A summary of some of the recently published, seminal papers in neuroscience

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The authors evaluated the impact of short (2-week) versus long (6-week) postoperative restrictions following lumbar discectomy on outcomes and reherniation for 1 year after surgery. This study included 108 patients who underwent lumbar discectomy, and they were randomized immediately following surgery between short and long postoperative restriction. There was no difference in the reherniation rates between short and long postoperative restriction groups (11% vs 7%, P = 0.52). Six patients (11%) in the 2-week restriction group and four patients (7%) in the 6-week restriction group had reherniation (P = 0.52). All the clinical measures, including VAS back pain, leg pain and ODI scores significantly improved for both cohorts as compared to baseline at the 2-week time point and remained significantly improved through 1-year. There were no significant differences in ODI, VAS back, or VAS leg scores between the 2- and 6-week postoperative restriction groups. The results of this randomized trial suggest equivalent clinical outcomes irrespective of the length of postoperative restriction. The authors concluded that there was no significant difference in outcomes after lumbar discectomy between short and long postoperative restriction cohorts.

Contributed by Mazda K Turel


The authors conducted this randomized controlled trial to study the differences in clinical outcomes in patients undergoing transforaminal endoscopic discectomy (TED) and microdiscectomy. A total of 143 patients, age 25-70 years and weight <115 kg, with a single level lumbar disc prolapse and radiculopathy, were recruited in the study and randomized between TED and microdiscectomy. After crossovers and dropouts, 70 patients underwent TED under conscious sedation and 70 underwent microdiscectomy under general anaesthesia. Oswestry Disability Index (ODI), visual analogue scores (VAS) of back and leg pain, and Short Form Health Survey indices (SF-36) were measured preoperatively and at 3, 12 and 24 months. There was significant improvement in all the above-mentioned measures postoperatively (P < 0.001). At 2 years, affected side leg pain was lower in the TED group (1.9 ± 2.6 vs 3.5 ± 3.1, P = 0.002). Hospital stay was shorter following TED (0.7 ± 0.7 vs 1.4 ± 1.3 days, P < 0.001). There was higher incidence of revision discectomy in patients undergoing TED as compared to those undergoing microdiscectomy (RR 2.62). The authors concluded that there was excellent functional improvement following both surgeries, and this was maintained at 2 years in both groups, with less ongoing sciatica after TED. There was a greater revision rate after TED, however the recovery following TED was quicker that following microdiscectomy.

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The impact of sagittal cervical alignment in the occurrence of C5 palsy following cervical laminectomy is unclear. The authors reviewed cervical alignment changes in patients who developed postoperative C5 palsy after cervical laminectomy and fusion. Eighteen of the 148 patients (12%) who underwent cervical laminectomy and fusion developed postoperative C5 palsy. Nine of these patients had required upright X-ray films, and this was compared with a randomly selected control group of 20 patients. There were no statistically significant differences between the 2 groups in age, proportion of males, and preoperative Nurick score. There was no significant difference in the measures of sagittal alignment between the 2 groups on preoperative and postoperative imaging. However, patients with C5 palsy had a statistically higher amount of average C4-C5 Cobb angle change (-2.53 vs 0.78°; \( P = 0.01 \)), when the amount of alignment change between preoperative and postoperative images on upright imaging was compared. On logistic regression analysis, lordotic change in both C4-C5 and C2-C7 Cobb angles were associated with development of C5 palsy. The authors concluded that lordotic cervical correction, as measured on upright imaging, was statistically larger in patients who had C5 palsy, and hence there might be a potential role of deformity correction in preventing C5 palsy.

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This retrospective analysis was performed to investigate the role of bone morphogenetic protein (BMP) in posterior cervicothoracic spine fusions, and to determine the reoperation rates for symptomatic non-unions in both groups. Posterior cervicothoracic spine fusion cases were identified from a large spine registry (Kaiser Permanente), and chart review was performed. There were 450 patients (32.7% with BMP) who underwent posterior cervicothoracic fusions, with a median follow-up of 1.4 years. Kaplan-Meier curves showed no significant difference in reoperation rates for non-unions using log-rank test (\( P = 0.088 \)). There were 260 patients (43.1% with BMP) with a follow-up period of greater than 1 year, and a median follow-up duration of 2.4 years. In this cohort too, there was no statistically significant difference in the symptomatic operative nonunion rates for posterior cervicothoracic fusions with and without BMP (0.0% vs 2.7%, respectively; \( P = 0.137 \)). The authors concluded that there was no statistically significant difference in the reoperation rates for symptomatic non-unions with or without BMP.

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The authors performed a retrospective analysis of patients undergoing anterior cervical disectomy and fusion in the prospective National Surgical Quality Improvement Program (NSQIP) database, to determine the most common reasons for readmission within 30 days after elective ACDF. A total of 17,088 patients undergoing elective ACDF were identified. There were 545 (3.2%) readmissions within 30 postoperative days. The commonest reasons for readmission following ACDF were nonsurgical site related reasons (293, 53.8%), which included neuropsychiatric issues (\( n = 44 \)), cardiovascular diseases (\( n = 39 \)), and pneumonia (\( n = 37 \)). Surgical site-related reasons were responsible for readmission in 184 patients (33.8%), which included surgical site infection (\( n = 42 \)), hemorrhage/hematoma (\( n = 42 \)), and dysphagia (\( n = 32 \)). A total of 84 patients (15.6%) had undocumented reasons for readmission. Only older age and higher American Society of Anesthesiologists class were independently associated with readmissions on multivariate analysis. The authors concluded that most readmissions after ACDF were due to nonsurgical site-related reasons, suggesting the importance of careful patient selection, optimization of preoperative medical conditions, and adequate postoperative management.

Contributed by Mazda K Turel


This retrospective analysis was performed to determine the importance of the modified Frailty Index (mFI) in predicting postoperative complications in patients undergoing surgery for adult spinal deformity (ASD). The mFI is an evaluation tool to describe the frailness of an individual and how their preoperative status may impact postoperative survival and outcomes. The data came from the American College of Surgeons National Surgical Quality Improvement Program, which is a large multicenter clinical registry. This registry prospectively collects preoperative variables, patient demographics, operative factors, and 30-day postoperative morbidity and mortality outcomes from about 400 hospitals nationwide. Current Procedural Terminology (CPT) codes were used to query the database for adults who underwent fusion for spinal deformity. Modified Frailty index (mFI) was calculated based on the number of positive factors, and univariate and multivariate logistic regression analysis were used to analyze the risk factors associated with mortality.

A total of 1001 patients were identified, and the mean mFI score was 0.09 (range: 0.0-0.545). Increasing mFI score was associated with higher complication, reoperation, and mortality rates (\( P < 0.05 \)). mFI of 0.09 and 0.18 was an independent predictor of any complication, mortality, requirement of a blood transfusion, pulmonary embolism/deep vein thrombosis,
Early disabling deficits and permanent disabling deficits occurred in 12.3% and 4.5% patients, respectively, whereas any permanent neurological deficit (modified Rankin Scale score ≥1) occurred in 16.1% patients. When the authors analyzed Spetzler-Martin grades 1 and 2 ubAVM patients, complete obliteration occurred in 99.2%, with early disabling deficits and permanent disabling deficits occurring in 9.3% and 3.4%, respectively. Major bleeding was the only significant predictor of early disabling deficits on multivariate analysis ($P < 0.001$). The authors concluded that microsurgery produced less disabling deficits than that reported in ARUBA trial. This also suggests that future controlled trials should focus on the safety and efficacy of microsurgery with or without adjunctive embolization in carefully selected ubAVM patients.

**Contributed by Mazda K Turel**


THRACE was a randomised controlled trial performed in 26 centres in France. Patients aged 18-80 years with acute ischemic stroke and proximal large vessel occlusion, were randomly assigned to receive either intravenous thrombolysis alone (IVT group) or intravenous thrombolysis plus mechanical thrombectomy (IVTMT group). Mechanical thrombectomy had to be started within 5 hours of symptom onset. The primary outcome measure was patients with functional independence, defined by modified Rankin scale (mRS) of 0-2. Out of 414 patients in the trial, 208 were randomly assigned to the IVT group, and 204 to the IVTMT group. Six patients in IVT group, and 4 patients in IVTMT group were excluded from analysis because of different reasons. A higher proportion of patients in IVTMT achieved functional independence at 3 months (85/202, 42% in the IVT group and 106/200, 53% in the IVTMT group, odds ratio 1.55; $P = 0.028$). There was no significant difference in mortality at 3 months (12% vs 13%, $P = 0.70$) or symptomatic intracranial hemorrhage at 24 h (2% vs 2%; $P = 0.71$) between the two groups. Common adverse events related to mechanical thrombectomy were vasospasm (33 [23%] patients) and embolization in a new territory (nine [6%] patients). The authors concluded that mechanical thrombectomy combined with standard intravenous thrombolysis improves functional independence in patients with acute ischemic stroke with large vessel occlusion, with no evidence of increased complications.

**Contributed by Mazda K Turel**


Even after the publication of ARUBA trial, which reported superiority of conservative management over any intervention in patients with unruptured brain arteriovenous malformations (ubAVMs), the management of these lesions is unclear. The principle criticism of the trial was that microsurgery occurred in only 14.9% of ARUBA intervention cases, raising concerns about the study’s generalizability. The purpose of this study was to evaluate the role of microsurgery in ARUBA-eligible ubAVM population. Out of 977 AVM patients, 155 ARUBA-eligible patients had microsurgical resection (71.6% surgery only and 25.2% with preoperative embolization). Mean follow-up was 36 months. Complete obliteration was achieved in 94.2% after initial surgery and in 98.1% on final angiography. Early disabling deficits and permanent disabling deficits occurred in 12.3% and 4.5% patients, respectively, whereas any permanent neurological deficit (modified Rankin Scale score ≥1) occurred in 16.1% patients. When the authors analyzed Spetzler-Martin grades 1 and 2 ubAVM patients, complete obliteration occurred in 99.2%, with early disabling deficits and permanent disabling deficits occurring in 9.3% and 3.4%, respectively. Major bleeding was the only significant predictor of early disabling deficits on multivariate analysis ($P < 0.001$). The authors concluded that microsurgery produced less disabling deficits than that reported in ARUBA trial. This also suggests that future controlled trials should focus on the safety and efficacy of microsurgery with or without adjunctive embolization in carefully selected ubAVM patients.

**Contributed by Mazda K Turel**


Atypical meningiomas (AM) are aggressive subset of meningiomas, and the role and advantage of adjuvant radiosurgery (ARS) over serial surveillance (SS) following subtotal resection (STR) remain unclear. The authors performed a systematic review to study recurrence rate (RR), 5-year progression-free survival (PFS), and 5-year overall survival (OS) between the treatment strategies (ARS versus SS following STR). Embase, PubMed and Cochrane databases were used to identify the studies reporting these outcomes in patients with atypical meningiomas. A total of 619 patients (263 ARS and 356 SS) were identified. Mean recurrence rates, 5-year PFS, and 5-year OS were 53.5%, 50.3%, and 74.9% for ARS versus 89.8%, 91.1%, and 89.8% for SS, respectively. The 5-year PFS between treatment strategies, ARS, and SS studies differed significantly ($P < 0.001$ and $P < 0.007$, respectively). This systematic analysis demonstrated significant differences in recurrence rates and 5-year PFS between ARS and SS, suggesting a potential benefit of ARS.

**Contributed by Mazda K Turel**


This authors conducted a deep genomic comparative analysis in eight tumors from ‘long-term’ glioblastoma survivors (average of 33 months) with tumors from ten ‘short-term’ survivors (7 months) in a cohort of patients receiving standard therapy (surgery plus concomitant radiation and temozolamide). They performed exome, RNA, whole genome sequencing, and DNA methylation for collection of deep genomic data from short-term survivors (STS) and long-term survivors (LTS). The authors found that the longest-living patients had the most genetically complex tumors. LTS GBM tumors showed frequent chromosomal gains in 4q12 (platelet derived growth factor receptor alpha and KIT) and 12q14.1 (cyclin-dependent kinase 4), and deletion in 19q13.33 (BAX, branched chain amino-acid transaminase 2, and cluster of differentiation 33). Patients with simple, but robust, cancer genomes had a shorter
Tumor consistency in meningiomas is a critical factor that influences operative strategy. The role of MRI in predicting the consistency of meningiomas has been analyzed in many studies. The authors performed a systematic review of the PubMed database since 1990. The studies that evaluated MRI appearance and tumor consistency to assess whether or not MRI can be used reliably to predict tumor firmness, were analyzed. They described the relationship between the preoperative imaging characteristics, intraoperative findings, and World Health Organization (WHO) histopathological subtype. While T2 signal intensity and MR elastography provided a useful predictive measure of tumor consistency, other techniques could not be validated. T1-weighted imaging was not found to offer any diagnostic or predictive value. A quantitative assessment of T2 signal intensity more reliably predicted consistency than inherently variable qualitative analyses. Based upon their review of the literature, the authors currently recommend the use of T2-weighted MRI for predicting consistency, which has been shown to correlate well with the tumor histological subtype.

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Contributed by Mazda K Turel


Though the Simpson grading system has been used for many years for grading extent of resection of meningioma and predicting recurrence, its role has been questioned in recent times, reflecting the changes in meningioma surgery over the years. The authors reviewed their experience in resecting WHO Grade I meningiomas, and assessed the association between extent of resection, as evaluated using the Simpson classification, and recurrence-free survival (RFS) of patients after meningioma surgery. A total of 458 patients were eligible for analysis. Overall tumor recurrence rates for Simpson resection Grades I, II, III, and IV were 5%, 22%, 31%, and 35%, respectively. Patients undergoing Simpson Grade I and II resections had significantly better RFS compared to patients undergoing Grade III and IV resections (P = 0.005). Extent of resection had a significant effect on recurrence rates for both skull base (P = 0.047) and convexity (P = 0.012) meningiomas. Female sex and Karnofsky Performance Scale score > 70 were also identified as independent predictors of RFS after resection of WHO Grade I meningioma. In the authors’ experience, Simpson grading system maintains its relevance and prognostic value, and can serve an important role for patient education.

Contributed by Mazda K Turel


Posttraumatic seizure (PTS) is a common complication following traumatic brain injury (TBI), and both levetiracetam and phenytoin have been used for seizure prophylaxis.

The authors performed a systematic review and meta-analysis to compare levetiracetam with phenytoin for seizure prophylaxis in patients with severe TBI. A random effects meta-analysis was performed. Out of 6079 articles addressing this topic, only 7 met the inclusion criteria. A total of 1186 patients were included. The seizure frequency was 35 of 654 (5.4%) in the levetiracetam cohort and 18 of 532 (3.4%) in the phenytoin cohort. Meta-analysis revealed no difference in the rate of early PTS with levetiracetam compared with phenytoin (relative risk, 1.02; 95% confidence interval, 0.53-1.95; P = 0.96). On the basis of currently available evidence, both levetiracetam and phenytoin can be used for post-traumatic seizure prophylaxis, and the incidence of PTS is similar with both medications.

Contributed by Mazda K Turel


The aim of this study was to see the difference between cranioplast using titanium and autologous bone for patients with skull defects following decompressive surgery. Sixty-four patients were enrolled and randomized to receive either their own bone, or a primary titanium cranioplasty. Primary and secondary outcome measures were assessed at 1 year after cranioplasty. There were no primary infections in either arm of the trial. There was no partial or complete cranioplasty failure at 12 months of follow-up in the titanium cranioplasty group (P = 0.002), and none needed revision (P = 0.053). There were 2 deaths unrelated to the cranioplasty, one in each arm of the trial. Of the 31 patients who underwent autologous cranioplasty, 7 (22%) had complete resorption of the autologous bone. Partial or complete autologous bone resorption appeared to be more common among younger patients than older patients (32 vs 45 years old, P = 0.013). The total cumulative cost between the 2 groups was not significantly different. The authors concluded that primary titanium cranioplasty should be considered for young patients who require reconstruction of the skull vault following decompressive craniectomy, as there was a high
rate of bone resorption in patients with autologous bone cranioplasty.

Contributed by Mazda K Turel


Gamma knife radiosurgery (GKRS) is one of the alternatives for the treatment of classical trigeminal neuralgia (TN). The authors analyzed long-term outcomes for 117 patients with medically refractory TN, treated with GKRS. Mean maximum dose was 86.5 Gy (range: 80-90 Gy; median: 90 Gy). Clinical response was defined based on the Burchiel classification. The authors considered classes I and II as a complete response, while for toxicity, they used the Barrow Neurological Institute facial numbness scale. All the patients had a minimum follow-up of 2 years, and the mean duration of follow-up was 66 months (range: 24-171 months). Complete response at last follow-up was seen in 81% of patients, with an excellent response while off medication prior to GKRS in 52%. Pain-free rates without medication (class I) were 85% at 3 years, 81% at 5 years, and 76% at 7 years. Complete response rates (classes I-II) were 91% at 3 years, 86% at 5 years, and 82% at 7 years. Poor treatment response rates differed significantly among patients who had undergone previous surgery and were refractory to management with medication prior to GKRS. New or worsening facial numbness was reported in 32.5% (30% score II and 2.5% score III) patients. However, there was no patient with anesthesia dolorosa. Permanent recurrence pain rate was 12%. The authors concluded that GKRS achieved favorable outcomes compared with surgery in terms of pain relief and complication rates, notwithstanding decreasing pain-free survival rates over time.

Contributed by Mazda K Turel


Ependymoma is the third most common pediatric brain tumor. Posterior fossa ependymoma comprises of two distinct molecular variants termed (ependymoma posterior fossa A and B) EPN_PFA and EPN_PFB, both of which have distinct biology and natural history. The authors investigated the effect of cytoreductive surgery and radiation therapy for patients with posterior fossa ependymoma, after accounting for the molecular subgrouping. Four independent non-overlapping retrospective cohorts of posterior fossa ependymomas were profiled using genome-wide methylation arrays. A total of 820 patients were analyzed. In this multicentric risk stratification study of 850 cases with posterior fossa ependymomas, the authors reported that the molecular subgroup is a powerful independent predictor of outcome. The prognosis of incompletely resected EPN_PFA ependymomas was very dismal, with a 5-year progression free survival range of 26.1% to 56.8% across all four cohorts. A large proportion of patients with EPN-PFB could be cured with surgery alone, while those with recurrence in this group could be treated with delayed external-beam radiation. On the other hand, first-line (adjuvant) radiation is beneficial for completely resected EPN_PFA. Though both the subgroups were helped by the increased extent of resection, subtotally resected EPN-PFA group (usually in infants) had dismal survival rates despite adjuvant external beam radiation therapy (EBRT). In contrast, patients with EPN-PFB (usually adults and children 10-17 years of age) had excellent progression free survival after gross total resection. They might be considered for observation alone regimen and adjuvant EBRT only at the time of relapse.

Contributed by Manjul Tripathi


At present, ultrasonography is the main diagnostic radiologic investigation for detection of fetal abnormalities. However, in-uteru MRI (iuMRI) has shown great promise as an adjunct to ultrasound in the prenatal diagnosis of fetal brain abnormalities. The author performed a multicenter, prospective cohort study in the United Kingdom, in 16 fetal medicine centers. The authors performed iuMRI in pregnant women with gestational age of 18 weeks of more, in whom ultrasound was suspicious of fetal brain abnormality. iuMRI was performed within 14 days of ultrasound. The cohort was divided between women of gestational age between 18-24 weeks (n = 369) and those of gestational age of 24 weeks or more (n = 201). iuMRI improved the diagnostic accuracy by 23% in 18 weeks to 24 weeks group, by 29% in the 24 weeks and older group (P < 0.0001 in both groups). The overall diagnostic accuracy was 68% for ultrasound, and 93% for iuMRI. iuMRI provided additional diagnostic information in 49%, changed prognostic information in 20%, and led to changes in clinical management in more than 33% cases. It also shows a high patient comfortability rate of >95%. Routine use of iuMRI in patients with suspected brain anomalies on ultrasonography would help in better patient counseling and management decisions including but not limited to continuation of pregnancy. Hence, the authors concluded that iuMRI improved the diagnostic accuracy for detection of fetal brain abnormalities significantly, and can lead to management changes.

Contributed by Manjul Tripathi


Olympic athletes are the symbol of strength, endurance, discipline and physical valor throughout the world. They are considered to be healthy and capable of performing extreme physical activity. The authors conducted this study to assess the prevalence and the type of cardiovascular abnormalities in selected Olympic athletes. They evaluated 2352 athletes...
Reversible cerebral vasoconstriction syndrome (RCVS) remains under-diagnosed, and factors predicting poor outcome in these patients have not been identified. Corticosteroids have had a controversial role in the management of RCVS. In this single-center, large retrospective series of 162 patients with RCVS (78% women), authors aimed at delineating the factors that prevailing diagnostic methodology such as physical examination and 12 lead electrocardiogram are not sufficient to diagnose all CV anomalies and needs supplementation with an echocardiogram. The screening methodology needs to be broad, and tailored as per requirement of the athletes.

**Contributed by Aastha Takkar**


Creutzfeldt-Jakob Disease (CJD) is a fatal neurodegenerative disease. The diagnosis of CJD is difficult, and there is a need for a non-invasive diagnostic test for the same. A previous report described the detection of abnormal prion protein in the urine of patients with variant CJD (vCJD) using protein misfolding by cyclic amplification. In this retrospective, cross sectional study, adaptation of the direct detection assay (developed originally as a blood test for vCJD) was used to detect disease-associated prion protein in urine samples from patients with sporadic CJD (sCJD). Anonymized urine samples from healthy non-neurological controls (91), patients with non-prion neurodegenerative diseases (34) and patients with prion disease (37) were studied. Of these 37 patients, 20 had sCJD. A total of 162 samples were analysed, including those from 91 normal controls, 34 from neurological disease controls and 36 from patients with prion disease. The assay’s specificity for prion disease was 100% with no false-positive reactions from 125 control individuals. This is probably the first demonstration of an assay that can detect sCJD infection in urine or any target analyte outside of the central nervous system. This can pave way for a rapid molecular diagnostic test for sCJD, and can also have implications for other neurodegenerative diseases.

**Contributed by Aastha Takkar**


Reversible cerebral vasoconstriction syndrome (RCVS) remains under-diagnosed, and factors predicting poor outcome in these patients have not been identified. Corticosteroids have had a controversial role in the management of RCVS. In this single-center, large retrospective series of 162 patients with RCVS (78% women), authors aimed at delineating the factors predicting a poor outcome. Persistent clinical worsening was noted in 14% patients at 6.6 ± 4.1 days after symptom onset, radiologic worsening in 27% patients (mainly new infarcts) and angiographic progression in 15% patients. Angiographic progression translated into clinical worsening. While infarction on baseline imaging predicted a poor outcome, prior serotonergic antidepressant use and intra-arterial vasodilator therapy predicted clinical and angiographic worsening. Intra-arterial vasodilator therapy was offered only to very poor cases. Interestingly, glucocorticoid treatment proved to be an independent predictor of clinical, imaging, and angiographic worsening and poor outcome. Out of the 23 patients with clinical worsening, 17 had received glucocorticoids. No significant differences were observed in baseline brain lesions and angiographic abnormalities between glucocorticoid-treated and untreated patients. Early diagnosis and prompt treatment is the key to management of patients with RCVS. Clinicians should be aware of iatrogenic factors such as glucocorticoid exposure, which may contribute to worsening.

**Contributed by Aastha Takkar**


In tetraplegic patients, damage to spinal pathways limits the corticomotor drive from motor cortex to spinal motor neurons. Corticomotor priming increases the descending drive, and hence can potentially increase the corticospinal transmission through the remaining spinal pathways, thus resulting in increased grip strength. This randomized study included 49 participants with chronic (>1 year) tetraplegia. It was aimed to assess changes in grip (precision, power) force and tactile sensation associated with two different corticomotor priming approaches and a conventional training approach. Participants were randomized to either of the corticomotor priming approaches: functional task practice plus peripheral nerve somatosensory stimulation (FTP + PNSS) or PNSS alone, or to conventional exercise training (CET). In a subset or patients, pre-intervention corticospinal excitability (CSE) of the thenar muscles was also assessed. Participants were trained 2 hours/day, 5 days/week for 4 weeks. Thirty-seven participants completed the study. Significant improvements in precision grip force were observed in both the stronger and weaker hand in the FTP + PNSS group and significant improvements in weak hand precision grip force were associated with both PNSS and CET. Change in precision grip strength correlated with measures of baseline CSE. The authors concluded that corticomotor priming with FTP + PNSS has the greatest influence in improving grip strength, and the results were better than those observed with conventional exercise training.

**Contributed by Aastha Takkar**


Huntington disease is a progressive neurodegenerative disease. At present, there is no disease modifying therapy available to halt the progression of the disease. Coenzyme Q10 is an antioxidant that improves oxidative phosphorylation. This multicentre trial enrolled 609 patients of early stage Huntington disease at 48 sites in United States, Canada and Australia.
Patients were randomized to receive high dose coenzyme Q10 (2400 mg/day) or placebo and were followed for a period of 60 months to document any change in 'Total Functional Capacity Score' (for patients who survived) combined with 'time to death' (for patients who died). No statistically significant differences were seen between treatment groups for the primary or secondary outcome measure. The trial was prematurely concluded for reasons of futility. The authors concluded that there was no evidence to support the use of coenzyme Q10 as a treatment to slow functional decline in Huntington disease.

Contributed by Sahil Mehta

Chen CB, et al. Risk and association of HLA with oxcarbazepine-induced cutaneous adverse reactions in Asians. Neurology 2017;88;78-86

The authors performed this trial to investigate the genetic associations of Oxcarbazepine-induced cutaneous adverse reactions (OXC-cADRS), including Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), in Asian population. They investigated the carrier rate of HLA-B*15:02 and HLA-A*31:01 of the patients with OXC-cADRS and compared them to OXC-tolerant controls. The authors prospectively enrolled 50 patients with oxcarbazepine induced cutaneous adverse reactions, including 20 with Steven Johnson Syndrome (SJS) and 6 of drug reaction with eosinophilia and systemic symptoms. The patients were enrolled in Taiwan and Thailand from 2006 to 2014 and were analysed for clinical course, latent period, drug dosage, organ involvement, complications as well as carrier rate of HLA –B*15:02 and HLA-A*31:01. The incidence of oxcarbazepine related SJS was compared with that of carbamazepine induced SJS. The authors found that oxcarbazepine related cutaneous reactions were of less severity. There was a significant association between HLA-B*15:02 and oxcarbazepine related SJS (OR 27.90). HLA –A 31:01 was not associated with SJS. The positive and negative predictive values of HLA-B*15:02 for OXC-SJS/TEN were 0.73% and 99.97%, respectively. The incidence and mortality of OXC-related SJS was lower than carbamazepine induced SJS. The authors concluded that HLA-B 15:02 is significantly associated with oxcarbazepine related SJS in Asian populations. However, the severity and incidence of oxcarbazepine related SJS was less than that of carbamazepine related SJS.

Contributed by Sahil Mehta


The study reports a randomized, double blind, placebo-controlled trial of amitriptyline (1 mg/kg/day), topiramate (2 mg/kg/day), and placebo in children and adolescents (8 to 17 years of age) with migraine. The primary outcome was a relative reduction of 50% or more in the number of headache days, in the comparison of the 28-day baseline period with the last 28 days of a 24-week trial. Secondary outcomes were headache-related disability, headache days, number of trial completers, and serious adverse events that emerged during treatment. A total of 361 patients were randomized, 132 in the amitriptyline group, 130 in the topiramate group, and 66 in the placebo group. The trial was terminated early for futility after an interim analysis. There were no significant between-group differences in the primary outcome between the active agents and placebo. The primary outcome of 50% or more reduction in the headache days occurred in 52% of the patients in the amitriptyline group, 55% of those in the topiramate group, and 61% of those in the placebo group. Adverse events were more in the active agent groups. This included fatigue (30% vs. 14%) and dry mouth (25% vs. 12%) in the amitriptyline group and paresthesia (31% vs. 8%) and weight loss (8% vs. 0%) in the topiramate group. The study documents the powerful placebo effect in migraine therapeutics.

Contributed by Srijithesh P.R. and Sahil Mehta


The study reports long term outcome of surgery for nonlesional neocortical epilepsy done for patients with normal MRI. They also aimed to identify the prognostic factors in these patients. The study included 109 patients who underwent surgical resection for drug-resistant neocortical epilepsy. In all these patients, the lesion was not identifiable by magnetic resonance imaging (MRI). It excluded patients who underwent functional hemispherectomy, corpus collosotomy, or those who had hippocampal sclerosis on MRI, or had medial temporal ictal onset area during the intracranial electroencephalographic (EEG) studies. At 1 year after surgery, 54.1% of patients achieved seizure freedom and one third of patients had seizure freedom without requirement of antiepileptic drugs. At the last follow-up, 59.3% of patients achieved seizure freedom. The favorable factors influencing surgical outcome were localizing patterns in functional neuroimaging like PET or SPECT, concordant results in pre-surgical diagnostic evaluations, and complete resection of areas of ictal onset during the intracranial electroencephalographic study.

Contributed by Srijithesh P.R.


Periodic discharges (PD) are the most common EEG phenomenon of unclear significance. They do not meet the criteria for seizures. Invasive monitoring in comatose patients with spontaneous subarachnoid hemorrhage (SAH) has revealed that electrographic seizures may be associated with adverse change in physiological parameters like partial pressure of oxygen in interstitial brain tissue (PbtO2), elevation of intracranial pressure and compensatory increase in regional blood flow. Whether similar adverse metabolic crisis occur in PD is unclear. In this prospective study, the authors recruited 90 patients with high-grade subarachnoid hemorrhage, who underwent continuous EEG and invasive multimodality monitoring. They were evaluated for association between...
periodic discharges and adverse effects in parameters of multimodality monitoring, like partial pressure of oxygen in interstitial brain tissue (PbtO2) and regional cerebral blood flow. Of the 90 patients, 21 (23%) patients had PDs visible on depth EEG only, while 32 (36%) patients had PDs visible on both surface and deep EEG recordings. Frequencies of PDs on depth EEG recordings were correlated with the multimodality variables. Median PbtO2 was significantly lower at 14.4 mmHg for a PD frequency of 2.5 Hz and 14.7 mmHg for a PD frequency of 3.0 Hz when compared with PbtO2 at 0 Hz (23.4 mmHg). Correlation between PD frequency and median cerebral blood flow and median cerebral perfusion pressure did not reach statistical significance, although there was trend with respect to cerebral blood flow. The authors concluded that similar to the seizures, there is increase in cerebral blood flow in patients with PD to compensate for the increased metabolic demand, which may be inadequate in patients with high frequency (>2 Hz) PDs.

Contributed by Srijithesh P.R.


Neuromyelitis optica spectrum disorders (NMOSDs) involve antibodies against water channels, aquaporin-4, which are highly expressed in area postrema syndrome located in the dorsal medulla. Area postrema syndrome, characterized by unexplained hiccough, nausea and vomiting is one of the core characteristics of the new diagnostic criteria for NMOSDs. In this retrospective records review, the authors evaluated whether the longitudinally extensive cervical cord lesions extending to dorsal medulla were specific to NMOSDs. The clinical records and MRIs of patients with cervical spinal cord lesions were assessed from 1996 to 2014. For the patients with involvement of dorsal medulla on MRI, the medical records were evaluated for symptoms of area postrema syndrome. Of the 236 case records analyzed, 180 patients had NMOSDs and 56 had other etiologies. Extension to dorsal medulla was noted in 47 cases (19.9%). There was no difference in the proportion of cases with extension of the lesion to dorsal medulla between NMOSDs and other etiologies (19% vs 21%; P = 0.44). Among the patients with extension to or involvement of dorsal medulla, a higher proportion of patients with NMOSDs had intractable nausea and vomiting, compared to other etiologies (51% vs 0%; P < 0.05; odds ratio, 23.6; 95% CI, 1.3-430.4). The authors concluded that if a spinal cord lesion extending to dorsal medulla is accompanied by intractable nausea and vomiting, it is highly specific for AQP-4 IgG–seropositive NMOSD.

Contributed by Srijithesh P.R.


Mechanical thrombectomy (MT) has been shown to improve outcomes in patients with acute ischemic stroke (AIS) with large vessel occlusion. However, it is not clear whether addition of intravenous thrombolysis (IVT) prior to MT gives any additional benefits. The authors did a posthoc analysis of data of 291 patients from two randomized controlled trials that evaluated MT for AIS, namely Solitaire with the Intention for Thrombectomy (SWIFT) and Solitaire Flow Restoration Thrombectomy for Acute Revascularization (STAR). They compared the outcomes of patients who underwent combined IV thrombolysis and mechanical thrombectomy (160, 55%) versus those who underwent mechanical thrombectomy alone (131, 45%). The outcome parameters were successful reperfusion, functional independence defined as modified Rankin scale score of 0-2, mortality at 90 days and symptomatic intracranial hemorrhage. The demographic parameters, NIHSS scores, and time from onset to groin puncture were similar in both the groups. There was no statistically significant difference between any of the outcome parameters. The reperfusion rates, functional independence at 90 days, mortality and embolization to new territory was similar in both groups, while vasospasm was higher in patients who had IVT plus MT as compared to MT alone. There was no difference in the symptomatic hemorrhage rates between the two groups. The authors concluded, that in view of these results, a randomized trial is warranted to provide conclusive evidence.

Contributed by Srijithesh P.R.


Myelin oligodendrocyte glycoprotein (MOG) is expressed at the lamellae of the myelin sheath in the central nervous system, and is used as an immunogen for experimental autoimmune encephalomyelitis (EAE). Although experimental models were suggestive, MOG has not been associated with any human autoimmune disease with distinct clinical characteristics until now. However, it was found in association with many other neuroimmunological diseases. This retrospective study reports the association of MOG antibody in the CSF in four patients with unilateral cortical encephalitis in an adult cohort of patients with steroid-responsive encephalitis of unknown etiology. The symptoms were generalized seizures with or without abnormal behaviour or consciousness. Two patients also developed benign optic neuritis. All the patients had unilateral hemispheric cortical hyperintense lesions in fluid-attenuated recovery (FLAIR) imaging. These MRI changes were not seen in any of the MOG antibody–negative patients. Other encephalitis-related autoantibodies, like aquaporin-4, glutamate receptor, and voltage-gated potassium channel antibodies were negative in the index patients. All the patients responded to high-dose methylprednisolone. The study warrants further prospective studies evaluating the association of MOG antibodies in the disease phenotype described.

Contributed by Srijithesh P.R.

Neurofibrillary pathology composed of tau protein is correlated with cognitive impairment in patients with Alzheimer’s disease (AD), and thus immunotherapy targeting the pathological tau proteins is an attractive strategy for the treatment of AD. The authors conducted the first human trial with this vaccine, in this phase 1, randomised controlled, double blind, placebo controlled study of the active vaccine against the pathological tau proteins, AADvac1. The primary endpoint was treatment related adverse events. Out of the 30 patients who received the tau vaccine AADvac1, 29 developed IgG immune response. Two patients withdrew due to side effects, and no patient developed any features of meningoencephalitis or vasogenic edema. The commonest side effect was injection site reaction. The authors concluded that AADvac1 had a favourable safety profile, and the immunogenicity was good in this first human study.

Contributed by Ravi Yadav


The authors investigated the effectiveness and cost-effectiveness of a brief psychological treatment (Health Activity Program, HAP) delivered by lay counsellors to the patients with moderately severe to severe depression. This was a randomised controlled trial, and patients scoring more than 14 on the patient health questionnaire 9, indicating moderately severe or severe depression, were recruited. HAP was delivered by lay counsellors, and patients were randomized into those who received enhanced usual care (EUC) combined with HAP, and those who received EUC alone. A total of 495 patients were recruited in the trial, 247 to the EUC plus HAP group and 248 to the EUC group alone. Participants in the EUC plus HAP group had significantly lower symptom severity and higher remission rates as compared to the participants with EUC alone. There was an 87% chance of this treatment being cost-effective in the study setting. The authors concluded that HAP delivered by lay counsellors plus EUC was better than EUC alone for patients with moderately severe to severe depression in routine primary care.

Contributed by Ravi Yadav


The authors conducted a phase 3 randomised, double blind, noninferiority trial to assess the efficacy, safety and tolerability of lacosamide as a first-line monotherapy for adults with newly diagnosed epilepsy. The authors recruited 888 patients from Europe, North America and Asia Pacific region with newly diagnosed epilepsy. The patients were assigned in 1:1 ratio to either the lacosamide monotherapy or controlled release carbamazepine twice daily. The primary outcome measure was freedom from seizure for 6 months after stabilization at the last assessed dose. The predefined noninferiority criteria were -12% absolute and -20% relative difference between the treatment groups. In the final analysis set, seizure freedom at 6 months following dose stabilization was achieved in 327 patients (74%) in the lacosamide group and in 308 (70%) in the carbamazepine group. The proportion of patients in the full analysis set predicted by the Kaplan-Meier method to be seizure-free at 6 months was 90% taking lacosamide and 91% taking carbamazepine, thereby achieving the predefined non-inferiority criteria when compared to carbamazepine. Serious treatment-emergent adverse events were seen in 32 (7%) patients with lacosamide and 43 (10%) patients with carbamazepine. Based on these results, the authors concluded that lacosamide might be useful as first line monotherapy in adult patients with newly diagnosed epilepsy.

Contributed by Ravi Yadav and Sahil Mehta


This study assessed the effectiveness and cost-effectiveness of Counselling for alcohol problems (CAP), a brief psychological treatment in patients with harmful drinking in primary health care settings in a village in Goa. This psychological treatment was delivered by lay counsellors to patients with harmful drinking, who attended routine primary health-care settings. The authors recruited male harmful drinkers, defined by an Alcohol Use Disorders Identification Test (AUDIT) score of 12–19, who were aged 18–65 years from ten primary health centres in Goa, India. Participants were randomly allocated (1:1) to enhanced usual care (EUC) alone, or EUC combined with CAP. Primary outcomes were remission, AUDIT score of less than 8 and mean daily alcohol consumption for 14 days. Out of the 377 patients included in the study, 188 received CAP treatment plus usual care, while 190 received usual care. Out of these participants, 336 (89%) completed the 3 month primary outcome assessment (164 in the EUC plus CAP group and 172 in the EUC alone group). The proportion of participants with remission was 36% in the CAP plus EUC group, compared to 26% in the EUC alone group (P < 0.01, CI 1.09-2.07), and the proportion abstinent in the past 14 days were 42% vs 18% (P < 0.0001). The authors concluded that CAP delivered by lay counsellors plus the usual care was better than usual care alone was, for harmful drinkers in routine primary health-care settings and suggested that it also could be cost effective.

Contributed by Ravi Yadav

In this multicentric randomized control trial, the authors evaluated the effect of induced hypothermia on neurological outcomes in patients with convulsive status epilepticus. A total of 268 patients on mechanical ventilation with convulsive status epilepticus were recruited in the trial. Out of these, 138 patients were subjected to hypothermia (32 to 34°C for 24 hours) in addition to standard care, while 130 patients received standard care alone. The primary outcome was Glasgow Outcome Scale of 5 (minimal or no neurological deficit). There was no difference between the hypothermia group and the control group with regard to the primary outcome. At 90 days, 49% of the patients in hypothermia group and 43% of the patients in control group had GOS of 5 (P = 0.43, Adjusted OR 1.22, 95% CI 0.75-1.99). Among the different secondary outcome measures, only the progression to EEG-confirmed status epilepticus on the first day was lower in the hypothermia group as compared to the controls (11% vs. 22%; P = 0.009). Other secondary outcome measures, including mortality at 90 days, refractory status epilepticus, status epilepticus refractory to general anesthesia, and functional sequelae were similar in both the groups. There were more adverse events in the hypothermia group.

The authors concluded that addition of induced hypothermia to the standard therapy did not result in significantly better outcomes in patients with convulsive status epilepticus compared to standard therapy alone.

Contributed by Kuntal K Das


The Pragmatic Ischaemic Thrombectomy Evaluation (PISTE) trial was a multicentre, randomized controlled clinical trial comparing intravenous thrombolysis (IVT) alone with IVT and intra-arterial mechanical thrombectomy (MT) in patients with acute ischemic strokes with large vessel occlusion in anterior circulation. The target interval time between start of IVT to arterial puncture for mechanical thrombectomy was less than 90 minutes. The primary outcome measure was patients achieving functional independence, as defined by modified Rankin scale (mRS) 0-2 at 90 days. There were 65 patients enrolled in this trial, and median NIHSS score was 16. In the intention to treat analysis, there was no difference in the primary outcome of the patients (mRS 0-2, adjusted OR 2.12, 95% CI 0.65-6.94, P = 0.20). However, the proportion of patients with full neurological recovery (mRS 0-1) was larger in the MT group (OR 7.6, 95% CI 1.6-37.2, P = 0.010). In the per-protocol analysis (n = 58), the primary and most secondary clinical outcomes significantly favored MT (absolute difference in mRS 0-2 of 22%, adjusted OR 4.9, 95% CI 1.2-19.7, P = 0.021). The authors concluded that even though MT did not affect disability free survival, early MT after IVT in patients with large vessel occlusion was safe and provided excellent clinical outcomes. In the per protocol population, MT also improved disability-free survival.

Contributed by Kuntal K Das


In this study on the dataset of ESCAPE trial (Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing CT to Recanalization Times), the authors aimed to determine whether the trajectory of neurological improvement after stroke treatment could predict the 90-day functional outcome. The stroke severity of the included patients was assessed at baseline, and 1, 2, 5, 30, and 90 days post stroke using the National Institute of Health Stroke Severity (NIHSS) Scale. The functional outcome of the patients was assessed at baseline, 30 days, and 90 days, using modified Rankin Scale. Patients were grouped into different subgroups based the longitudinal trajectories of NIHSS measured over the first 2, 5, and 30 days. Other variables such as baseline NIHSS, infarct volume, 24-hour change in NIHSS and disease severity trajectory subgroups for predicting 90-day outcome were analyzed using logistic regression analysis. The trajectory model of the 2-day longitudinal NIHSS data revealed 3 distinct subgroups of NIHSS trajectories—large improvement (41.6%), minimal improvement (31.1%), and no improvement (27.3%) subgroups. Individuals in the large improvement group were more likely to have good outcome at 90 days, as compared to those in the minimal or no improvement subgroup. Among all the above-mentioned variables, the 2-day trajectory subgroup predicted the 90-day modified Rankin Scale with an accuracy of 84.5%. Thus, the authors concluded that 2-day longitudinal NIHSS trajectory was a better predictor of 90 day functional outcome as compared to the other commonly used variables.

Contributed by Kuntal K Das

Hänggi D, et al. Randomized, open-label, phase 1/2A study to determine the maximum tolerated dose of intraventricular sustained release nimodipine for subarachnoid hemorrhage (NEWTON [Nimodipine Microparticles to Enhance Recovery While Reducing Toxicity After Subarachnoid Hemorrhage]). Stroke 2017; 48: 145-151

This randomized, open-label, phase 1/2a, dose-escalation study of intraventricular sustained-release nimodipine (EG-1962) was performed to determine its safety, tolerability, pharmacokinetics, and clinical effects in aneurysmal subarachnoid hemorrhage. Patients with aneurysmal subarachnoid hemorrhage patients, who were either clipped or coiled, belonging to World Federation of Neurological Surgeons grade 2 to 4, and who
had an external ventricular drain placed during surgery, were enrolled in this trial. Fifty-four patients were randomized to receive EG-1962, while 18 patients received oral nimodipine. The patients were divided into 12 cohorts (6 each for two randomized groups) based on the administered dosage of the drugs as 100, 200, 400, 600, 800 and 1200 mg). The maximum tolerated dose of EG-1962 was 800 mg. There was one serious adverse event at 400 mg dose, and two dose-limiting toxicities with EG-1962 without any clinical sequelae. Unlike oral nimodipine, EG-1962 was not associated with drug-induced hypotension. The authors noted significantly higher rates ($P = 0.027$) of favorable outcome at 90 days on the extended Glasgow outcome scale with EG-1962. Moreover, there was lower incidence of delayed cerebral ischemia (31% vs 61%), and the need for rescue therapy (24 vs 56%) was also lower with EG-1962 therapy as compared to oral nimodipine. The authors concluded that EG-1962 was safe and could be tolerated upto 800 mg dose, and was associated with better clinical outcomes as compared to oral nimodipine therapy.

Contributed by Kuntal K Das


This prospective, observational, multimodality monitoring study was done to explore the use of diffusion tensor imaging (DTI) tractography for characterization and prognostication in patients with traumatic brain injury (TBI) and aneurysmal subarachnoid hemorrhage (aSAH). The study subjects included 20 patients of severe TBI and 23 patients of aSAH. These patients underwent whole brain DTI tractography at a median time of 12 days after injury or ictus. The parameters quantified were average fractional anisotropy, mean diffusivity, tract length, and the total number of reconstructed fiber tracts. These variables were compared between TBI and aSAH patients, and were correlated with mortality and 6-month functional outcome. Fractional anisotropy values ($P = 0.01$), total number of tracts ($P = 0.03$), and average tract length ($P = 0.002$) differed significantly between the survivors and the non-survivors. The results were consistent between TBI and aSAH patients for various DTI measures. Therefore, the authors concluded that DTI done at 12 days could act as a possible early biomarker in patients with severe TBI and aSAH, and could be used as an early endpoint for clinical studies, and as predictor of late mortality.

Contributed by Kuntal K Das


Progression of asymptomatic carotid stenosis in patients with >50% stenosis is predictive of stroke, and there is evidence of involvement of several microRNAs (miRNAs) in this process. This study looked at a wide panel of micro RNAs (miRNAs) in the peripheral blood exosomes of the patients with asymptomatic carotid artery stenosis (ACAS) to find out if some of these could predict progression of carotid stenosis. Sixty patients with ACAS with >50% luminal narrowing were included in the study. The authors initially determined miRNA expression profiles of the circulating exosomes using Affymetrix microarrays in the plasma samples of 16 patients. Thereafter, the most differentially expressed miRNAs in patients with ACAS progression were quantified in 39 patients utilizing the real-time polymerase chain reaction. The authors found that the expression of miR-199b-3p, miR-27b-3p, miR-130a-3p, miR-221-3p, and miR-24-3p was significantly higher in those patients with ACAS progression. The study concluded that specific circulating miRNA expression profiles could act as novel subclinical biomarkers and could predict the progression of ACAS, thus complementing the clinical monitoring for ACAS progression. This strategy could improve the therapeutic approaches to prevent ischemic stroke.

Contributed by Kuntal K Das

**Ellingson BM, et al. Baseline pretreatment contrast enhancing tumor volume including central necrosis is a prognostic factor in recurrent glioblastoma: evidence from single and multicenter trials. Neuro Oncol 2017;19: 89-98**

In this study, the authors aimed to determine the prognostic significance of the baseline contrast enhancing tumor volume prior to second- or third-line therapy in patients with recurrent glioblastoma. In total, 497 patients with recurrent GBM were included in this study, and the patient population was taken from two single-center sites of Toronto and Los Angeles, and two 2 phase II multicenter trials (AVF3708G, Bevacizumab ± Irinotecan, NCT00345163; XL184-201, Cabozantinib, NCT00704288). The volume of pretreatment contrast enhancing tumor, including central necrosis, was determined using T1 subtraction maps. Analysis was done both with continuous measure of baseline tumor volume, and with tumor dichotomized between large (>15cc) and small (<15cc). Baseline tumor volume was significantly predictive of OS ($P < 0.001$) both in the continuous and dichotomized measure of baseline tumor volume. This was independent of age and adjuvant treatment. On univariate analysis, significant differences of OS were found between large (≥15cc) and small (<15cc) tumors under all therapeutic scenarios, except for patients treated with cabozantinib who previously failed anti-angiogenic therapy. The authors concluded that baseline tumor volume was an independent predictor of overall survival in patients with recurrent GBM.

Contributed by Kuntal K Das


The authors conducted a randomised controlled, double-blind, parallel-arm, phase 3 study at 115 centres across 16 countries to assess the safety and efficacy of Leuco-methylthioninium bis (hydromethanesulfonate; LMTM) in modifying disease
progression in patients who suffer from mild to moderate Alzheimer’s disease. Out of the 891 participants, 357 patients were assigned to the control group (4 mg LMTM twice a day to maintain blinding with respect to urine or faecal discoloration), 268 patients to 75 mg LMTM twice a day, and 266 patients to 125 mg LMTM twice a day. The primary outcomes were progression on the Alzheimer’s Disease Assessment Scale–Cognitive Subscale (ADAS-Cog) and the Alzheimer’s Disease Co-operative Study–Activities of Daily Living Inventory (ADCS-ADL) scales from baseline assessed at week 65 in the modified intention-to-treat population. For both the outcomes, primary analyses did not show any benefit at either of the doses as compared to placebo. At both the high doses of LMTM, urinary and gastrointestinal adverse events were the commonest, and were also the most common cause of discontinuation. Reduction of haemoglobin was dose-dependent, and was the most common laboratory abnormality, though it was clinically non-significant. Amyloid-related imaging abnormalities were noted in less than 1% (8/885) of participants. The authors concluded that the results do not suggest benefit of LMTM as an add-on treatment for patients with mild to moderate Alzheimer’s disease.

Contributed by Anant Mehrotra


The authors conducted a multicentre, open-label, randomised trial over 102 hospitals, where they enrolled 377 children with infantile spasms and a hypsarrhythmic (or similar) EEG no more than 7 days before enrolment. Randomisation was done on 1:1 basis into either the hormonal therapy only group (n = 191), or to the hormonal therapy and vigabatrin group (n = 186). An additional randomisation (1:1) of type of hormonal therapy used (prednisolone or tetracosactide depot) was done. The minimum doses were intramuscular tetracosactide depot 0·5 mg (40 IU) on alternate days, or prednisolone 10 mg four times a day with or without vigabatrin 100 mg/kg per day. The primary outcome was cessation of spasms, which was defined as no witnessed spasms on and between day 14 and day 42 from trial entry, as recorded by parents and carers in a seizure diary. A total of 133 (72%) out of 186 patients on hormonal therapy with vigabatrin, and 108 (57%) of 191 patients on hormonal therapy alone, had no spasms between days 14 and 42 (difference 15·0%, 95% CI 5·1–24·9, P = 0·002). In 33 infants, there were serious adverse effects which necessitated admission (17 on hormonal therapy with vigabatrin and 16 on hormonal therapy alone). The authors concluded that hormonal therapy with vigabatrin is significantly more effective at stopping infantile spasms than hormonal therapy alone.

Contributed by Anant Mehrotra


The authors conducted a study on 5 cadavers for the feasibility and limitations of endonasal endoscopic surgery for approaching lesions in the anterior portion of the brainstem. The authors performed extended transphenoidal and transclival approaches to expose the brainstem, and also to perform white matter dissection through the endoscopic window. They found that sella limited the rostral exposure and pituitary transposition was necessary for exposure of the mesencephalon. Laterally, the exposure was limited by the cavernous carotid artery at the sellar level, by the petrous carotid artery at the petrous apex, and by the inferior petrosal sinuses toward the basion. Partial resection of the anterior arch of Cl and odontoid was needed for caudal exposure. In all the specimens, midline pons and medulla were exposed. Access to the peritrigeminal safe zone for gaining entry into the brainstem is limited medially by the pyramidal tract, with a mean lateral pyramidal distance (LPD) of 4·8 ± 0·8 mm. The mean interpyramidal distance was 3·6 ± 0·5 mm, which progressively reduced toward the pontomedullary junction. The small caliber of the medulla with very superficial corticospinal tracts left no room for a safe ventral dissection. The mean pontobasilar midline index averaged at 0·44 ± 0·1. The authors concluded that endoscopic endonasal approaches are best suited for midline pontine intraaxial tumors strictly anterior to the corticospinal tracts, or for exophytic lesions.

Contributed by Anant Mehrotra


In this study, the authors analyzed prospectively maintained database of 208 consecutive patients with basilar apex aneurysms between 2000 and 2012. Out of these 208 cases, 161 were managed by endovascular methods and 47 were managed microsurgically. A total of 116 patients (56%) had ruptured aneurysms. Ninety-two (57%) of the aneurysms treated with endovascular treatment were ruptured, while 24 (51%) of those treated with microsurgery were ruptured. The average Hunt and Hess grade was 2·4 (2·4 in the endovascular group and 2·2 in the microsurgical group; P = 0·472). Cranial nerve involvement and hemiparesis in the post-operative period was more commonly seen in the microsurgical group (55·3% vs 16·2%, P < 0·05; and 27·7% vs 10·6%, P < 0·05, respectively). However, aneurysm remnants and need for retreatment were more common in the endovascular than the microsurgical group (41·3% vs 2·3%, P < 0·05; and 10·6% vs 0·0%, P < 0·05, respectively). Rehemorrhage rates and average GOS score at discharge and 1 year after treatment were not statistically different between the two treatment groups. The authors concluded that as compared with microsurgically managed cases of basilar apex aneurysm, the rates of recurrence and need for retreatment was higher in the endovascular group. There was higher incidence of postoperative deficits in the microsurgical group, but at 1 year, there were no difference in the outcomes between both groups.

Contributed by Anant Mehrotra

Immune responses to antigen in the brain after stroke contributes to a poorer outcome. The authors hypothesized that splenectomy would reduce the immune response, thereby improving the outcome. Male Lewis rats (275-350g) underwent middle cerebral artery occlusion immediately after splenectomy or sham splenectomy. Immune response to myelin basic protein was determined at euthanasia at 4 weeks (672 hours). Infarct volume was determined in a subset of animals euthanized at 72 hours. Behavioral outcomes were assessed up to 672 hours. Splenectomy was associated with worse neurological scores early after stroke, but infarct size at 72 hours was similar in both groups. Behavioral outcomes and immune responses to myelin basic protein were also similar among splenectomized and sham-operated animals 672 hours after middle cerebral artery occlusion. The authors concluded that splenectomy has no benefit in improving outcomes following stroke.

Contributed by Anant Mehrotra