percentage points short of millennium development goal (MDG) 5: to reduce the maternal mortality ratio by three quarters during that time period. For this achievement, Nepal, which has been recovering from a decade-long civil war between 1996 and 2006, was selected out of 49 least-developed countries by the United Nations in 2010 to receive an award for its leadership, commitment and progress towards the achievement of MDG 5. Over the past decade, more women in Nepal are giving birth in a health facility than at home – another factor that has reduced the risk of postpartum haemorrhage (loss of blood following the birth), which is the leading cause of maternal deaths worldwide. Twenty-five years ago in the hilly regions of Nepal women had to deliver at home and maternal mortality was very high," says Dr. Kiran Regmi, chief specialist at the health ministry. "Now, caesarean sections are available, even in remote areas. There are birthing centres and health posts across the country, where safe delivery is assisted by skilled birth attendants," says Regmi, a former director of the health ministry's family health division.

Bulletin of the World Health Organization 2016;94:318-319

IUDS, implants may be best birth control for women with diabetes

The two most effective hormonal birth control methods for women in general are also excellent options for women with diabetes, according to a new study. Intrauterine devices (IUDs) and contraceptive implants that are placed under the skin, both of which are highly effective, were linked with the lowest risk of blood clots in these higher-risk women. Hormonal contraceptives boost women's risk for clots, which can lead to heart attack and strokes. That's a particular problem for women with diabetes, who are at increased risk for blood clots to begin with. While many contraceptives use a combination of two hormones, estrogen and progestin, the World Health Organization advises that women at increased risk of a blockage caused by a blood clot - known as a thromboembolism - use contraceptives containing only progestin.

Dr. Eleanor Bimla Schwarz of the University of California, Davis in Sacramento and her colleagues analyzed data on 146,080 U.S. women with diabetes, ages 14 to 44. As reported in Diabetes Care, the majority were not using hormonal contraceptive pills or devices during the study. Only 28 percent were using hormonal contraception, and most of those were taking estrogen-containing pills. Only 4 percent were using progestin-only contraception. During the study, the researchers identified 3,012 so-called thrombotic events. Blood clots were most common among women using estrogen-containing contraceptive patches, with 16 events each year for every 1,000 women. Rates of blood clots were lowest for women using progestin-only IUDs and under-the-skin (subdermal) contraceptives. There were an average of only 3 events each year for every 1,000 women using the IUDs and less than 1 event per year among women using the subdermal implant. Dr. Natalie Whaley, an obstetrician/ gynecologist and family planning provider at the University of Rochester Medical Center in New York, said the findings confirm earlier research about women's risk for thromboembolism with diabetes.

"Spinal Cord Injury Following Thoracic and Thoracoabdominal Aortic Repairs"

Dr. Nirmal Panthee
Cardiac Surgeon
SGNHC, Bansbari

Introduction

Spinal cord injury (SCI) remains a devastating complication after Thoracobdominal Aortic Aneurysm (TAAA) repairs. Its incidence ranges from 1% to 32%; 2.3% to 32% with open surgery, and 1% to 19% with Thoracic Endovascular Aneurysm Repair (TEVAR). This large difference among series is due to varying proportions of high-risk patients, use of different surgical adjuncts for spinal cord protection, and selection bias, which is the rule in current clinical practice. Despite so many years of experience, we have not been able to completely eliminate these devastating complications, although we have reduced the incidence by using various adjuncts and with better understanding of cord perfusion physiology.

Method

We carried out a PubMEd search of publications listed upto 2013, using the Medical Subject Headings : arotic aneurysm/surgery" and "spinal cord ischemia"; "arotic aneurysm, thoracic/surgery" and "spinal cord ischemia/cerebrospinal fluid"; "aortic aneurysm/surgery" and "paraplegia." By excluding review articles, case reports, letters to the editor, commentaries, editorials, guidelines, author replies, surgical techniques, original articles with acute traumatic rupture of the aortic isthmus, articles in languages other than English, reports of animal experiments, and those without the full text available through the medical library system of the University of Tokyo, we analyzed 190 original articles with a patient pool of 38,491. Spinal cord injury has been reported after repair of acute traumatic aortic isthmus rupture, but these patients are usually young, often have associated polytrauma, and lack the atherosclerotic risk factors associated with TAAA; therefore, we excluded them from the analysis. We divided the publications into 3 broad groups based on year of publication: before 2000, between 2001 & 2007, & between 2008 & 2013.

Data were analyzed using SPSS version 20. One way analysis of variance was utilized for statistical tests, with a p value <0.05 being considered statistically significant.

Discussion

Spinal cord injury remains a devastating complication after TAAA repair. Its incidence is reported to range from 1 to 32%. Despite various adjuncts and surgical techniques, complete elimination of this complication is virtually impossible. Our analysis of the data of over 38,000 patients showed the overall incidence of SCI to be 7.1 ± 6.1 %. Because this result is an average of a varying pool of patients in different series, the actual incidence of SCI was different in each patient pool (0-32)%. An important finding demonstrated by this analysis is the decreasing trend of SCI over the last few years. The extend of disease almost remained the same in the 3 time periods, except for the higher proportion of patients with type I TAAA before 2000. Nevertheless, the incidence of SCI decreased significantly from 9.0 ± 6.7% to 5.9%. Use of adjuncts such as distal perfusion, hypothermia, CSF drainage, epidural cooling, naloxone, and MEP and SSEP monitoring has contributed to reducing SCI over recent years. Significantly, more patients received distal perfusion after 2000, and although it did not reach statistical significance, a clear trend of increased use of CSF drainage was found after 2000. Neuromonitoring with MEP (Motor-Evoked Potentials) and SSEP (Somatosensory-Evoked Potentials), and preoperative artery of Adamkiewicz identification with magnetic resonance angiography and computed tomography-angiography were also increasingly utilized after 2000. ICA reimplantation showed an increasing trend between 2001 and 2007 compared to before 2000, and every effort was made to reimplant each pair of ICA. However, after 2007, surgeon were concerned about the longer operative time needed to reimplant ICA, and they started to sacrifice intercostals that were not crucial to spinal circulation by monitoring MEP. Monitoring MEP helped surgeons to identify crucial ICA to reimplant, thus decreasing the total aortic clamp time. With the knowledge of the above mentioned predictors of paraplegia, a large number of strategies have been utilized in various centers to combat SCI following TAAA surgery. Because of postoperative paraplegia, careful preoperative planning and use of multiple adjuncts can reduce SCI in these high-risk patients.

Distal Perfusion is an important strategy to reduce postoperative SCI. The simple clamp-and-sew technique results in more SCI. However, if combined with selective epidural cooling to a CSF temperature of 26.4°C, the simple clamp-and-sew technique also offers spinal cord protection. Distal perfusion has routinely been included in TAAA repairs in recent years. Several authors have shown that aortic clamp time is a predictor of post-operative SCI. Biglioli and collegues, reported that in descending thoracic aortic aneurysm repair, spinal cord perfusion can be adequately maintained without reimplantation of segmental vessels or use of atrial-distal bypass when the arotic crossclamp time is short ($<$15-20 min). Arotic crossclamp time $>$ 30 minutes was associated with SCI and $>$ 60 min was associated with an increased incidence of SCI. Use of left heart bypass has been shown to lower the risk of SCI, mainly because it unloads the proximal circulation during aortic occlusion while maintaining adequate distal perfusion allowing a longer time for all distal intercostal reimplantation. However, Coselli & Collegues found that left heart bypass was not a predictor of SCI. Use of cardiopulmonary bypass (partial or fully) has also been shown to lower the risk of SCI .Use of shunts (Gott Shunt) significantly reduced SCI during descending aortic surgery.

Hypothermia has always been regarded as an important adjunct during any cardiac surgery procedure. Most authors routinely used a moderate degree of hypothermia to perform thoracoabdominal arotic surgeries. Failure to cool actively with bypass was described as a predictor of paraplegia by Svensson and Collegues. Hypothermia and circulatory arrest offers excellent protection against SCI during aortic aneurysm repair. When the arch is involved along with the descending thoracic aorta or thoracoabdominal aorta, institution of deep hypothermia

circulatory arrest is preferable. However, even without arch involvement, the use of deep hypothermic circulatory arrest resulted in a decreased incidence of SCI.

Neuromonitoring has been extensively utilized during TAAA repairs. Use of MEP and SSEP allows surgeons to perform staged clamping and identify critical ICA supplying the spinal cord. The combination of Neuromonitoring with ICA reimplantation, CSF drainage, and distal perfusion has yielded consistently good results with respect to SCI.

TEVAR has recently been increasingly utilized in the management of thoracic aortic aneurysms. Because SCI is also associated with TEVAR, we included TEVAR along with open repairs during our analysis. Our review showed that the incidence of SCI ranges from 2.3% to 32% in open surgical repair and from 1% to 19% in endovascular procedures. This is mostly because of proper patient selection in the TEVAR group, whereas high-risk patients underwent open surgical repair. Furthermore, when a larger extent of the thoracic aorta was planned for coverage, adjuncts such as CSF drainage, MEP/SSEP monitoring, and maintenance of high normal blood pressures have been instituted even with TEVAR. However, a few studies have shown a similar incidence of SCI following TEVAR and open surgery. During TEVAR, branched or fenestrated grafts have been used to prevent SCI, with good results.

Use of fewer stents also results in a reduced incidence of postoperative SCI. Maldonado and colleagues showed a paraplegia rate of only 3.7% with the use of a single stent vs. 10% with 53 stents. Coverage of the left subclavian artery without revascularization during TEVAR appeared to increase SCI in some series, probably due to the presence of collateral circulation to the spinal cord from the subclavian artery. However, other studies have refuted this finding. Maldonado and colleagues showed that left subclavian artery coverage does not appear to result in an increased incidence of SCI or cerebrovascular accidents when a strategy of selective revascularization is adopted. They also showed that left subclavian artery revascularization was not protective against SCI. Holt and colleagues argued that aneurysms involving the aortic arch vessels can be effectively treated by staged endovascular surgical hybrid procedures, with good outcomes that can be further improved through prior revascularization of the left subclavian artery. Implications for management of the left subclavian artery to prevent SCI following TEVAR thus still remain controversial.

With better understanding of the risk factors associated with postoperative SCI, combinations of modalities have been utilized by various authors. Patel and colleagues reported a 4.5% incidence of SCI after combining a neuroprotective cocktail (intravenous methylprednisolone 1g, phenobarbital 1g, and mannitol 25g) with deep hypothermic circulatory arrest at 20°C, ICA reconstruction, and CSF drainage. Intravenous steroid (methylprednisolone 30mg.kg^{-1}) with mannitol (12.5g) and thiopental (32mg.kg^{-1}) was utilized by Acher and colleagues. Because of its ability to reduce spinal cord metabolism, thiopental is administered to maintain burst suppression on the electroencephalogram immediately before and during aortic occlusion.Combining CSF drainage with a continuous intravenous infusion of naloxone at 1μg.kg^{-1}.h^{-1} started before induction and continued for 48h after surgery resulted in a markedly low incidence of SCI of 1.6% vs. 22.4% in a control group. Combining CSF drainage with intrathecal papaverine 30mg introduced 20min before aortic crossclamping resulted in reduced SCI (11.8% vs. 43.8% in a control group). Tabayashi and colleagues showed only a 3.9% incidence of SCI with the use of epidural cooling to 23.3°C started 30min before aortic crossclamping along with distal perfusion, CSF drainage, and ICA reconstruction. Preventing SCI after TAAA surgery is a multidisciplinary approach. By identifying patients at high risk of SCI, a combination of various adjuncts should be considered. Avoiding hypotension (intraoperative and early postoperative) is a simple but crucial step. Combined use of distal perfusion, CSF drainage, critical intercostal artery reimplantation, and early detection with prompt intervention for cord ischemia by monitoring MEP has shown promising results in preventing SCI. Also, pharmacological intervention by the use of naloxone and avoidance of morphine may be another strategy. The limitations of this study include the fact that we analyzed only data from papers available in PubMed, thus a large number of papers from other databases including EMBASE were not considered. Although we truly believe that the incidence of SCI following TAAA repairs is decreasing, there remains the possibility of underreporting of data with worse results in journals yet to be listed in PubMed.

We performed a generalized analysis of the data we gathered, and analyzed surgical repairs and endovascular repairs together in a heterogeneous sample. Although we know that type II TAAA has the highest risk of paraplegia, we were not able to review the risk of SCI based on the extent of disease because the majority of studies reported an overall incidence of SCI rather than according to the extent of disease. We included only those studies that clearly mentioned the numerical values of percentages in their analysis. So, for each variable, the number of studies utilized to calculate the means was different.

We concluded that spinal cord injury after TAAA repair poses a real challenge to cardiovascular surgeons. However, over recent years, with evolving surgical strategies, identification of predictors of SCI, and use of various adjuncts, the incidence of SCI after thoracic or thoracoabdominal aortic repair is on the decline. Embracing a multimodality approach offers good insight to combat this grave complication.

(This is an article adopted from Asian Cardiovascular & Thoracic Annals, 2015. Vol 23(2) 235-246 with permission of author)

स्तन पुनर्निर्माण
(Breast Reconstruction)

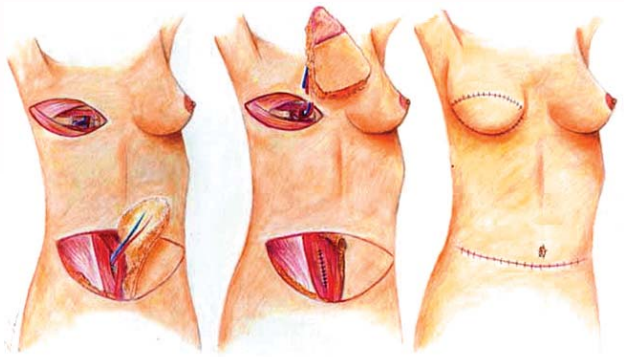
डा. अमर बज्राचार्य
स्तन पुनर्निर्माण विशेषज्ञ
काठमाडौं मेडिकल कलेज

परापुर्वकाल देखीनै नारी वा महिलाहरुको सुन्दरताको वर्णन गर्दाहोस् वा नारी आफै परीपूर्णताको एक हिसाबले स्तन एक आकर्षक अंगको रुपमा लिइन्छ । यसले नारीको शारिरिक रुपमा मात्र नभई मानसिक रुपमा पनि एउटा महत्वपूर्ण भूमिका खेलेको हुन्छ । तसर्थ हरेक शारिरिक बिकास र परिवर्तनमा नारीहरुले यसलाई एकदम नजिकबाट नियाली राखेका हुन्छन् ।

पश्चिमी बिकसित मुलुकहरुमा नारीहरु, पुरुषहरुको तुलनामा अधिकार तथा समानताको हिसाबले बराबर छन् । तर हाम्रो जस्तो कम बिकसित मुलुकमा अज्ञानताले गर्दा महिलाहरु आफ्नो शरीरको समस्या बारे खुलस्थ रुपमा प्रस्तुत हुन सक्ने अवस्था देखिएको छैन । तसर्थ स्तन क्यान्सर जनचेतनाको कमिले गर्दा ढिलो (last stage) अवस्थामा देखिँदै आएको छ ।

स्तन पुनर्निर्माण (Breast Reconstruction)

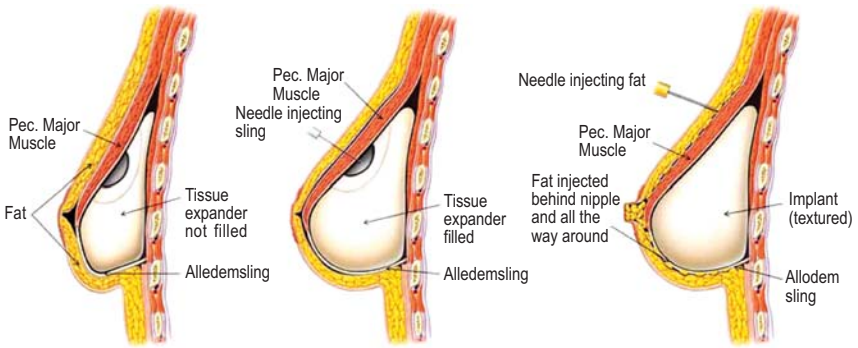
स्तन पुनर्निर्माण भन्नाले स्तन क्यान्सरबाट अप्रेशन पश्चात स्तन निकालिएको अवस्थामा शरीरको कुनै भाग जस्तै पछाडिको भागको मासु तथा बोसो (LD flap), पेटको नाइटो मुनिको मासु तथा बोसो (TRAM flap, Diep flap) बाट स्तन पुनर्निर्माण (Breast Reconstruction) गरिन्छ । यसैगरी आजकल बिज्ञान र प्रबिधिको बिकासले गर्दा silicon बाट निर्मित बिभिन्न आकार प्रकारको Breast implant हरु पाइन्छ ।



तसर्थ स्तन क्यान्सर पश्चात महिलाहरुमा एक प्रकारको अपूर्णतालाई स्तन पुनर्निर्माणद्वारा एक प्रकारको मनोबैज्ञानिक हिसाबले पनि आत्मसन्तुष्टिको अनुभुति प्राप्त गर्दछ । बिभिन्न अनुसन्धानबाट स्तन क्यान्सरका महिलाहरुमा स्तन पुनर्निर्माणले survival rate (रोगपश्चातको आयु) को पनि दर बढेको देखिन्छ । आजकल बिज्ञान र प्रबिधिको बिकासले धेरै बिधामा फड्को मारेको छ । त्यही क्रममा क्यान्सर रोगको उपचार विधिमा पनि उल्ले खनिय उपलब्धि अपनाउनु पर्दछ ।

हरेक रोगको पहिचानको लागि त्यस रोग सम्बन्धि जनचेतनाको आवश्यकता पर्दछ । बिकसित मुलुकको दाजोमा हाम्रो जस्तो कम बिकसित मुलुकमा जनचेतनाको कमी पुर्ति गर्न हरेक क्षेत्र निजी, तथा नेपाल सरकारबाट पर्याप्त मात्रमा जनचेतना मुलक कार्यक्रमहरुको आवश्यकता देखिन्छ ।

Breast Reconstruction Stage



त्यसमध्ये पनि संचार माध्यम तथा पत्रपत्रिकाको उल्लेखनिय योगदान रहन्छ । हरेक महिलाले आफ्नो स्तनमा कुनै नौलो फरक अनुभुति जस्तै आकारमा फरक, स्तनमा घाऊ, स्तनमा गाठागुठि, काखीमा गाठागुठि, मुन्टोबाट पिप तथा रगत आउने आदि इत्यादी भएको खण्डमा चिकित्सकको परामर्श लिइहाल्ने गुर्न पर्दछ । यसको लागि एउटा सजिलो उपाय भनेको हरेक महिलाले स्नान गर्दा आफ्नो शरीरको हरेक अंगहरुलाई राम्रो सँग नियाल्नु पर्दछ र त्यसमा पनि स्तनलाई आफ्नो हातको स्पर्शको माध्यमले छाम्नु पर्दछ, यसबाट साजिलै गाठागुठि पत्ता लाग्ने गर्दछ ।

हरेक महिलाले आफ्नो स्तनलाई महिनाको एक पल्ट आफैद्वारा जाँच गरेको खण्डमा समयमानै गाठागुठिहरु पत्ता लाग्ने गर्दछ । Self Breast Examination बारे बेलाबेलामा पत्रपत्रिकामा लेखहरु पढ्न पाइन्छ ।

स्तन पुनर्निर्माण भन्नाले खाली स्तन क्यान्सर भएका महिलाहरुले मात्र गर्ने बिधि भन्ने बुझाईराख्नु पनि एक प्रकारको गलत बुझाई हुनजान्छ । ठुलो वा सानो आकारको स्तनलाई पुनर्निर्माण बाट ठुलो वा सानो आफ्नो ईच्छा अनुसार बनाउने सकिन्छ । यो प्रकृयालाई Breast reduction वा Breast agumentation भनिन्छ ।

स्तन ठुलोलाई सानो बनाउने प्रबिधिलाई reduction mammoplasty भनिन्छ भने सानो स्तनलाई ठुलो बनाउने प्रबिधिलाई agumentation mammoplasty भन्ने गरिन्छ । ठूलो बनाउने क्रममा Breast silicon implant हरुको प्रयोग हुन्छ । आजकल बजारमा बिभिन्न प्रकारका आकर्षक implant हरु पाइन्छ । जसको प्रयोगले महिलाहरुको सुन्दरतामा ठुलो परिवर्तन आएको छ । तसर्थ आजकल बिज्ञान तथा प्रबिधिको बिकासले गर्दा नेपालमा पनि बिस्तारै महिलाहरुमा जनचेतना र सुचना प्रवाहले गर्दा स्तन पुनर्निर्माण सम्बन्धि आवश्यकता महसुस हुने अवस्था सिर्जना हुने आशा छ । बिदेशमा हासिल गरेको ज्ञान तथा सीप अवश्य पनि एकदिन नेपालमा काम लाग्ने अवस्था आउने छ । यही नै एक प्रकारको नारीहरुको लागि सुन्दरताको उपहार हुनेछ ।

मृगौंलाको पत्थरीबारे जान्नै पर्ने कुराहरू

डा. कुशल कार्की
क. मूत्र विशेषज्ञ
सुमेरु अस्पताल

पत्थरी, पत्थर या ढुङ्गा मानवजातिलाई आदिमकाल देखि लाग्ने रोग हो । मृगौंलामा हुने ढुङ्गाको अवशेष ४,५०० BC पहिला Egyptian Mummy मा पाइएको प्रमाण भेट्न सकिन्छ । यसपछिका मानव सभ्यताहरुमा पनि यस रोगको वर्णन पाईन्छ । यो रोग ५-१०% मानिसहरुलाई लाग्न सक्छ । सामान्य तया यो रोग महिला भन्दा पुरुषलाई हुने गरेपनि सबै उमेर समूहका मानिसलाई मृगौंलाको पत्थरी हुन सक्छ ।

किन हुन्छ मानिसलाई पत्थरी ?

१. वातावरण र भूगोल
   विशेषगरी गर्मी ठाउँमा यो विमारी हुने गर्छ, दक्षिण एशिया तथा खाडी मुलुकमा धेरै हुन्छ । पश्चिम मुलुकको जीवन शैली, junk food, धेरै रातो मासुको सेवन, बोसो, मोटोपन, मधुमेह अनि cholesterol ले गर्दा यसको प्रकोप दिनानुदिन बढ्दो छ ।
२. पिसाबको संक्रमण: महिलामा ज्यादा
३. कम पानी पिउने र धेरै पसिना जाने काम
४. वंशाणुगत
५. मृगौंलाको अप्राकृतिक बनोट: पिसाब मृगौंलामा जमेर बस्ने

केही लक्षणहरु

१. कोखा तथा तल्लो पेट दुख्ने
२. ज्वरो आउने
३. पिसाब बन्द हुने

इमरजेंन्सीमा जानु पर्ने अवस्था के हुन सक्छ ?

१. पिसाब आउन बन्द भएमा या साविक भन्दा कम भएमा
२. काम ज्वरो आएमा
३. दुखाई अत्याधिक भएमा

कसरी यो रोग पत्ता लगाउने ?

१. सही चिकित्सककोमा जाने, urologist (मूत्र विशेषज्ञ)कोमा जाने
२. विरामीको लक्षण अनि शरीर जाँचको आधारमा अन्य जाँच गर्नुपर्छ जस्तै पिसाबको जाँच,
   - मृगौला/पिसाब थैलीको X-ray (X-ray KUB), अल्ट्रासाउंड (भिडियो एक्सरे)
   - IVP (नशाबाट दवाई दिएर गरिने एक्सरे)
   - CT Scan (लगभग १००% accuracy को साथ CT scan ले पत्थर भएको नभएको बताउन सक्छ ।)

ढुङ्गा एक, जात अनेक

पत्थरीको रसायनिक बनोटको आधारमा ढुङ्गालाई २५ भन्दा धेरै जातमा बाढिएको पाइन्छ । तर नेपालीहरुमा हुने पत्थरीमा Calcium Oxalate 70-80%, Struvite 10-15%, Uric Acid 5-10% ढुङ्गा पाइन्छ ।

कसरी हुन्छ पत्थरीको उपचार ?

सबै पत्थरीको उपचार गर्नुपर्छ भन्ने छैन । पत्थरीको किसिम, आकार, मृगौंलाको अवस्था र बिरामीको पेशाको आधारमा चिकित्सकले निर्णय गर्दछन् । ढुङ्गा रहेको भाग (मृगौंला, नली, पिसाब थैली) ढुङ्गाको सारोपना, आवश्यक उपकरण, जन शक्ति, बिरामीको खर्च गर्न सक्ने अवस्था हरेर चिकित्सकले निर्णय गर्दछन् ।

उपायहरु

१. औषधीको सेवनबाट
२. चिरफार गरेर गर्ने (परम्परागत तरीका)
३. मृगौंलालाई प्वाल पारेर निकाल्ने (PCNL)
४. पिसाब आउने बाटोबाट दुरबीन छिराएर गरिने (URS)
५. अल्ट्रासोनिक तरंगबाट (ESWL)
६. RIRS (पिसाबको नलीबाट दुरबीन मृगौंलामा पठाई गरिने)

औषधी खाएर पत्थर पग्लन/निक्लीन सक्छ ?

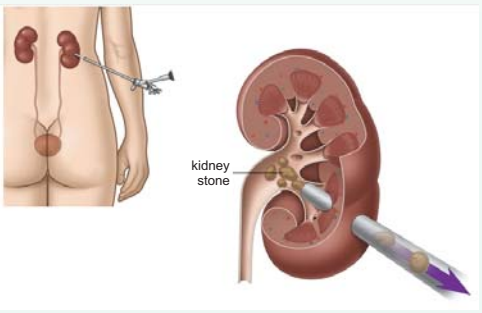
Allopathy औषधीले पत्थरको केहि जात मात्र (Uric acid, Cysteine stone) पगाल्न सक्छ, त्यो पनि सानो आकारको । अनि सधै यो तरीका सफल हुन सक्छ भन्ने छैन । ठुला पत्थर या अरु जातको पत्थर औषधी खाएर जान्छ भन्नुमा वैज्ञानिक आधार छैन ।

फलानो ढुङ्गा औषधी खाएर पिसाबबाट गयो रे ?

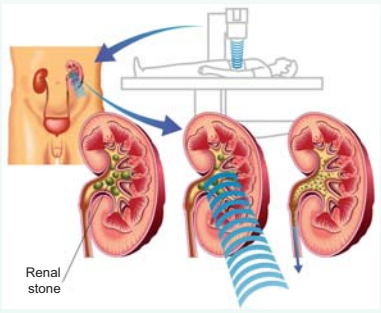
सानो आकारको ढुङ्गा (मृगौंलाको) र मुत्रनली (Ureter) को ढुङ्गा धेरै पानी र Ureter को मुख खोल्ने औषधी खाँदा जान सक्छ ।

पत्थरी हुँदा कुर्न सकिन्छ ?

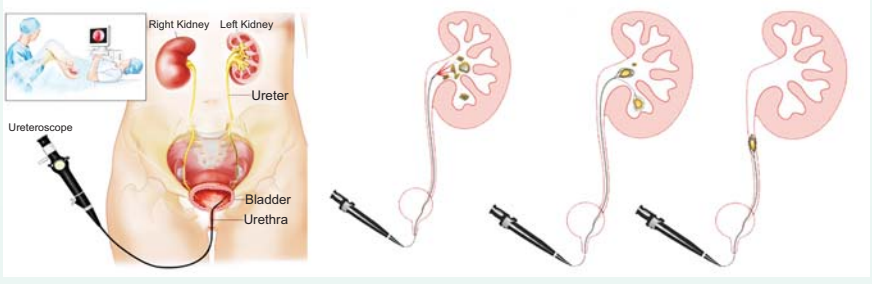
ढुङ्गाको आकार र यसले मृगौंलालाई गरेको असरको आधारमा चिकित्सकले निर्णय गर्छन । यदि मृगौंला सुन्निएको छ भने बढी मा ४-६ हप्ता सम्म कुर्न सकिन्छ तर अरु धेरै तथ्य बिचार गर्नुपर्ने हुन्छ ।



Percutaneous Nephrolithotomy (PCNL)



Extracorporeal Shock Wave Lithotripsy



Retrograde intratenal surgery

How to prevent KIDNEY STONES


Drink enough water to keep urine diluted

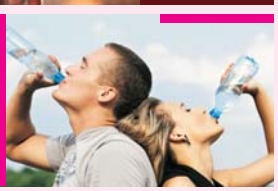
Take fruits that prevent stone formation like lemon and other citrus fruits


Take fruits rich in water soluble fiber- apple, watermelon, sugarcane

Limit salt intake to reduce sodium level


Avoid carbonated drinks and excess caffeine

Limit oxalate rich foods like dark chocolate, spinach, beetroot, rhubarb, tomato, eggplant, cauliflower



Limit red meat consumption

Need of New Thoughts: Pharmaceutical Technology Transfer

Background

It is evident that the entry of private sector pharmaceutical producers after 1990s changed scenario in Nepal and has changed the face of the domestic drug market which was once overwhelmingly dominated by foreign products. According to a study carried out by South Asia Watch on Trade Economics and Environment (SAWTEE), the share of domestic companies in the country's pharmaceutical market was only about 30 percent in 2005. But the scene has changed remarkably today and according to industry insiders, domestic companies have gone up to an impressive share of 45 percent.

The most sensitive part of pharmaceutical product is quality, efficacy and integrity. Major breakthrough is the implementation of WHO GMP by Nepali Pharmaceuticals which has been accorded to quite a number of pharmaceutical producers of Nepal. The march of all producers is focused to the quality pharmaceutical products which can assure and build the trust of all the stakes of healthcare system of Nepal. As the various phases of development of pharmaceuticals are concerned in Nepal, Research and Development has always been the least priority sector. It could be because of the scale of investment desired by it or could be the non availability of manpower and infrastructure. Though the pharmaceutical industries contribution in the GDP has grown tremendously in the last years, similar is the condition with the investment in pharmaceuticals industries which has reached nearly NRs 20 billion.

One of the basics of market mix is the product. The ranges and the portfolios of products are the key for building the market strategy. Once there is strength in the portfolios by encompassing the current demand analysis,the company can cater all the ranges to the market. The fact that all the dosage forms are not technically possible to manufacture in Nepal is because of the lack of technical know how, which has always been a constraint in the development of our pharmaceutical products. Where there are much advanced technologies adapted for the manufacturing of the pharmaceuticals in different parts of the world, the need of new thoughts to grasp and adapt such technologies in Nepal can bring a massive change in the pharmaceutical business in Nepal. In this aspect pharmaceutical Technology Transfer can be a key tool in transferring the know how to nepali pharmaceutical fraternity.

Technology Transfer

Technology Transfer is the process of transferring (disseminating) technology from the places and in groups of its origination to wider distribution among more people and places. It occurs along various axes: among universities, from universities to businesses, from large businesses to smaller ones, from governments to businesses, across borders, both formally and informally, and both openly and surreptitiously. Often it occurs by concerted effort to share skills, knowledge, technologies, methods of manufacturing, samples of manufacturing, and facilities among governments or universities and other institutions to ensure that scientific and technological developments are accessible to a wider range of users who can then further develop and exploit the technology into new products, processes, applications, materials, or services. It is closely related to (and may arguably be considered a subset of) knowledge transfer. Horizontal transfer is the movement of technologies from one area to another. At present Transfer of Technology (TOT) is primarily horizontal. Vertical transfer occurs when technologies are moved from applied research centers to research and development departments.

In the pharmaceutical industry, "technology transfer" refers to the processes that are needed for successful progress from drug discovery to product development to clinical trials to full-scale commercialization or it is the process by which a developer of technology makes its technology available to commercial partner that will exploit the technology.

Pharmaceutical Technology Transfer in Nepali context can be executed with the identification of 'developer of pharmaceutical technology' which can be a foreign partner with defined scope of pharmaceutical technology to make available to exploit for the commercial purpose to nepali commercial partner. Regulatory consensus and modalities also play a vital role in the effective implementation of technology transfer.

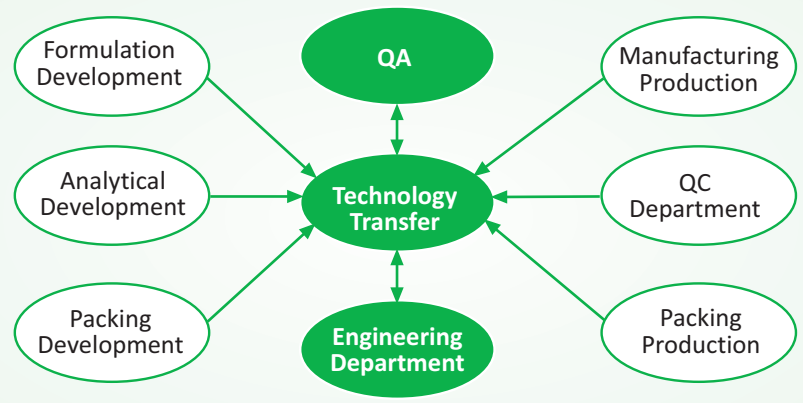
Ashesh Bhandary
Factory Operation Director
TIME Pharmaceuticals (P.) Ltd

Various stages of formulation development science are to be taken during technology transfer which are:

1. Preformulation studies.
2. Bench scale - (1/1000th of X)
3. Lab scale – (1/100th of X)
4. Scale up- (1/10th of X)
5. Commercial (X)

Where X is the final commercial scale batch size.

Technology transfer is both integral & critical to the drug discovery & development process for new medicinal products. The decision to transfer products between manufacturing sites is frequently driven by economics. Key stages of the process include data collection, data review, regulatory impact with particular emphasis on any change approvals, analytical validation, pilot or full-scale process batch, stability studies etc. The process has to be carried in a very coordinated and synchronized relation with the functional departments like Quality Assurance, Engineering, Quality Control, Research & Development and Production.



Typical technology transfer flow chart

Technology Transfer Team:

A technology transfer team should be formed as mentioned in the table below with defined responsibilities.

The process of technology transfer is considered to be completed after successful completion of three validation batches by exhibition batches of the manufacturing process by R&D personnel to production personnel. Ensure that the development team reliably transfer all relevant quality, technical information to the receiving site such that the process must operate consistently and the critical process parameters are well defined and understood by the production personnel.

Technology Transfer Team	Responsibilities
Process Technologist (From Donor)	a. Central focus for transfer activities. b. Collates documentation from donor site c. Performs initial assessment of transferred project for Feasibility, Compatibility with site capabilities and Establishes resource requirements.
QA Representative	a. Reviews documentation to determine compliance with marketing authorization (DDA). b. Reviews analytical methods with QC to determine capability, equipment training requirements. c. Initiates conversion of donor site documentation into local systems or format. d. Initiates or confirms regulatory requirements, e.g., change to manufacturing license; variations to national guidelines if process changes needed, etc.
Production Representative	a. Reviews process instructions (with process technologist) to confirm capacity and capability. b. Considers any safety implications, e.g., solvents; toxic; sanitizing materials. c. Considers impact on local standard operating procedures (SOPs). d. Considers training requirements of supervisors or operators.
Engineering Representative	a. Reviews (with production representative) equipment requirement. b. Initiates required engineering modifications, change or part purchase. c. Reviews preventative maintenance and calibration impact, e.g., use of more aggressive ingredients; more temperature sensitive process, and modifies accordingly.
QA Representative	a. Reviews analytical requirement. b. Availability with instruments. c. Responsible for analytical method transfer for drug substance and drug product.

Conclusion:

Technical up gradation of the Nepali Pharmaceutical industries with appropriate technology transfer is important to upgrade the quality of design to ensure stable and high quality of the pharmaceutical products . The technology transfer does not mean one-time actions taken by the transferring party toward the transferred party, but means continuous information exchange between the both parties to maintain the manufacturing pharmaceutical products of consistent quality.

References:

1. *Analytical Procedures Technology Transfer. ISPE Draft Guidelines. International Society of Pharmaceutical Engineers, ISPE European Office, 7 Avenue des Gaulois, 1040 Brussels, Belgium.*
2. *Draft Guidelines for Validation of Analytical Procedures. International Committee for Harmonization (ICH).*
3. *Guideline for Technology Transfer (Draft), Cited 2009 December 12. Available from:URL: nihs.go.jp/drug/GMP/04BDH0149-1post.pdf*
4. *Technology Transfer from R & D to production, Cited 2010 February 6. Available from URL: bioqc.org/workshopdata/1Technology.pdf*
5. *Singh Amanjeet, Aggarwal Geeta. Technology Transfer In Pharmaceutical Industry: A Discussion. International Journal of Pharma and Bio Sciences. July-September 2009; 1, Issue-3.*
6. *YUE Feifei and YUE Yingming. Research on Technology Transfer in the Pharmaceutical Industry. Available from: 2010cygchy01 a3.pdf*

20th Anniversary Celebration

Puja at Factory

Honouring staff who worked for more than 15 years

Training at factory

Inauguration of one-horned rhinoceros statue

Futsal Competition among health care professionals of Naraynagarh

Breaking the pot game

Female LUTS and Alpha Blockers

Dr Amit Kumar Shah
Consultant Urologist
B and C Teaching Hospital
Birtamode, Jhapa

The alpha-blockers has been the keystone for the medical management for men with lower urinary tract symptoms (LUTS) and benign enlargement of prostate (BEP) but still its with unknown data for supporting the use of alpha-blockers in women with voiding dysfunction or the female LUTS (FLUTS). Recently few urologists are now advocating for alpha-blockers for women with lower urinary tract symptoms associated with or without bladder outlet obstruction (BOO) or underactive detrusor muscle. Questions continues for the advocacy.

Overactive Bladder (OAB) is the most common term used in clinical medicine to describe a complex of LUTS[1]. OAB which is presumed to be due to involuntary contractions of detrusor muscle during filling phase, consists of nocturia, frequency and urge incontinence. Lifestyle modification, behaviour therapy, pelvic floor muscles exercise with bladder training and the drugs muscarinic receptor antagonists remain integral in management of OAB in females as first line treatment[2]. But, these drugs are associated with anticholinergic side effects as dry mouth, somnolence, constipation, blurred vision and thus the compliance can be considered poor[3].

Currently, alpha-adrenergic receptor antagonists are used for men with LUTS. Treatment benefits alpha-adrenergic receptor antagonists occur mainly through reducing smooth muscle tone in prostate and bladder neck and decreasing bladder outlet resistance.

The α_{1D} alpha-adrenergic receptor predominates in the female detrusor and the α_{1A} alpha-adrenergic receptor is expressed at higher levels than other α_1 alpha-adrenergic receptor subtypes in the female urethra (including the bladder neck). Therefore, the efficacy of α_1 adrenoceptor antagonists for the treatment of FLUTS may be explained by the targeting of two possible mechanisms. The first is dysfunction of the bladder neck and urethra, causing functional outlet obstruction and secondary detrusor overactivity, which is similar to bladder outlet obstruction in men with BPH. The second possibility is increased α_{1AR} activity in the detrusor, causing frequency and urgency[4].

In a study of terazosin therapy for FLUTS, 100 women with LUTS and IPSS=8 were treated with terazosin or a placebo. The response rate was found to be 80% among the terazosin treated patients vs. 55% in placebo group ($p<0.02$). But improvement was only in frequency and straining items in IPSS[5]. A study with **alfuzosin**, symptoms subjectively improved, and patients' satisfaction significantly increased in 64% of the patients (16 out of 25). Most urodynamic parameters were also significantly improved after treatment with **alfuzosin. Alfuzosin** significantly improved urodynamic parameters and alleviated bother score in almost two thirds of patients and can be an effective first-line treatment in FLUTS[6].

Among the alpha-blockers **Alfazosin** is associated with minimal side effects. Many studies these days are being conducted using terazosin and dexazosin but these drugs are associated with orthostatic hypotension. So alpha blocker, **alfazosin** can be preferred for FLUTS.

References

1. *Abrams P, Cardozo L, Fall M, et al: The standardisation of terminology of lower urinary tract function: Report from the standardisation subcommittee of the International Continence Society. Neurourol Urodyn 2002; 21:167-178*
2. *Andersson KE: The overactive bladder. Pharmacologic basis of drug treatment. Urology 1997; 50(Suppl 6A):74-89.*
3. *Hampel C: Long-term management of overactive bladder with antimuscarinic agents. Eur Urol Suppl 2007; 6:432-437.*
4. *Zhang, P., Hu, W., Cheng, B., Cheng, L., Xiong, X."α_1-adrenergic receptor antagonists versus placebo for female lower urinary tract symptoms: A meta-analysis". Experimental and Therapeutic Medicine 10.1 (2015): 251-256.*
5. *Costantni E, Lazzeri M, Bini V, et al: Open-label, longitudinal study of tamsulosin for functional bladder outlet obstruction in women.Urol Int 2009; 83:311-315.*
6. *Athanasopoulos, A., Gyftopoulos, K., Giannitsas, K. et al. Int Urogynecol J (2009) 20: 217. doi:10.1007/s00192-008-0749-x*

Meditime 19th Issue Winner List

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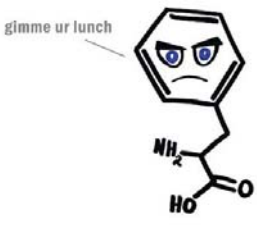
Jokes

WHAT DO YOU CALL AN ACID WITH AN ATTITUDE?



A-mean-oh acid.

Husband Talks in Sleep

A woman askes a doctor : "My husband has a bad habit of talking in sleep! What should I give him to cure?"

"Give him an opportunity to speak when he is awake", replies the doctor.

Review of COX Inhibitors

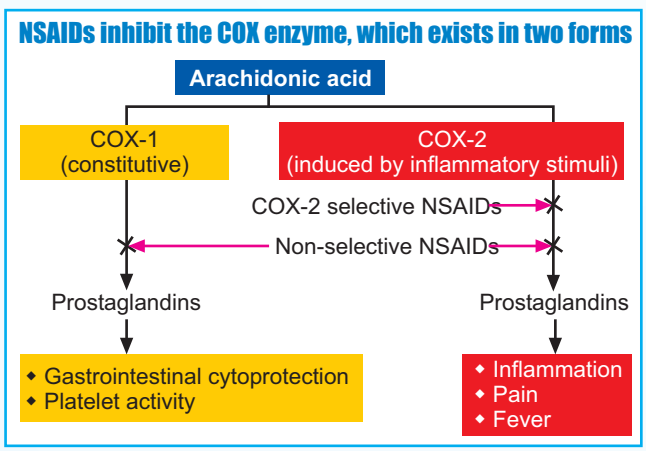
Sabin Raj Shakya
MPD

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely used therapeutics. Through their anti-inflammatory, anti-pyretic and analgesic activities, they represent a choice of treatment in various inflammatory diseases such as arthritis, rheumatisms as well as relieving pain of everyday life. The cyclo-oxygenase enzyme was first identified as the therapeutic target of NSAID by Vane in 1971, showing that these anti-inflammatory substances block the biosynthesis of prostaglandins (PGs) that contribute to a variety of physiological and patho-physiological functions[1]. In healthy individuals, prostaglandin mediate a range of normal biological functions including gastric protection, renal homeostasis, vascular homeostasis, uterine function, embryo implantation & labor, regulation of the sleep wake cycle, body temperature and inflammation.[2] The cyclo-oxygenase (COX) enzyme includes two isoforms, COX-1 and COX-2. COX-1 is expressed in most cells throughout the body. Products of COX-1 are involved in regulation of platelet function, renal function, electrolyte balance and protection of gastrointestinal mucosa.[3] COX-2 is responsible for the production of prostaglandins that mediate inflammation and pain. The following are type of NSAIDs:

Non-selective COX inhibitors	Selective COX-2 inhibitors
Aceclofenac	Etoricoxib
Diclofenac	Valdecoxib
Piroxicam	Rofecoxib
Ibuprofen	Celecoxib
Naproxen	

Adverse effects of Selective and non-selective COX Inhibitors

The main adverse effects of the non-selective NSAIDs involve the GI tract. Since PGs mediate a variety of physiological functions, inhibiting their production likely accounts for some of the adverse events associated with NSAID therapy. Cytoprotective PGs in the stomach are thought to be synthesized primarily by COX-1 which is widely distributed throughout the GIT. In the stomach, PGE2 and PGI2, the type of prostaglandin, inhibit gastric acid secretion stimulated by feeding, histamine or gastrin. Both PGE2 and PGI2 are vasodilators in the GI mucosa, and PGI2 may be directly involved in the regulation of blood flow. Mucous secretion in the stomach and small intestine is increased by PGEs. These effects help to maintain the integrity of the GI mucosa. In addition, PGEs and their analogues inhibit gastric damage caused by a variety of ulcerogenic agents and promote healing of duodenal and gastric ulcers.[2]



COX-1 may contribute to the inflammation process whereas COX-2 is constitutively expressed in several tissues and organs such as brain, kidneys and reproductive tract[1]. Also, the COX-2 inhibitors can increase the risk of cardiovascular events in patients with preexisting cardiovascular disease. This prothrombotic risk results from thromboxane A2–mediated vasoconstriction and platelet aggregation, which will remain unbalanced and unopposed when prostacyclin activity is suppressed via COX-2 inhibition.[2] Care should be exercised in prescribing COX-2-selective NSAIDs for patients with renal insufficiency, cardiac disease and thromboembolic disease. The drugs are contraindicated in pregnancy and in patients with aspirin-sensitive asthma.[2]

Selective and Non-selective COX inhibitors: Choice for treatment

The NSAID market is undoubtedly crowded and competitive, with new compounds being introduced frequently and older drugs being almost withdrawn or relabeled. NSAIDs involves the activity by inhibiting two isozymes COX-1 and COX-2, which have quite different biological properties and functions. NSAIDs have varying degree of specificity for the two forms of cyclo-oxygenase. In recent years, COX-2-selective NSAIDs appear to be drugs of choice for patients with gastric sensitivity to non-selective NSAIDs. COX-2-selective NSAIDs seem also to be an appropriate option for elderly patients (over the age of 65 years) with RA or OA who at high risk for adverse GI events with non-selective NSAIDs. [2] But further studies are required to prove its efficacy compared with other adverse effect related to CVS and renal system.

Many COX-2-specific inhibitors (Valdecoxib and Rofecoxib) have been removed from the U.S. market. Rofecoxib was withdrawn from world market in 2004. Valdecoxib and rofecoxib were about 300 times more potent at inhibiting COX-2 than COX-1, but too toxic for the heart.[4] Celecoxib is approximately 30 times more potent at inhibiting COX-2 than COX-1, with Etoricoxib being more potent than Celecoxib but Etoricoxib is not approved in the US, where the Food and Drug Administration fails to find the safety of efficacy data of its use in people.[6] The USFDA had withdrawn the selective COX-2 inhibitors introduced in market by 2005 due to lack of adequate data on the cardiovascular safety, reports of serious and potentially life-threatening skin reactions, including deaths and lack of comparative advantages of using Selective COX-2 inhibitors over non-selective COX-2 NSAIDs.[4] In 2007, the American Heart Association (AHA) addressed the concern that selective COX-2 inhibition may potentiate a cardiovascular event in patients who are at an increased risk. The AHA states that physicians and patients must weigh the risks and benefits of each agent before choosing a treatment plan for pain relief. Patients should be treated only for the shortest amount of time and with the lowest dosage of drug necessary to gain symptom relief.[5]

In Europe, a warning is introduced for prescribers to exercise caution when prescribing COX-2 inhibitors for patients and serious attention should be given for patients who are with risk factors for heart disease such as hypertension, hyperlipidemia, diabetes and smoking, as well as for patients with peripheral arterial disease. A contraindication is introduced for all selective COX-2 inhibitors in patients with ischemic heart disease or stroke.[4]

Non-selective COX inhibitors are considered as associated with gastrointestinal complications. COX-2 selective inhibitors have anti-inflammatory effects without gastrointestinal side effects

compared to Non-selective COX inhibitors. However, the increased incidence of gastrointestinal lesions and decrease in PG levels induced by NSAIDs are not always linked with each other. For example, higher doses of NSAIDs were required for producing gastric lesions than were required for inhibiting COX at the gastric mucosa[7]. There is no study reported about superiority of COX-2 selective to prevent GI adverse effects compared with NSAIDs co-prescribed with PPIs. Among non-selective COX-inhibitors, Aceclofenac can be considered as gold standard NSAIDs, as it has more preference to inhibit COX-2 compared to COX-1. GI adverse events are the most common tolerability problems with NSAIDs. However, evidence indicates that among NSAIDs aceclofenac has a particularly good GI tolerability. Aceclofenac has also shown stimulatory effects on Glycosaminoglycan (GAG) synthesis in human osteoarthritic cartilage and chondroprotective effects mediated by the suppression of metalloprotease production and proteoglycan release. Beside this no important drug interactions have been identified with aceclofenac; those that have been observed are similar to those seen with other NSAIDs. These include interactions with anticoagulants, cyclosporine, diuretics, quinolone antibiotics, lithium, digoxin and methotrexate[8].

Conclusion

Among the overcrowded NSAIDs, COX-2 selective inhibitors are promoted as NSAIDs with GI safety but it outweigh the risk benefit ratio in terms of cardiac and renal toxicity. Whereas, Aceclofenac appears to be particularly well tolerated and safer drug amongst the NSAIDs, with a lower incidence of gastrointestinal adverse effects. This good tolerability profile results in a reduced withdrawal and hence greater compliance with treatment.

References

1. Iranian Journal of Pharmaceutical research (2011), 10(4); 655-683
2. National Prescribing Service ACN 082 034 393
3. International Orthopedics (SICOT) (2011) 35:3–8
4. WHO, Essential Medicines and Pharmaceutical Policies Quality Assurance and Safety: Medicines Health Systems and Services (WHO/EMP/QSM/2008.3)
5. US Pharm. 2014; 39(3):35-38
6. Wikipedia ()
7. Pharmaceuticals (2010), 3, 1614-1636
8. Expert Opinion on Pharmacotherapy (2004), 5(6); 1347-1357

Recognizing Hypoglycemia

Amrita Acharya
Sr. PDO

Hypoglycemia is the most common side effects from sulfonylurea, glinide, or insulin. The ultimate goal of the glycemic management of diabetes is a lifetime of euglycemia without hypoglycemia. Hypoglycemia puts patients at risk for injury and death. As a group, people with diabetes fear hypoglycemia more than they fear the long-term complications of diabetes.

Symptoms

Especially when the blood glucose level falls autonomic symptoms such as (but are not limited to) palpitations, tremor, hunger, and sweating may occur. Neuroglycopenic symptoms often include behavioral changes, difficulty thinking, and/or frank confusion, but neuroglycopenic manifestations can include seizure, coma, and even death. The degree of cognitive-motor dysfunction, particularly slowing of cognitive and motor processing speed, during an episode depends on the magnitude of hypoglycemia. Hypoglycemia may occur during the night or early morning hours while the patient is asleep, producing such symptoms as nightmares, night sweats, and headaches.

Causes

Although there are several cause of hypoglycemia, by far the most frequent cause in the insulin dependent diabetic is not eating at the proper times. Working through lunch or making a late dinner engagement are other common causes. Unfortunately insulin's onset, peak, and duration of action are not as flexible. A significant increase in exercise or taking too much anti-diabetic medication also produce hypoglycemia. Another cause of hypoglycemia, especially in insulin dependent diabetic is a defect in glucagon secretion. Another counter regulatory mechanisms may also be adversely affected, such as the impairment of epinephrine's action resulting from the administration of a beta-adrenergic blocking agents.

American Diabetes Association Workgroup on Hypoglycemia describes an hypoglycemic events which could be:

1) Severe hypoglycemia.
An event requiring assistance of another person to actively administer carbohydrate, glucagons, or other resuscitative actions. These episodes may be associated with sufficient neuroglycopenia to induce seizure or coma. Plasma glucose measurements may not be available during such an event, but neurological recovery attributable to the restoration of plasma glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose concentration.

2) Documented symptomatic hypoglycemia.
An event during which typical symptoms of hypoglycemia are accompanied by a measured plasma glucose concentration =70 mg/dl (3.9 mmol/l).

3) Asymptomatic hypoglycemia.
An event not accompanied by typical symptoms of hypoglycemia but with a measured plasma glucose concentration =70 mg/dl (3.9 mmol/l). Since the glycemic threshold for activation of glucagon and epinephrine secretion as glucose levels decline is normally 65–70 mg/dl (3.6–3.9 mmol/l) and since antecedent plasma glucose concentrations of =70 mg/dl (3.9 mmol/l) reduce sympathoadrenal responses to subsequent hypoglycemia, this criterion sets the lower limit for the variation in plasma glucose in nondiabetic, nonpregnant individuals as the conservative lower limit for individuals with diabetes.

4) Probable symptomatic hypoglycemia.
An event during which symptoms of hypoglycemia are not accompanied by a plasma glucose determination (but that was presumably caused by a plasma glucose concentration =70 mg/dl [3.9 mmol/l]). Since many people with diabetes choose to treat symptoms with oral carbohydrate without a test of plasma glucose, it is important to recognize these events as "probable" hypoglycemia. Such self-reported episodes that are not confirmed by a contemporaneous low plasma glucose determination may not be suitable outcome measures for clinical studies that are aimed at evaluating therapy, but they should be reported.

5) Relative hypoglycemia.
An event during which the person with diabetes reports any of the typical symptoms of hypoglycemia, and interprets those as indicative of hypoglycemia, but with a measured plasma glucose concentration >70 mg/dl (3.9 mmol/l). This category reflects the fact that patients with chronically poor glycemic control can experience symptoms of hypoglycemia at plasma glucose levels >70 mg/dl (3.9 mmol/l) as plasma glucose concentrations decline toward that level. Though causing distress and interfering with the patient's sense of well-being, and potentially limiting the achievement of optimal glycemic control, such episodes probably pose no direct harm and therefore may not be a suitable outcome measure for clinical studies that are aimed at evaluating therapy, but they should be reported.

Diabetic Foot

Dr. Prabhat Jha
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Alka Hospital

Diabetic foot is a common complication of diabetes mellitus. It is a result of long term uncontrolled diabetes. Lifetime risk of foot ulcers in patients with diabetes mellitus is between 15% to 25%. According to American Podiatric Medical Association, 14% to 24% of Americans with diabetic foot ulcers have amputations.

Pathogenesis includes peripheral nerve dysfunction along with peripheral microangiopathy. Patients cannot feel pain from minor trauma which often go unnoticed. Besides increased HbA1c causes defective oxygen dissociation. Due to reduced blood supply, wounds take a long time to heal. Diabetic ulcers are most common under big toes and balls of feet.

Risk factors include poorly controlled diabetes mellitus along with poorly fitting shoes, poor hygiene, obesity, smoking.

Symptoms

Symptoms include drainage from foot, swelling, irritation, redness, partial or complete gangrene

Wegner's classification

Diabetic foot has been classified into six grades by Wegner.

Grade 0- Foot at risk and no ulceration

Grade 1- Superficial ulcer

Grade 2 – Deep ulcer (cellulitis)

Grade 3- Ulcer with bone involvement (osteomyelitis with ulcer or abscess)

Grade 4 – Gangrenous patches (partial foot gangrene)

Grade 5 – Gangrene of entire foot

Treatment

Treatment includes management of infection with broad spectrum antibiotics. Choice of antibiotics depend on the severity of infection, culture and sensitivity pattern.

Regular dressing of wound with debridement is required.

Hyperglycemia should be managed with insulin therapy, diabetic diet.

In cases of extensive tissue destruction with unsalvageable limbs amputation should be considered.

Prevention

Preventive measures include optimization of blood glucose levels, identification and screening of people at risk of diabetic foot ulceration.

Patient education include

- Washing foot everyday
- Trimming toenails
- Keeping foot dry and moisturized
- Changing socks frequently
- Wearing proper fitting shoes
- Protect feet from hot and cold

Needle, Window, Mountain, Shoe, Keyboard

Brain Teaser

1. What has an eye but cannot see?

2. What invention lets you look right through a wall?

3. What has roots as nobody sees, Is taller than trees. Up, up, up it goes, And yet never grows?

4. I have a soul but I cannot see or hear. What am I?

5. I have a key but no lock and a space but no door. What am I?

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