

7TH INTERNATIONAL NEUROLOGY UPDATE

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The International Neurology Update, a regular feature of the neurology winter calendar in Pakistan now in its 7th year, was held this year at Aga Khan University in Karachi. As in previous years, eminent Pakistani-origin neurologists from Europe and North America provided updates on innovations and advances in the neurological sciences.

Dr. Naweed Syed, a neurobiologist at the University of Calgary, has focused his research on defining neuronal development to control rhythmic behaviors, such as respiration and locomotion. More recently, in collaboration with a group in Germany, he has developed brain chip interfacing technology that offers the potential for future brain-controlled prosthetic devices. Dr. Syed's team cultured nerve cells from a snail and placed them on a specially designed silicon chip. The chip operates as a transmitter and a receptor, stimulating one nerve cell which would transmit a signal to a neuronal network. This can be potentially used to develop electronic devices that can be implanted in the brain to, for example, control prosthetic limbs, artificial eyes or restore memory. On questioning from the audience, Dr Syed admitted that there are ethical considerations that will have to be sorted out as the research develops.

Dr Rafey Faruqui is at Kemsely National Center for Brain Injury in Northhampton, UK. He also works at Imperial College in London. He spoke on acquired brain injuries and associated personality changes. He pointed out alarming figures of head injuries, even in the developed world, approximately 200-300/100,000 in the UK and 175-365/100,000 in the USA. Severe disabilities can occur in up to 150-200/million per year. Dr. Faruqui also pointed out that structural brain damage, especially in the orbito-frontal and ventro-medial frontal regions of the brain, can cause impulsivity, aggression, and lack of empathy. Aggression can be seen in patients who have temporal lobe injury, while an injury to amygdala causes more excitation and low sociability. Studies, especially coming out of Finland, point towards increasing risk of mental disorders, as high as two-fold, in patients with traumatic brain injury (TBI). Interestingly, there are cases of serial killers who had suffered TBI. Dr. Faruqui emphasized that the management of these patients requires a holistic approach where patient needs neuro-physical, cognitive, communication, behavioral and

psychiatric support. Family and social support is also needed for such patients. Judicious use of medications was also emphasized.

Dr Naeem Dean works as a clinical associate professor and directs the stroke program at Royal Alexander Hospital in Edmonton, Canada. He gave two talks on stroke prevention. In Alberta (Canada), figures show 5000 new strokes per year with a cost of \$300 million per year. Dr. Dean suggested that stroke incidence in low income countries such as Pakistan may be 5-10 times higher than in countries such as UK and USA. He quoted figures from the Pakistan Stroke Society estimating 250 strokes per 100,000 and nearing 350,000 strokes per year. Thirty percent of individuals in Pakistan above 45 have hypertension and 5 million are estimated to have diabetes mellitus, both potent risk factors for stroke. Even in Canada, only very small numbers of patients are able to get thrombolytics, accounting for only 4.1 to 6.3 % of acute strokes; hence prevention remains the main stay for the management of strokes. Dr. Dean cited several studies pointing towards 30-day recurrence rates of strokes of about 18% for patients with atherosclerosis. He pointed toward 'iatrogenesis' as a potentially preventable cause of early stroke. Dr. Dean spoke about life style modifications with reference to the DASH diet, exercise of 20-60 minutes of moderate cardiopulmonary activity 3-5/week, and weight loss of 5 kg with avoidance of smoking and alcohol. Adherence and compliance to life style change is very low, even in Canada. Dr. Dean also discussed more recent and important stroke trials including PROGRESS, SPARCLE, CAPRIE and MATCH. Early carotid endarterectomy for stroke prevention was also illustrated by several studies. He explained the working of a new device called WATCHMAN(r) - Left Atrial Appendage System for prevention of strokes from atrial fibrillation. The WATCHMAN device is comprised of a self-expanding nitinol frame structure with fixation barbs and a permeable polyester fabric that covers the atrial face of the device. Deployment of this device reduces the chance of embolic strokes.

Dr. Ismail Khatri from Shifa International spoke on dementia. More people are now living longer and there is rapid increasing in the numbers of nuclear families, with many elderly living by themselves. There are no systematic

data on dementia from Pakistan. Unfortunately, there are very few neurologists in Pakistan and the disease will increase over the next decades and will have an impact on health management and society at large.

Dr. Fayyaz Ahmed Sheikh is at Hull Headache Clinic, University of Hull, UK.

He discussed the latest trends in the management of headaches and migraines. He talked about 'stepped and stratified care' within an attack that delays relapses and reduces clinic visits. He discussed the different types of triptan drugs and their differences. He pointed that placebo rates are unusually low in the eletriptan trials, and high in the almotriptan trial. Other notable facts were that when using the 2-hour response rate (Glaxo), after subtraction of placebo responses, all differences disappear except for with 80 mg eletriptan. Using the 2 hour pain-free rates, rizatriptan 10mg and eletriptan 80mg remained superior. Using sustained pain-free rates, rizatriptan 10mg, eletriptan 80mg and almotriptan 10 mg stood out. In lowest adverse events, naratriptan and almotriptan stand out.

Dr. Mubeen F. Rafay is a pediatric neurologist from Winnipeg Canada. Her talk was titled 'Arterial Ischemic Strokes (AIS) in Neonates and Children.' She discussed that strokes in children are within the top ten causes of death and can cause permanent motor/cognitive disability in over 50%. Twenty to thirty percent of children with AIS have recurrent strokes. The reported incidence of childhood AIS, based on population studies and hospital discharge data bases, ranges from 1.2 to 7.9 per 100,000 children per year, with 5% - 10% mortality in Canada. Dr. Rafay, who is also an investigator in the Canadian Pediatric Stroke Study, showed some interesting statistics. The study included patients with AIS and presumed perinatal AIS. This study looked at 6708 children and 1041 cases were included in the study with 701 non- neonates, 232 neonates. One hundred and eight were presumed pre- or perinatal stroke (PPERI). Nine hundred and thirty three (15%) had definitive AIS. According to her study, 49% diagnosis of AIS is delayed for more than 24 hours. Neonates with AIS usually presents with seizures. Most likely cause is arteriopathy in older children while it is mixed in neonates including prothrombotic states, cardiac, acute and chronic illnesses. Most neonates and older children were now being treated with medications. Comparing 1992 data of 30.8% treated to 51.55% treated in 1998-2002 shows a positive trend towards treatment. Outcome of most of the children was normal or mild disability. Neonatal mortality was 9% and older children mortality was 15%. Predictors of poor outcome included delayed presentation, large cortical stroke, Broca's or Wernicke's speech areas involvement, sub cortical stroke with basal ganglia or internal capsule

involvement, combined cortical and sub-cortical stroke, and evidence of Wallerian degeneration in corticospinal tracts in the brain stem.

Dr. N. Dean's second talk was on high risk TIAs and importance of the emergency ABCD score. The ABCD Score is assigned as follows:

| | |
|------------------------------------|----------|
| Age 60 years | 1 point |
| BP 140/90 | 1 point |
| Unilateral weakness | 2 points |
| Speech impairment without weakness | 1 point |
| Duration 60 minutes | 2 points |
| Duration 10-59 minutes | 1 point |
| Diabetes mellitus | 1 point |

Depending on the above score, risk is stratified as follows:

| | Score | 2-day risk |
|---------------|-------|------------|
| High risk | 6-7 | 8.1% |
| Moderate risk | 4-5 | 4.1% |
| Low risk | 0-3 | 1.0% |

Risk stratification in the ER by the ABCD score significantly reduces admission rates of TIA patients. He quoted a study in which appropriateness of admissions was greater and no inappropriate discharges were noted.

Dr. Ashfaq Shuaib, a renowned stroke specialist from the University of Alberta, spoke on 'Ongoing clinical trials: How can Pakistani centres participate?' He discussed his recent study on NXY-059. It failed to show benefit in humans despite very good results in lower animals. He then talked about recent and ongoing trials in the field of stroke, as follows:

Field Administration of Stroke Treatment-Magnesium

(FAST-MAG) Trial - This is a placebo-controlled, double-blind, randomized multicenter, single region trial involving 69 hospitals of Los Angeles County. It uses 4 g Mg delivered emergently to stroke patients in the field, with 16 g Mg maintenance for 24 hours. Enrollment period is 3.5 years. Primary endpoint of this study is functional activity assessed by the Rankin Scale

MINUTES : Multiple Interventions for Neuroprotection Utilizing Thermal regulation in the Emergent

treatment of Stroke - This trial is using multiple concurrent neuroprotective strategies, including magnesium (NMDA antagonist), albumin (multiple effects

including free-radical scavenging, improved astrocyte function, and improved endothelial function), atorvastatin (anti-inflammatory function and inhibition of nitric oxide synthetase), minocycline (inhibition of inflammation and apoptotic cell death pathways), and hypothermia (multiple effects at different levels). The Minutes protocol is the first randomized open label trial investigating combination neuroprotection with clinically induced hypothermia. Preliminary data suggests viability and safety of the MINUTES protocol with an early trend towards efficacy.

SENTIS: Safety and Efficacy of Neuro-Flo Treatment

for Ischemic Stroke - Neuro-Flo is a catheter device that causes partial occlusion of the descending aorta, diverting blood flow to the cerebral vasculature. It requires aortic balloon catheterization via the femoral artery and is positioned at infra- & supra-renal positions. It is deliverable by interventionalists, neuroradiologists, neurologists or cardiologists. This trial is planned for 40 North American centers and is actively screening for patients. Twenty five centers have enrolled 99 patients as of Dec 2007. No unanticipated adverse events.

Dr. Shuaib emphasized that in order to promote research in Pakistan, infrastructure (personal and financial support), political willingness, projects specific to the local environment, and centralized core lab facilities are needed.

Dr. Ayeesha Kamran Kamal, who directs the stroke program at Aga Khan University Hospital in Karachi, discussed intracranial stenosis. She presented the latest developments in the management of acute stroke in Pakistan and showed an excellent example of a complicated stroke successfully treated in collaboration with interventional neuroradiology. She also spoke about a newly planned study, KISS (Karachi Intracranial Stenosis Study), which will be a non-randomized observational case-control study looking at risk factors, disease mechanisms, genetic factors, radiological presentation and prognosis.

Dr. Muhammad I. Akhtar is an academic neurologist from Charlotte, USA. He spoke on the latest modalities of neuroimaging including MRI with newer protocols, MR spectroscopy, SPECT, neurosonology, CT, PET, transcranial doppler, carotid ultrasound, and other neuroimaging modalities. He described in detail how MRI functions and what are the different machines and techniques available in MRI technology. He showed interesting pictures of 'stand up' MRI where patient is actually sitting or stand in a relatively open space. Dr. Akhtar elaborated on the recent development of diffusion tensor imaging (DTI), which visualizes the location, orientation, and anisotropy of white matter tracts. This

technique enables brain maps of fiber directions and allows examination of the connectivity of different regions in the brain (so-called 'tractography'), which is expected to help in examining areas of neural degeneration and demyelination in diseases such as multiple sclerosis.

Dr. Mubashira Hashmi from Karachi's Liaquat National Hospital presented a free paper titled 'Carbamazepine and Atherosclerosis: Is there any link?' She showed that lipid profiles of subjects on carbamazepine were found to be significantly altered. The atherogenic index however was not affected. The HDL promoting effects of carbamazepine were noted. The data are interesting and demand further investigation.

Next year's neurology update is scheduled for December 2008 at Shifa International Hospital in Islamabad.

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