A summary of some of the recently published papers in Neuroscience

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The prognostic significance of the right or left hemispheric intracerebral haemorrhage (ICH) is not known. It is believed that right hemispheric strokes have a greater chance of major disability but the reports derived from the previous studies show conflicting results. This study publishes the subsidiary analysis of the randomized controlled trials of patients with spontaneous acute ICH with elevated systolic blood pressure, randomly assigned to intensive (target systolic BP <140 mm Hg) or guideline-based (<180 mm Hg) blood pressure (BP) management (INTERACT Pilot and INTERACT 2) studies. The study aimed to determine the relationship between laterality of acute ICH and poor clinical outcomes. A total of 2708 patients, whose modified Rankin Score information at 90 days was available, were included. Patients with a right hemispheric ICH (1327, 49%) had a higher risk of death at 90 days compared to those with left hemispheric ICH after adjustment for potential confounding variables that included hematoma volume, deep versus lobar location, intraventricular location and randomization into intensive versus guideline based treatment groups (OR, 1.77; 95% CI 1.33 to 2.37). However, on assessing the combined end point of mortality/major disability, and of major disability alone, there were no significant differences between patients with a right or left hemispheric ICH. The authors discussed that higher mortality among patients with a right hemispheric ICH was presumably because of judgment of right ICH as milder because of a lower National Institutes of Health Stroke Scale [NIHSS] assessment of the right sided ICH (due to the hemispheric bias within the NIHSS). Thus, the standard intensive care during the first 7 days of admission like intensive care unit admission, and nasogastric feeding were often not offered to patients with a right sided ICH.

Contributed by Dr. Vimal Paliwal


Intravenous lorazepam is well established as a first-line drug for bringing about the cessation of acute convulsive seizures and acute convulsive status epilepticus. However, in certain healthcare settings, establishing a venous access...
is not possible and therefore, nonvenous medications may be urgently required for achieving seizure cessation and for preventing the conversion of an acute convulsive seizure to a convulsive status epilepticus. Since the Rapid Anticonvulsant Medication Prior to Arrival Trial (RAMPART) study was published, there is a greater recognition of the role of intramuscular midazolam in the cessation of acute convulsive seizures by healthcare workers before the arrival of a patient in the emergency room. This is a network meta-analysis of all the randomized controlled trials (RCTs) from 1997 to 2012 that used nonvenous drugs in at least one arm. A network meta-analysis is used in place of a conventional meta-analysis in situations where pair-wise comparison between drugs is not possible because of different drugs/routes being used in different studies. Thus, it can be used to compare efficacy of drugs that are not compared head-to-head in any of the included randomized control trials (RCTs). Sixteen RCT were included. Drugs/their routes of administration studied in the different RCTs were intramuscular midazolam, buccal midazolam, intranasal midazolam, rectal diazepam, intranasal lorazepam, sublingual lorazepam, and intramuscular paraldehyde. An intramuscular midazolam was superior to other nonvenous medications for its better time-to-seizure termination (2.145 minutes, 95% credible interval [Crl] 1.308-3.489), time-to-seizure cessation after arrival in the hospital (3.841 minutes, 95% Crl 2.697 – 5.416), and time-to-initiate treatment (0.779 minutes, 95% Crl 0.495-1.221). Intranasal midazolam was found to be most efficacious for seizure cessation within 10 minutes of administration (90.4% of participants, 95% Crl 79.4%-96.9%). The authors discussed that the present report studies the efficacy of the studied medications but not their safety profile owing to variability present in defining the adverse events across the studies.

**Contributed by Dr. Vimal Paliwal**

**Zeiler FA, et al. Magnesium sulfate for non-eclamptic status epilepticus. Seizure 2015;32:100-8**

The role of magnesium sulfate infusion is well known in the prevention and treatment of eclampsia. The role of magnesium sulfate is also often discussed in the treatment of status epilepticus, and especially refractory status epilepticus. The authors conducted a meta-analysis of all the published studies regarding the use of magnesium sulfate in the non-epileptic status epilepticus. They found 19 articles that comprised a total of 28 patients (11 adults, 9 children and 8 subjects of unknown age). The majority were single patient retrospective case reports or case series. Seizures were classified as generalized status epilepticus in 1 patient, generalized refractory status epilepticus in 13 patients, focal refractory status epilepticus in 2 patients, non-convulsive refractory status epilepticus in 1 patient and status epilepticus/refractory status epilepticus in 9 patients. With the use of intravenous magnesium sulfate, seizure reduction/control occurred in 14 of 28 patients (50%), with 2 (7.1%) and 12 (42.9%) of the patients displaying partial and complete responses, respectively. Seizure recurred upon withdrawal of magnesium sulfate in 50% patients. Three patients reported adverse events secondary to magnesium sulfate in the form of limb weakness in 1, and heart block in 2 patients. The authors concluded that there was a trend towards improved seizure control with the use of intravenous magnesium sulfate therapy for non-eclamptic status epilepticus/refractory status epilepticus. However, the level of evidence in favor of magnesium sulfate treatment remains low (Oxford level 4, Grade D). The authors also discussed that there was a high likelihood of publication bias in the studies, as those with negative results often remain unpublished.

**Contributed by Dr. Vimal Paliwal**


Experiential hallucinations (EH) are also called reperceptual hallucinations. They are defined as lively visual, auditory or compound hallucinations depicting a scene experienced previously by the affected individual. Another psychic hallucination is a feeling of abnormal familiarity or déjà vu (DV). Both EH and DV occur in temporal lobe epilepsy and both are known to arise from the mesial temporal lobe. However, there are conflicting reports regarding the lateralization of EH and DV. In this study, the authors systematically compared the epileptogenic or putative epileptogenic zone in 28 patients with temporal lobe epilepsy presenting with DV and EH in order to determine the lateralizing value of both DV and EH. All patients underwent a thorough presurgical examination including magnetic resonance imaging, positron emission tomography, single photon emission computed tomography and electroencephalography as well as neuropsychological examination. They found that EH were strongly lateralized to the left mesial temporal lobe whereas DV was due to the right or left mesial temporal lobe affliction. They also found more interictal language deficits in patients suffering from EH. The authors discussed that the EH usually comprise auditory, and more specifically verbal hallucinations from the past experiences, and that the episodic memory and visuo-spatial imagery in autobiographical memory is linked...
to a left-lateralized neural network that includes the left mesial temporal lobe and the left temporo-parietal junction.

**Contributed by Dr. Vimal Paliwal**


Migraine with an aura is associated with a two-fold increase in the incidence of ischemic stroke in adults. The relationship of migraine with childhood stroke, however, is not known. In this study, the authors compared the incidence of ischemic and hemorrhagic stroke in a large cohort of children (2–17) years with migraine and those without headache. Among the 88,164 children with migraine, eight had a stroke (three [38%] hemorrhagic, five [63%] ischemic). Eighty strokes occurred in 13,23,142 children without headache (53 [66%] hemorrhagic; 27 [34%] ischemic). The incidence of ischemic strokes was 0.9 per 100,000 person-year in migraineurs as compared to 0.4 per 100,000 person-year in those without headache [IR 2.0 (95% CI 1.2-9.5)]. The incidence rate of hemorrhagic stroke was 0.5/100,000 person-year in migraineurs, and 0.9/100,000 person-years in those without headache [IR 0.6 (95% CI 0.2-2.0)]. A post-hoc analysis of adolescents (12–17 years) showed an increased risk of ischemic stroke among those with migraine (IR 3.4 (95% CI 1.2-9.5)]. The authors concluded that there is no increase in the risk of ischemic or hemorrhagic stroke among children with migraine as compared to those without migraine. However, there is a trend towards a greater risk of ischemic stroke among adolescent patients with migraine. The strength of the study was a large cohort, whereas the limitation was the presence of only a few strokes in the population having a migraine. The authors discussed that the trend towards a higher incidence of ischemic stroke in adolescents with migraine may be related to age-related hormonal changes similar to that seen in women in the reproductive age having a migraine who have a two-fold increased risk of developing an ischemic stroke.

**Contributed by Dr. Vimal Paliwal**


Migraine with an aura is a risk factor for ischemic stroke. The authors based their study on the fact that the migraine mutant mice show an enhanced accelerated sensitivity to cerebral ischemia. This, therefore, led to an early recruitment of hypoperfused but viable brain tissue into the infarct core. They hypothesized that the patients with migraine would exhibit increased recruitment of the ischemic brain tissue into the infarct zone. They retrospectively recruited all those consecutive patients with an acute ischemic stroke in whom the MRI was done within 72 hours of the stroke onset and whose diffusion-weighted and perfusion imaging were available. They found that significantly larger proportion of migraineurs (n = 45) had no diffusion-perfusion mismatch pattern as compared to controls (n = 27). They concluded that by the time the MRI was performed, more migraineurs had developed complete infarction of the hypoperfused brain area when compared to controls. This finding supported the hypothesis proposed by the authors. The authors discussed that the migraineurs may, therefore, have a narrower window for thrombolysis in the setting of acute ischemic stroke. The latter also required a more stringent monitoring of the risk factors responsible for stroke. The prophylactic treatment for migraine may also have some role in reducing the vulnerability of brain to ischemic injury.

**Contributed by Dr. Vimal Paliwal**


Epileptic encephalopathy with electrical status epilepticus in sleep (ESES) is a pediatric epileptic syndrome characterized by acquired impairment of cognition, behavior and sleep-related epileptic discharges on electroencephalography (EEG). It is believed that early treatment may improve cognition and EEG changes. However, there are knowledge gaps in the effective treatment options and factors associated with a favorable outcome. In this study, the authors conducted a pooled analysis of all those patients who were included in the published literature from 1977 to 2013. They analyzed 112 articles and 950 treatments in 575 patients. The inclusion criteria used included the availability of information regarding the cognitive or EEG outcome. To limit the publication bias associated with inclusion of case reports and case series, the authors conducted a subgroup analysis of studies reporting all consecutive patients fulfilling the inclusion criteria in a specific period. The primary outcomes assessed were an improvement in cognition, EEG, or any other forms of improvement. The authors found that antiepileptic drugs were associated with improvement (in cognition or in the EEG findings) in 49% subjects. Administration of benzodiazepine resulted in improvement in 68%, and steroids in 81% subjects. Surgery resulted in improvement in 90% patients. In the subgroup analysis, improvement was associated with antiepileptic drugs in 34% patients. Administration of benzodiazepine resulted in an improvement in 59%, and steroids in 75% patients; and, performance of surgery
resulted in improvement in 93% patients. The possible predictors of an improved outcome were the treatment category, normal development before the onset of ESES and the absence of a structural abnormality. The surgical procedures performed included multiple subpial resection, hemispheric surgery, corpus callosotomy, lobar/multilobar resection or disconnection, and cysteroperitoneal shunt. The authors concluded that this pooled analysis suggested the superior efficacy of steroids and surgery in encephalopathy associated with ESES. A randomized controlled European multicenter trial was recently initiated (RESCUE ESES, Randomized European trial of steroid versus clobazam usage for encephalopathy with electrical status epilepticus in sleep) that may provide further directions.

**Contributed by Dr. Vimal Paliwal**


Small vessel disease (SVD) is known to produce depression and apathy. SVDs in various white matter tracts are previously shown to be associated with late-life depression. But it is not known if these regions are also associated with apathy. Therefore, the authors determined the prevalence of, and the overlap between, apathy and depression, in patients with SVD using diffusion tensor imaging (DTI) and analyzed the fractional anisotropy and mean diffusivity maps using voxel-based analysis. They also studied the impact of depression and apathy on the quality of life. One hundred and eighteen patients with SVD and 398 controls were included in the study. All the participants underwent neuropsychological tests for depression and apathy, and stroke-specific quality-of-life scale evaluation to ascertain the quality of life. They found that depression ($r = -0.41, P \leq 0.001$) and apathy ($r = -0.23, P \leq 0.001$) were independent predictors of the quality of life. They found that depression ($r = -0.41, P \leq 0.001$) and apathy ($r = -0.23, P \leq 0.001$) were independent predictors of the quality of life. They found that depression ($r = -0.41, P \leq 0.001$) and apathy ($r = -0.23, P \leq 0.001$) were independent predictors of the quality of life. They found that depression ($r = -0.41, P \leq 0.001$) and apathy ($r = -0.23, P \leq 0.001$) were independent predictors of the quality of life. Apathy was significantly associated with a reduced median fractional anisotropy ($r = -0.38, P \leq 0.001$) but no such relationship was seen with depression ($r = -0.16, P = 0.09$). On voxel-based analysis, apathy was associated reduced fractional anisotropy in limbic association tracts like the anterior cingulum, fornix and uncinate fasciculus. However, no significant relationship was found between the white matter parameters and depression after controlling for apathy.

The authors concluded that apathy and not depression is related to damage to the white matter networks which are associated with regulation of emotion, reward and goal-directed behavior in patients with SVD. The authors discussed that their study suggests that depression and apathy may be dissociable and distinguishable based on the imaging in a patient with SVD. This has clinical implications in designing therapy as most serotonin-reuptake blocking drugs are effective in depression but may not work in apathy.

**Contributed by Dr. Vimal Paliwal**


Wernicke-Korsakoff syndrome (WKS) is a common condition characterized by a triad of confusion/memory impairment, ophthalmoplegia and ataxia. However, a myriad of clinical features are associated with the condition. It occurs as a result of thiamine deficiency and the condition is associated with chronic alcoholism. WKS in non-alcoholic patients is considered rare and thought to present with a different set of clinical features. It is believed that the well-known triad of WKS is infrequently seen in these patients. Therefore, to ascertain the clinical presentation and causes of WKS in non-alcoholics, the authors conducted this meta-analysis. They searched for all the published cases with WKS from 1867 to 2014. They found 623 cases. The illnesses that precipitated WKS included gastrointestinal tract disease or surgery, hyperemesis gravidarum, dietary insufficiency, starvation or vomiting, leukemia or cancer of the lymphoid system, hyperalimentation, psychiatric disorders, dialysis, HIV/AIDS and other unspecified causes. Non-alcohol related cases presented with the triad of clinical features with a similar frequency as alcohol-related WKS ($P = 0.662, \text{Cohen’s } w = 0.12$) but with more signs when diagnosed in the antemortem state ($P < 0.001, \text{Cohen’s } w = 0.46$). Ongoing memory impairment of Korsakoff syndrome was reported in 25% of the non-alcohol related WKS patients. Non-alcoholic WKS was associated with female gender, younger age, a shorter duration of precipitating illness, and better survival as compared to alcohol-related WKS. Authors concluded that non-alcohol-related WKS presents in a similar fashion as alcohol-related WKS. Authors discussed that the nonalcohol-related WKS may be under-reported because of the ingrained belief that thiamine deficiency cannot occur in the absence of chronic alcoholism.

**Contributed by Dr. Vimal Paliwal**


Aneurysmal subarachnoid hemorrhage (aSAH) has a high case fatality rate often being greater than 50%. In this study,
the authors evaluated the relationship of various early inflammatory parameters with the functional outcome based on the modified Rankin Scale score (mRS) at discharge (primary objective) and at six months after the precipitation of aSAH. A total of 81 patients with a mean age of 53.8 ± 13.2 years were included. The patients were grouped into those having a favorable (mRS: 0-2) or an unfavorable outcome (mRS: 3-6). All deaths (mortality occurred in 13 patients) occurred before discharge. During discharge, 48% (n = 39) had a favorable outcome. At six months, reevaluation showed a favorable outcome in 56% (n = 33) patients and a poor outcome in rest of the 44% (n = 26) patients. The univariate analysis at discharge showed a significant correlation of serum log interleukin-6 (IL-6) and log leukemia inhibitory factor (LIF) with an unfavorable outcome (mRS: 3-6). The multivariate analysis showed only the correlation of log IL-6 with unfavorable outcome to be significant. No significant correlation was found with the serum levels of C-reactive protein, E-selectin, intercellular adhesion molecule 1, matrix metalloproteinase 9 and the leucocyte count. Similarly, in the cerebrospinal inflammatory parameters, only log LIF showed a significant difference with regard to outcome at discharge (P = 0.043). To conclude, a poor outcome at discharge in patients with aSAH shows correlation with higher IL-6 serum levels at admission.

**Contributed by Dr. Neeraj Kumar and Dr. Ravindra Kumar Garg**


The prodromal stage of Alzheimer’s disease, when only mild cognitive impairment (MCI) exists, is the best stage for potential disease modifying interventions. Due to the poor beneficial effects of pharmacological interventions, the focus is changing towards non-pharmacological interventions. The authors assessed the improvement in cognition that occurred in patients with MCI with anodal transcranial direct current stimulation (anodal-tDCS) in a double-blind, sham controlled, cross-over study. Stimulation was given to the left inferior frontal cortex in the resting state and during task-related functional magnetic resonance imaging (fMRI). Eighteen patients were enrolled based on the core clinical criteria for the diagnosis of “MCI due to AD” and tested by the standardized testing using the Consortium to Establish a Registry for Alzheimer’s Disease (CERAD) test battery. Eighteen matched healthy controls were included in study. During sham stimulation, the patients with MCI showed hyperactivity in bilateral prefrontal regions with lesser correct semantic word retrieval when compared to controls. Anodal-tDCS resulted in significant reduction in the task-related prefrontal hyperactivity with improved performance in the semantic word retrieval task. The authors showed improvement in cognition and brain functions with the anodal-tDCS in MCI and proposed a systematic evaluation of repeated stimulation sessions for sustained benefits.

**Contributed by Dr. Neeraj Kumar and Dr. Ravindra Kumar Garg**


The authors studied the effect of donepezil on the rate of hippocampal atrophy in prodromal Alzheimer’s disease (AD). In this double blind, randomized, placebo-controlled study, donepezil (10mg/day) was given in patients with suspected prodromal AD and two brain MRI studies (baseline and final visit) were done. After screening 332 patients, 216 were randomized into the placebo (n = 103) or the donepezil (n = 113) group.

A slower rate of hippocampal atrophy was observed in the donepezil group versus the placebo group (Annualized percentage changes [APC] = –1.89%[standard error (SE) = 0.34] versus -3.47% [SE = 0.32], respectively, n = 174, P < .001). Annualized percentage changes showed a significant difference between the donepezil and placebo groups in term of the left and right hippocampal volume (P = 0.001 and P = 0.008). Similar differences were found in the APC of the global cerebral volume and ventricular volume (P = 0.005 and P < 0.001). This study showed the significant role of donepezil in decreasing hippocampal atrophy rate by as much as 45% in patients with AD with prodromal symptoms.

**Contributed by Dr. Neeraj Kumar and Dr. Ravindra Kumar Garg**


The authors studied the effect of glucocorticoid (GC) treatment on upper limb function in non-ambulant boys and adults with DMD. This study was done to resolve the controversies surrounding the appropriate time of initiation and continuation of corticosteroids. The cohort included DMD patients who had lost their ambulation for at least
2 years. Retrospectively, they were divided into the first group with continued glucocorticoid treatment after the loss of ambulation, the second group with no corticosteroid administration after the loss of ambulation, and the third group who had either never taken glucocorticoids (GC) or had only taken them in the ambulatory stage for less than a year. The Performance of Upper Limb (PUL) test that included 22 items was used for evaluation. Out of the 91 included patients, 48 were still taking GCs, 25 had stopped their GCs at the time of loss of ambulation, and the remaining 18 patients had not been administered GCs. There was a significant increase in the baseline PUL score from shoulder (mean = 1.85) to middle (mean = 19.14) to distal (mean = 20.21, \( P < 0.01 \)) domains. Moreover, the baseline PUL score was significantly higher in the GC taking group than in the group of patients in whom GC had been discontinued (\( P < 0.001 \)). The 12-month PUL change in the middle region showed a lesser decrease (-10%) in the GC group than in the non-GC group (-34%). Thus, the authors concluded that continuation of GC in the non-ambulant patients would be beneficial for maintaining upper limb functions especially at the middle domain leading to retaining of self-feeding functions for a longer duration.

**Contributed by Dr. Neeraj Kumar and Dr. Ravindra Kumar Garg**


Myasthenia gravis (MG) is an autoimmune disorder with an associated dysregulation of the helper T lymphocytes (Th) and regulatory T lymphocytes (Tregs). In this prospective study, the authors evaluated the outcome of thymectomy with or without immunosuppressive (IS) treatment in patients with nonthymomatous myasthenia gravis. Additionally, the study assessed their effect on regulatory T cells as it has a role in maintaining peripheral tolerance. The patients were divided into 3 groups. The first group consisted of patients with nonthymomatous generalized MG treated with pyridostigmine only; the second group had patients with nonthymomatous generalized MG treated with corticosteroids only; and, the third group had patients with generalized nonthymomatous MG treated with a combination of ISs (corticosteroids and azathioprine). The therapeutic outcome in terms of the quantified myasthenic score (QMGS) showed a reduction in 89% of all patients with a nonthymomatous MG measured at 1 year following the thymectomy. The QMGS score was maximally reduced in the group treated with steroids [a decrease by 2.27 points (\( P = 0.015 \))] as compared to the group with combined ISs in which the mean score decreased by 2.22 points (\( P = 0.044 \)). Complete stable remission (CSR) after a 2 year follow-up was present in 38% of patients in the corticosteroid group and 24% in the combined IS group, while it was present in only 8% in the pyridostigmine therapy group. One year after surgery, there was a significant increase in the Treg cell proportion (2.7%, \( P < 0.001 \)) in the corticosteroid group and in the combined IS group (1.75%, \( P = 0.008 \)). No significant change was found in the pyridostigmine group. The authors concluded that an increase in the circulating CD4 + CD25 + regulatory T cells leads to the stabilization of the disease in the thymectomized patients.

**Contributed by Dr. Neeraj Kumar and Dr. Ravindra Kumar Garg**


Neuromyelitis optica (NMO) is an autoimmune demyelinating disorder affecting predominantly the spinal cord and optic nerves. The treatment options are limited and therefore, search for an effective medication is the need of the hour. In this retrospective study on six diagnosed patients with NMO, the benefits of rituximab infusion were evaluated. The treatment cycles comprised of 2 infusions of 1000 mg, 15 days apart, repeated every 6 to 8 months. The follow-up and outcome were assessed in terms of the EDSS (Kurtzke) scale, overall condition of the patient, CD19 + count, relapse rate, and presence of anti-NMO antibodies. A stable EDSS score and a lower yearly relapse rate occurred in 4 patients. Anti-NMO antibodies were positive in 50% (3/6) patients and became negative in one patient at follow up. To conclude, rituximab may be considered as an attractive treatment option for NMO and requires larger randomized controlled trials to substantiate its efficacy.

**Contributed by Dr. Neeraj Kumar and Dr. Ravindra Kumar Garg**


The authors performed this study in an attempt to diagnose dementias based on the metabolic profile of the cerebrospinal fluid (CSF). Magnetic resonance spectroscopy was used to evaluate the CSF of patients with dementia who were grouped into the four common dementia syndromes namely the Alzheimer’s disease (AD), vascular dementia (VaD), Lewy body disease (LBD) and frontotemporal dementia (FTD). The included patients were classified into the following...

In this study, the authors evaluated the success of the extradural selective peripheral denervation (SPD) procedure in patients with cervical dystonia unresponsive to botulinum toxin (secondary non-responders). After the magnetic resonance imaging and the electromyographic study, surgery was performed using the method of Bertrand. Evaluation was done using the Tsui scale for dystonia (0-25), Visual analogue scale (VAS) for pain, and Fugl-Meyer life-satisfaction questionnaire for quality of life (Qol). Out of the 54 patients operated for cervical dystonia (SPD procedure), 6 developed recurrence and had to be operated again, resulting in a total of 61 operations. The immediate post-surgery improvement in dystonia was seen in all but one patient. The mean score of the Tsui scale was 10 preoperatively which improved to 4.5 (p < 0.001) at 6 months; VAS for pain improved from 6.5 preoperatively to 4.2 (p < 0.001) at 6 months. The Fugl-Meyer score for Qol improved from a preoperative figure of 43.3 to 46.6 (p < 0.05) at 6 months. The authors concluded that selective peripheral denervation is a less invasive procedure than deep brain stimulation and can be performed in those patients who are unresponsive to conservatively managed cervical dystonia.

Contributed by Dr. Neeraj Kumar and Dr. Ravindra Kumar Garg


The authors retrospectively reviewed patients with refractory status epilepticus without an identifiable etiology within 48 hours of admission. The outcome was assessed at discharge based on the modified Rankin Scale. Out of the 130 included cases, etiology was ultimately found in 63 (47%) patients. The majority (23/63, 40%) comprised of non-paraneoplastic autoimmune etiology and the next common cause was paraneoplastic (19/63, 16%). An infectious cause was detected in 16% patients. Anti-NMDAR antibodies related encephalitis was the most frequent etiology. Even in the cryptogenic group (67/130, 52%), the paraneoplastic panel detected anti-Hu in 66, anti-CRMP5/CV-2 in 59, anti-amphiphysin in 57, and anti-Ma2/Ta in 41. Anti-VGKCC, anti-NMDAR, anti-GAD65, anti-AMPAβ, and anti-GABAB-receptor antibodies were tested in 48, 42, 40, 5, and 5 cryptogenic cases, respectively. Despite aggressive treatment, 22% died and 62% had a poor outcome at discharge. The outcome improved during the follow up period. The authors concluded that autoimmune encephalitis is the most commonly detected cause of new onset refractory status epilepticus. In half of these patients, the etiology still remains cryptogenic.

Contributed by Dr. Neeraj Kumar and Dr. Ravindra Kumar Garg


Authors evaluated the risk factors associated with rupture of unruptured cerebral aneurysms (UCA) in the elderly Japanese groups: 76 patients with probable AD, 33 patients with mild cognitive impairment (MCI), 26 patients with an early stage AD (EAD), 16 patients with VaD, 16 patients with FTD, and 10 patients with LBD. Controls were selected from psychiatric patients who did not have an AD marker profile in their CSF. Quantitative analysis and spectral model obtained with MRS showed 31 metabolites (17 known, 7 unknown and 7 with overlapping signals). The composition of CSF contains adequate information of the neurological state of a given patient with a specific dementia. Thus, the method may be used to diagnose various types of dementia with extremely high accuracy.

Contributed by Dr. Neeraj Kumar and Dr. Ravindra Kumar Garg
patients. The patient data was included from 3 prospective studies namely the Unruptured Cerebral Aneurysm Study of Japan (UCAS Japan), UCAS II, and the prospective study at the Jikei University School of Medicine. The mean aneurysm size was 6.2 mm in the included study patients (n = 1896). Subarachnoid hemorrhage occurred in 68 (3.6%) patients during the follow up. The multivariate analysis showed significant association of the aneurysm rupture with age 80 or more (P = 0.012), aneurysm size [7mm or larger (P = 0.007), 7-9mm (P = 0.001), 10-24 mm (P < 0.001) and >25mm (P < 0.001)] and location (internal carotid–posterior communicating artery aneurysms, P = 0.011).

**Contributed by Dr. Neeraj Kumar and Dr. Ravindra Kumar Garg**


The authors studied the histopathological correlation of the hippocampal region with pre-operative seizure burden and post-operative outcomes. The cohort of children and adults who underwent epilepsy surgery (n = 43) were included along with controls (n = 15).

Increased reactive astrocitic number in the CA3 zone was associated with a poor post-operative seizure outcome at 1 and 3 years. Changes in lower cortical astrocitic and upper cortical microglial number also correlated with post-operative outcome at 1 year. The focal, lobar and generalized atrophy visualized on neuroimaging in the preoperative period correlated with the degree of cortical gliosis in the surgical specimen.

**Contributed by Dr. Neeraj Kumar and Dr. Ravindra Kumar Garg**


To investigate the role of hypothermia in severe traumatic brain injury (TBI), the authors conducted a multi-center randomized controlled trial enrolling 387 patients treated at 47 centers in 18 European countries from November 2009-14. Researchers randomly assigned adults with severe closed TBI with an intracranial pressure of more than 20 mm Hg despite initial treatments (including mechanical ventilation and sedation management) to standard care (control group) or hypothermia (32 to 35°C) plus standard care. Barbiturates and decompressive craniectomy were used if all other treatments failed to control intracranial pressure. The primary outcome was the score on the Extended Glasgow Outcome Scale (GOS-E; range, 1 to 8, with lower scores indicating a worse functional outcome) at 6 months. Results showed that only 26% of patients treated with hypothermia had a favorable outcome (GOS-E; 5 to 8) compared with 37% who were given the standard of care (P = 0.03). Barbiturates and decompressive craniectomy were required to control the intracranial pressure in 44% of the patients in the hypothermia group and in 54% of the patients in the control group. Patients undergoing therapeutic hypothermia were 1.53 times more likely to have a lower GOC-E score indicating a worse outcome than those in the control group. The authors concluded that in patients with an intracranial pressure of more than 20 mm Hg after traumatic brain injury, therapeutic hypothermia plus standard care to reduce intracranial pressure did not result in outcomes better than those with standard care alone. The results of the Eurotherm3235 Trial, may lead to the demise of hypothermia as yet another pillar of therapy for intracranial hypertension. Completely new approaches are needed for the control of intracranial pressure in order to design trials and treatments for severe TBI.

**Contributed by Dr. Mazda Turel**


Despite the past failures, the promise of clinical neuroprotection in traumatic brain injury continues to drive the assessment of new compounds. The latest of these compounds is erythropoietin, which has also been proposed to having neurocytoprotective effects. The authors aimed to study the effect of erythropoietin on neurological recovery, mortality, and venous thrombotic events in patients with moderate-to-severe traumatic brain injury. In this multi-center, randomized controlled trial conducted between May 2010 and Nov 2014, 606 patients suffering from traumatic brain injury (TBI) were recruited from 29 centers in 7 countries and randomly assigned to erythropoietin (n = 308; 40,000 units subcutaneously) or placebo (n = 298; 0·9% sodium chloride subcutaneously) once per week for a maximum of three doses. The primary outcome, assessed at 6 months, was improvement in the patients’ neurological status, summarized as a reduction in the proportion of patients with an Extended Glasgow Outcome Scale (GOS-E) of 1-4 (death, vegetative state, and severe disability). Compared with a placebo, erythropoietin did not reduce the proportion of patients with a GOS-E
level of 1-4 (44% in the erythropoietin group versus 45% in the placebo group). In terms of safety, erythropoietin did not significantly affect the 6-month mortality versus the placebo (11% died at 6 months in the erythropoietin group versus 16% in the placebo group); it also did not increase the occurrence of deep venous thrombosis of the lower limbs (16% vs 18%, P = 0.44). The authors concluded that following moderate-to-severe TBI, erythropoietin neither reduced the number of patients with severe neurological dysfunction (GOS-E; level 1-4) nor increased the incidence of deep venous thrombosis of the lower limbs.

**Contributed by Dr. Mazda Turel**


Astrocytic brain tumors, including glioblastomas, are incurable neoplasms characterized by diffusely infiltrative growth. To study the occurrence and the dynamics of membrane tube protrusions in mammalian tumors, the authors followed gliomas growing in the mouse brain (n = 6) by an *in vivo* multiphoton laser-scanning microscopy for up to one year. They showed that many tumor cells in astrocytomas extend ultra-long membrane protrusions, and use these distinct tumor microtubes as routes for brain invasion, proliferation, and to interconnect over long distances. The resulting network allows multicellular communication through microtube-associated gap junctions. When damage to the network occurred, tumor microtubes were used for repair. Moreover, the microtube-connected astrocytoma cells, but not those remaining unconnected throughout tumor progression, were protected from cell death inflicted by radiotherapy. The neuronal growth-associated protein 43 was important for microtube formation and function, and drove microtube dependent tumor cell invasion, proliferation, interconnection, and radioresistance. Oligodendrogial brain tumors were deficient in this mechanism. In summary, they concluded that astrocytomas can develop functional multicellular network structures. Disconnection of astrocytoma cells by targeting their tumor microtubes emerges as a new principle to reduce the treatment resistance of this disease.

**Contributed by Dr. Mazda Turel**

**Schalto B, et al.** Outcomes after combined use of intraoperative MRI and 5-aminolevulinic acid in high-grade glioma surgery. *Neuro Oncol 2015;17:1560-7*

In this retrospective study of 200 patients who underwent surgery for high-grade gliomas, the authors compared rates of progression-free (PFS) and overall survival (OS) using multivariable regression analysis, between patients who underwent surgical resection with the combination of 5-aminolevulinic acid (5-ALA) and intraoperative (iMRI) and a control group without iMRI. The mean age was 57 ± 12 years and 176 deaths were observed in the follow-up period. The long-term survival rate (>2.5 years) of this cohort was 25%. Gross total resection (GTR) was achieved in 132 (66%) patients. The median PFS was 7 months in the non-iMRI group, and 10.6 months in the iMRI group (P = 0.19) The median OS was 13.8 months in the non-iMRI group, and 17.9 months in the iMRI group (P = 0.043). Patients receiving 5-ALA were 3 times more likely to achieve GTR at surgery than patients who did not receive 5-ALA. However, no effect on PFS and OS was observed. The authors concluded that GTR is the key surgical variable that influences progression and survival in patients with high-grade gliomas and is more likely when surgical adjuncts, such as iMRI in combination with 5-ALA, are used to enhance resection. To determine which of these adjuncts has a higher impact on survival would require a complex study design with many groups and will be likely remain elusive.

**Contributed by Dr. Mazda Turel**


The standard of care for a newly diagnosed glioblastoma (GBM) is maximal safe surgical resection, followed by chemo-radiation therapy. The authors assessed the efficacy and safety of carmustine wafer implantation when used in combination with standard care. This study was conducted from 18 centers in France. Included were adult patients with (n = 354, implantation group) and without (n = 433, standard group) carmustine wafer implantation during the first surgical resection followed by chemo-radiation standard protocol. The median age was 58 years. The median progression-free survival (PFS) was 12 months in the implantation group and 10 months in the standard group and the median overall survival (OS) was 20 months and 18 months, respectively. Carmustine wafer implantation was independently associated with a longer progression free survival in patients with subtotal/total surgical resection in the whole series (P = 0.005), whereas no significant difference was found in the OS. Surgical resection at progression, whether alone or when combined with carmustine wafer implantation, was independently associated with a longer OS in the whole series. The higher postoperative infection rate in the implantation group (7.1% versus 1.5%, P < 0.001) did not affect survival. The authors
concluded that carmustine wafer implantation during surgical resection followed by the standard chemo-radiation protocol for newly diagnosed GBMs in adults resulted in a significant PFS benefit and may represent a promising first-line treatment option in newly diagnosed supratentorial GBMs in adults. These results warrant a multicenter randomized control trial to clearly assess the actual impact in terms of overall survival in this patient population.

*Contributed by Dr. Mazda Turel*


This report serves to update the last intracerebral hemorrhage (ICH) guidelines published in 2010. The clinically relevant Class 1 recommendations are these: A baseline severity score should be performed as part of the initial evaluation; the most widely used and externally validated one is the ICH score. Rapid neuroimaging with CT or MRI is recommended to distinguish an ischemic stroke from an ICH. Coagulopathies should be reversed and the international normalized ratio (INR) should be corrected. Patients should have intermittent pneumatic compression for prevention of venous thromboembolism, beginning from the day of hospital admission. For ICH patients presenting with SBP between 150 and 220 mm Hg and without contraindication to acute BP treatment, acute lowering of SBP to 140 mm Hg is safe and can be effective in improving the functional outcome. Initial monitoring and management of ICH patients should take place in an intensive care unit or a dedicated stroke unit. Glucose should be monitored. Both hyperglycemia and hypoglycemia should be avoided. Clinical seizures should be treated with antiseizure drugs. A formal screening procedure for dysphagia should be performed in all patients before the initiation of oral intake to reduce the risk of pneumonia. Patients with cerebellar hemorrhage, who are deteriorating neurologically or who have brainstem compression and/or hydrocephalus from ventricular obstruction, should undergo surgical removal of the hemorrhage as soon as possible. Patients with a change in mental status who are found to be having electrographic seizures on electroencephalography should be treated with antiseizure drugs. Class 2 and 3 evidence is as follows. For most patients with supratentorial ICH, the usefulness of surgery is not well established. A policy of early hematoma evacuation is not clearly beneficial compared with hematoma evacuation when the patients deteriorate. Decompressive craniectomy with or without hematoma evacuation might reduce mortality for patients with supratentorial ICH who are in a coma, have large hematomas with significant midline shift, or have elevated intracranial pressure refractory to medical management. The effectiveness of minimally invasive clot evacuation with stereotactic or endoscopic aspiration with or without thrombolytic usage is uncertain (Class 2). Prophylactic antiseizure medication is not recommended (Class 3).

*Contributed by Dr. Mazda Turel*


With advances in the endovascular techniques at one end of the vascular neurosurgical spectrum, vascular surgeons performing open surgical approaches too are pushing the envelope to address intracranial aneurysms at the other end of the spectrum. The authors in Finland from Dr Hernesniemi’s group conducted the largest retrospective study till date to identify anatomic parameters based on imaging that would favor a unilateral approach to address bilateral aneurysms located between the two middle cerebral artery (MCA) bifurcations. Of the 51 patients with bilateral MCA aneurysms, 38 patients underwent a single craniotomy with a contralateral microsurgical approach (group 1) and 13 patients underwent bilateral craniotomies (group 2). All aneurysms approached contralaterally were unruptured and without wall calcifications. Of the contralaterally approached aneurysms, 97% were smaller than 14 mm. The median length of the contralateral A1 was 13.2 mm and the median length of the contralateral M1 was 14.2 mm. There was no difference in the length or projections of the aneurysm between the two groups. The saccular shape of the contralateral aneurysm was a significant feature when choosing the approach. The contralateral group had a good postoperative outcome (modified Rankin Scale 0-3) in 86% of the unruptured cases. The median surgical time was 120 minutes, which was 43% shorter than the bilateral group. The authors concluded that the contralateral approach for bilateral MCA aneurysms in selected patients (unruptured aneurysms, without calcification, of simple configurations but with any projection, less than 15 mm in size, and with a contralateral median M1 and A1 length of around 15 mm) is feasible in experienced hands, with acceptable morbidity and mortality. The contralateral approach requires a meticulous preoperative analysis of the characteristics of the aneurysm to be clipped and of the anatomic constraints of the microsurgical operative corridor. The disadvantage of the contralateral approach is the potential for olfactory dysfunction seen in 21% of their patients.

*Contributed by Dr. Mazda Turel*
In recent years, less invasive procedures and microdecompression through smaller incisions are frequently being performed for lumbar canal stenosis. This shift towards minimally invasive surgery (MIS) has not been backed by solid evidence. To determine if MIS was as effective as traditional laminectomy, 885 patients with central stenosis of the lumbar spine who underwent laminectomy \( n = 414 \) or microdecompression \( n = 471 \) at 34 Norwegian centers, from October 2006 to December 2011 were included in this multicenter observational study. Among 81% patients with a complete one-year follow-up, 70% achieved a minimal clinically important difference predefined as an improvement of eight points or more in the Oswestry disability index (ODI) score from the baseline. For both groups combined, the mean ODI score at the baseline was 40, and at one-year follow-up was 22.2, the difference of 17.8 being significant \( (P < 0.001) \). In the propensity-matched cohort, the mixed linear model showed a mean reduction in ODI score at one-year follow-up of 16 in the laminectomy group and 19 in the microdecompression group—a difference of 3 points, not meeting the predefined criteria of an improvement of 8 points. The mean duration of hospital stays were 1.6 and 2 days longer in the laminectomy group for single level and two-level decompressions, respectively \( (P < 0.05) \). The numbers of patients experiencing complications were significantly higher in the laminectomy group \( (15.0\% \text{ v} 9.8\%, P = 0.018) \), but after propensity matching, the groups were equal \( (14.6\% \text{ v} 10.6\%, P = 0.23) \). There was a comparable significant improvement in the quality of life scales in both the groups. The authors concluded that the effectiveness of microdecompression was equivalent to that of laminectomy in the surgical treatment of central stenosis of the lumbar spine in this registry based multicenter observational study. This finding was consistent in both unmatched and propensity matched populations.

This knowledge will enable clinicians to identify meaningful functional improvements in patients with DCM.

**Contributed by Dr. Mazda Turel**


The authors conducted this multi-center, prospective study across 17 centers to determine the preoperative patient characteristics that predict the postoperative quality of life (QoL) and survival in patients who undergo surgery for spinal metastases. A total of 922 patients were analyzed. The mean age at surgery was 60 years. About half of the patients survived 1 year after surgery, and a quarter survived for 2 years. The multivariate analysis revealed that the main factors associated with survival were the metastatic tumor type, the number of visceral metastases and the number of spinal vertebral levels involved with the tumor \( (P < 0.05) \). Better Karnofsky scores showed a trend towards an increased survival \( (P = 0.08) \). Factors that predicted the QoL after surgery were the preoperative EuroQual group 5 dimensions (EQ-5D) scale, the preoperative Frankel score, and the preoperative Karnofsky Performance Status. Surgery for patients with a poor Karnofsky Performance...
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This study compared the safety and efficacy of treatment with the PRESTIGE LP cervical disc (n = 280) versus a historical control (n = 285) comprising of anterior cervical discectomy and fusion (ACDF). The patients having an intractable radiculopathy and/or myelopathy recalcitrant to nonoperative treatment modalities were considered candidates for a single-level stand-alone discectomy. The median age was 44 years. The investigational and control groups were similar demographically. There was no significant difference in the blood loss (51 ml versus 57 ml) or hospital stay (0.98 days versus 0.95 days) in the investigational and control groups, respectively. The investigational group had a significantly longer operative time (1.49 hrs versus 1.38 hrs). Significant improvements when compared to the preoperative scores in the neck disability index, neck/arm pain, 36-Item Short Form Health Survey, and neurological status were achieved by 1.5 months in both the groups and were sustained at 24 months. Neurological success at 24 months was 94% in the investigational group and 84% in the control group. At 24 months, 12% of the investigational and 16% of the control patients had an adverse effect classified as device or device/surgical procedure related; and, 14 (5.0%) of the investigational and 21 (7.9%) of the control patients had a second surgery at the index level. The median return-to-work time for the investigational group was 40 days compared with 60 days for the control group (P = 0.020). Following implantation of the PRESTIGE LP device, the mean angular motion was maintained at 12 months (7.9°) and 24 months (7.5°). At 24 months, 90% of investigational and 88% of control patients were satisfied with the results of surgery. The authors concluded that this device maintains the mean postoperative segmental motion while providing the potential for biomechanical stability. The patients reported significantly improved clinical outcomes compared with the baseline, which were at least not inferior to the ACDF, up to 24 months after surgery.

### Contributed by Dr. Mazda Turel


The aim of this multi-center randomized control trial was to determine the safety and efficacy of the lumboperitoneal shunt surgery in normal pressure hydrocephalus (NPH). Using strict inclusion and exclusion criteria, eligible participants (60-85 years of age) with idiopathic NPH, with ventriculomegaly, and tightness of the high-convexity and medial subarachnoid spaces on MRI, were recruited from 20 centers in Japan. The eligible participants were then randomly assigned in an 1:1 ratio to either the immediate shunt surgery group within one month of randomization (n = 46; immediate group) or the postponed shunt surgery group after 3 months of randomization (n = 41; postponed group). At 12 months after surgery, 63% of the entire cohort of patients showed improvement in their functional status. More patients in the immediate treatment group than in the postponed treatment group had an improvement of one point or more on the modified Rankin scale (mRS) at 3 months: (65% versus 5%; P < 0.0001). The numbers of patients who had an improvement of one point or more on the mRS at 12 months after surgery were similar between the two groups (67% versus 58%; P = 0.496). The proportions of patients with serious adverse events did not differ significantly between the groups during the 3 months post-randomization (15% versus 2%; P = 0.060). The authors concluded that lumboperitoneal shunt surgery might be beneficial for patients with idiopathic normal pressure hydrocephalus and, if these findings are confirmed in larger studies, this could be a first-line treatment option for this disease.

### Contributed by Dr. Mazda Turel


The authors evaluated the role of abobotulinumtoxinA injection in the upper limb muscles on muscle tone,
spasticity, active movement, and function in patients with stroke or traumatic brain injury. In this randomized, placebo-controlled, double blind study, the authors enrolled adults (aged 18–80 years) at least 6 months after stroke or brain trauma from 34 neurology or rehabilitation clinics in Europe and the USA. 243 patients were randomly allocated to placebo (n = 81), abobotulinumtoxinA 500 U (n = 81), or abobotulinumtoxinA 1000 U (n = 81). The primary endpoint was the change in the muscle tone (Modified Ashworth Scale [MAS]) from baseline to 4 weeks. The mean change in MAS score from baseline at week 4 was −0.3 in the placebo group, −1.2 in the abobotulinumtoxinA 500 U group, and −1.4 in the abobotulinumtoxinA 1000 U group (P < 0.0001 versus placebo). There was a significant improvement in the Physician Global Assessment and Disability Assessment Scale in the latter group. Adverse events that were thought to be treatment related occurred in two (2%), six (7%), and seven (9%) patients in the placebo, abobotulinumtoxinA 500 U, and abobotulinumtoxinA 1000 U groups, respectively. The most common treatment-related adverse event was mild muscle weakness. All adverse events were mild or moderate. The authors concluded that AbobotulinumtoxinA at doses of 500 U or 1000 U injected into upper limb muscles provided tone reduction and clinical benefit in hemiparesis.

**Contributed by Dr. Mazda Turel**


The objective of this Norwegian study was to review the surgical outcome, mortality, social outcome, and health-related quality of life in middle-aged patients treated for hydrocephalus during the years 1967-1970 when they were less than 14 years old. A total of 128 patients were included in the study, with no patient lost to follow-up. Sixty-one (48%) patients died (tumor = 22; myelomeningocele = 13) during the 42-45 years of observation. The mortality rate was lowered to 39% if the patients with tumors were excluded. The overall mortality rates at 1, 2, 10, 20, and 40 years from the time of initial shunt insertion were 16%, 24%, 31%, 40%, and 48%, respectively. The incidence of shunt-related mortality was 8%. The majority of the patients had between 1 and 5 procedures, with a mean revision number of 3.3. No revision of the shunt was performed in 27 patients (21%), of whom 4 patients (3.1%) were still alive at follow-up. The majority of children graduated from a normal school (67%) or from a school specializing in education for physically handicapped children (20%). Self-perceived health was significantly poorer in 6 out of 8 domains assessed by SF-36 as compared with the background population. A total of 56% of the patients were socially independent, and 42% of the patients were employed. Approximately half of the patients were still alive. The late mortality rate was low, but not negligible. Twelve patients died during the last 2 decades, 1 of whom died because of acute shunt failure. Although the shunt revision rate was decreasing during the study period, many patients required shunt surgery during adulthood. Forty-one revisions in 21 patients were performed during the last decade. The authors concluded that there was an obvious need for life-long follow-up in these patients.

**Contributed by Dr. Mazda Turel**


The authors conducted a systematic review of the literature that reported results of surgery in previously coiled aneurysms. The authors analyzed 26 such retrospective and non-comparative studies, which included 466 patients having 471 intracranial aneurysms. They carried out a subgroup analysis to compare direct clipping versus coil removal, clipping versus parent vessel occlusion, early (less than 4 weeks post-coiling) versus late surgery, and anterior versus posterior circulation. They noted that patients undergoing direct clipping had a lower perioperative morbidity (5.0%, 95% CI = 2.6–7.4%) compared to those undergoing simultaneous coil removal and clipping (11.1%, 95% CI = 5.3–17.0%) or parent vessel occlusion (13.1%, 95% CI = 4.6–21.6%; P = 0.05). Patients receiving early surgery (less than 4 weeks post-coiling) were found to have significantly lower rates of good neurological outcome (77.1%, 95% CI = 69.3–84.8%) when compared to those undergoing late surgery (92.1%, 95% CI = 89.0–95.2%; P < 0.01). There were higher rates of long-term neurological morbidity (23.1% versus 4.7%, P < 0.01) and long-term neurological mortality (4.4% versus 2.8%, P < 0.01) in the posterior circulation group. The authors concluded that the surgical treatment is safe and effective in such cases. While noting that the aneurysms that are amenable to direct clipping and the patients having late surgeries had fared better, the authors emphasized on the poor outcomes in recurrent posterior circulation aneurysms.

**Contributed by Dr. Kuntal Kanti Das**

The authors intended to share their experience of surgically managing patients with essential hypertension concomitantly presenting with hemifacial spasm. They identified 48 such patients (all but one patient had severe hypertension) out of 201 (23.8%) patients admitted for surgery of hemifacial spasm under their care. In all these patients, demonstrable neurovascular complex (NVC) around the root entry/exit zone of the ninth and tenth cranial nerves (CN IX-X) and adjacent ventrolateral medulla was identified using MRI, in addition to that seen at the CN VII root exit zone [REZ] (the vascular compression of the latter being responsible for the hemifacial spasm). They performed microvascular decompression (MVD) of the IX/Xth nerve in all these patients. The effect of the procedure on hypertension was assessed using the World Health Organization classification during the follow-up (mean = 7 years, range 2-16 years). They also evaluated the comparative changes in blood pressure following the right and left sided MVDs. Following the surgical procedure, 28 of their patients had become normotensive with or without medication. They also found that 10 out of 18 patients having an unstable blood pressure measurement preoperatively attained stable blood pressure control after surgery (P < 0.02). Although the majority of their patients underwent a left sided MVD (30 versus 18), there was no statistically significant difference in outcome according to the side of decompression. They concluded that MVD can be very effective in attaining control of uncontrolled hypertension in patients with medically refractory essential hypertension in whom high-resolution MRI clearly demonstrates neurovascular compression at the CN IX-X REZ and adjacent ventrolateral medulla.

Contributed by Dr. Kuntal Kanti Das


The authors reviewed the outcomes following Gamma Knife radiosurgery (GKRS) in cerebral arteriovenous malformations (AVMs) and their correlation with post-radiosurgery adverse radiation effects (AREs). From a prospectively maintained database, the authors identified 105 patients with a minimum of 2 years of follow-up for analysis. They looked at the incidence and quantitative changes in the AREs as a function of time after GKRS. Statistical analysis was performed to identify factors related to the development of ARE and changes in the ARE index. Majority of the patients had a Spetzler-Martin grade ≥ III AVM (47.6%). The median administered margin and maximum doses were 22 and 40 Gy, respectively. Appreciable ARE was defined as an ARE index > 8. At a median clinical follow-up of 53.8 months (range 24–212.4 months), the authors noted an overall AVM obliteration rate of 70.5%. Among the patients showing complete AVM obliteration, 74.4% developed AREs within 4–6 months after GKRS. 58.1% of patients who developed appreciable AREs proceeded to have a complete nidus obliteration. Thus, the ARE was highly predictive of AVM obliteration (P = 0.043). Appreciable AREs were found to be influenced by the AVM nidus volume >3 ml, lobar location, number of draining veins and feeding arteries, prior embolization, and a higher marginal dose. The authors concluded that the development of ARE after radiosurgery typically peaks at 7–12 months after the therapy. They also stressed the importance of ARE index as an important adjunct enabling outcome prediction for such patients during their follow-up.

Contributed by Dr. Kuntal Kanti Das


The authors reviewed 139 patients treated with a pipeline embolization device between 2011 and 2013 for the presence of in-Pipeline stenosis (IPS). For the determination of predictors of IPS, multivariable logistic regression analysis was used. At a mean follow up of 6.7 months, 21 patients (15.8%) had some degree of IPS. Mild stenosis (<50%) was seen in 11 patients, moderate stenosis (50%-75%) in 5, and >75% stenosis was observed in 6 patients. Despite the presence of stenosis, no patient was symptomatic or required any further intervention. 73% of these patients had detection of their stenosis within 6 months. 16.7% of patients with an anterior circulation aneurysm had an IPS as compared to 7.6% in patients of posterior circulation aneurysms. The rate of IPS was higher in patients who were not on aspirin as compared to patients who were on aspirin (60% versus 14.2%; P = 0.02). No aspirin therapy (odds ratio, 10.0; 95% confidence interval, 1.4-67.7; P = 0.02) and internal carotid artery (ICA) aneurysm location (odds ratio, 3.1; 95% confidence interval, 1.1-8.8; P = 0.03) were strong independent factors predicting an IPS. The authors concluded that patients with ICA aneurysms are more likely to develop IPS and aspirin plays an important role in the prevention of IPS.
Sridhar, et al.: The fourth dimension

Contributed by Dr. Anant Mehrotra


The authors conducted a phase 2 study in 47 centers distributed among various countries and enrolled 202 patients with Hoehn and Yahr stage II-IV of Parkinson’s disease (PD) to determine the analgesic efficacy of prolonged–release oxycodone-naloxone (OXN PR) in patients with PD and chronic severe pain. The patients had at least one type of severe pain with an average 24 hour pain score of at least 6 (as assessed on an 11 point scoring system ranging from 0 to 10 with 0 indicating no pain and a score of 10 indicating pain as bad as one can imagine). 93 patients were randomly assigned to the OXN PR group (starting dose oxycodone 5 mg, naloxone 2·5 mg, twice daily) and 109 to the placebo group. The full analysis population consisted of 88 patients versus 106 patients. At 16 weeks, the least squares mean average score of 24-h was 5.0 in the OXN PR group versus 5.6 in the placebo group (difference — 0·6, 95% CI: —1·3 to 0·0; P = 0·058). Adverse events were similar in the two groups (60/92 [65%] versus 76/109 [70%]). Treatment-related nausea was more common in the OXN PR group than in the placebo group (16/92 [17%] versus 10/109 [9%]), as was treatment-related constipation (16/92 [17%] versus 6/109 [6%]). The authors concluded based on full analysis of the population at week 16 that the difference between the two groups was not significant though OXN PR has potential efficacy.

Contributed by Dr. Anant Mehrotra


The authors have assessed the neural placode derived from myelomeningocele as a potential source of neural stem and progenitor cells. During the surgical repair of meningomyelocele in infants, the neural placode was harvested and was further analyzed by in vitro studies, flow cytometry and immunofluorescence. Neural placode-derived neurospheres were subjected to differential media growth for assessment of lineage potential. Through assessment of platelet-derived growth factor receptor α (PDGFRα) and CD15 cell marker expression, Sox2 + Olig2 + putative oligodendrocyte progenitor cells were successfully isolated. The highest rate of self renewal capacity and multipotency of cell progeny was observed in PDGFRαhi CD15hi cell population. It was observed that the neurospheres were more likely to differentiate into oligodendrocyte progenitor marker, CNPase. They, however, also showed differentiation to neurons and astrocytes although to a lesser extent. The authors concluded that neural placode tissue derived from meningomyelocele is a novel source of multipotent progenitor cells and can be used in various neurological diseases.

Contributed by Dr. Anant Mehrotra