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Snippets from the Journals

Welcome to the second issue of the ASN Neurology Update. We know it can be difficult to stay on top of the latest research and discussion in the field of neurology. To save you time, we have highlighted the most topical recent articles to keep you up to date. We have also included papers published in reputed and indexed international journals by our own researchers. If you have comments to further improve this format please email us at: office@asn.lk

Co-editors Manjula Caldera
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Efficacy of rasagiline and selegiline in Parkinson's disease: a head-to-head 3-year retrospective case-control study.
Cereda E, Cilia R, Canesi M, Tesei S, Mariani CB, Zecchinelli AL, Pezzoli G.
J Neurol. 2017 May 26. doi: 10.1007/s00415-017-8523-y. [Epub ahead of print]

Data on long-term efficacy of MAO-B inhibitors are limited with no head-to-head comparison available to date. This case-control retrospective study analyzed data from patients with Parkinson Disease (PD) who attended the Parkinson Institute (Milan, Italy) over a 6-year period (2009-2015) and compared the effects of selegiline and rasagiline on levodopa treatment outcomes. Patients with PD treated with either selegiline (n = 85) or rasagiline (n = 85) for 3 years as well as a control group of patients (N = 170) who had never received MAO-B inhibitors, were matched for gender, disease duration (±1 year) and age (±1 year) at baseline assessment (ratio 1:1:2). The Unified PD Rating Scale and the Hoehn-Yahr staging system were used for clinical comparisons. At baseline, mean PD duration was 6.5 years and clinical features were comparable across all three groups. After a mean follow-up of approximately 37 months, no differences in clinical progression of motor and non-motor symptoms were observed between the 3 groups. However, MAO-B inhibitor use was associated with ~2-fold lower change in daily dose of levodopa ($p < 0.001$) and lower dyskinesia scores ($p = 0.028$) than non-users. No intra-class differences were observed between selegiline and rasagiline.

Conclusion: Long-term use of MAO-B inhibitors resulted in a significant reduction in levodopa requirements and a lower frequency of dyskinesias in patients with PD. Selegiline and rasagiline had equal efficacy in controlling motor symptoms in PD patients on optimized therapy.

Individualised prediction model of seizure recurrence and long-term outcomes after withdrawal of antiepileptic drugs in seizure-free patients: a systematic review and individual participant data meta-analysis.
Lamberink HJ, Otte WM, Geerts AT et al.
Lancet Neurol. 2017 May 5. pii: S1474-4422(17)30114-X. doi: 10.1016/S1474-4422(17)30114-X. [Epub ahead of print]

One of the most frustrating aspects of epilepsy is the absence of indicators of the likelihood that, in the absence of medication, a seizure would happen on any given day. Thus, a dilemma is created—should medication be withdrawn if seizure freedom is achieved on antiepileptic drugs, despite not knowing whether epilepsy is still present? Lamberink and colleagues have shed some light on this question.
This was a systematic review and meta-analysis, which identified articles which reported on cohorts of patients with epilepsy who were seizure-free and had started withdrawal of antiepileptic drugs, using PubMed and Embase databases with a last update on Nov 6, 2014. Articles contained information regarding seizure recurrences during and after withdrawal. 45 studies with 7082 patients were identified; ten studies (22%) with 1769 patients (25%) were included in the analysis. Median follow-up was 5·3 years. Prospective and retrospective studies and randomised controlled trials were included.
Relapse occurred in 812 (46%) of 1769 patients; 136 (9%) of 1455 for whom data with regards to timing of relapse were available had seizures in their last year of follow-up, suggesting enduring seizure control was not regained by this time point. Independent predictors of seizure recurrence were epilepsy duration before remission, seizure-free interval before antiepileptic drug withdrawal, age at onset of epilepsy, history of febrile seizures, number of seizures before remission, absence of a self-limiting epilepsy syndrome, developmental delay, and epileptiform abnormality on electroencephalogram (EEG) before withdrawal. In 812 (46%) of 1769 patients, and 136 (9%) of 1455 patients overall were not seizure-free in their last year of follow-up, suggesting that reintroduction of antiepileptic drugs had failed to return them to a seizure-free state.

Conclusion: The concept of removing antiepileptic drugs at 2 years in all patients is an outdated and artificial construct, and should be discarded in favour of an individualised risk– benefit assessment for every patient.

Clinical manifestations of the anti-IgLON5 disease
Carles Gaig, Francesc Graus, Yarko Compta, et al.
Neurology. 2017 May 2;88(18):1736-1743. doi: 10.1212/WNL.0000000000003887. Epub 2017 Apr 5.

This retrospective study described the clinical presentations, main syndromes, Human Leucocyte Antigen (HLA) association and immunoglobulin G (IgG) subclass association in a newly described antibody, IgLON5.

The study was an analysis of 22 patients positive for IgGLON5. Median age of the patients was 64 (46-83). The presenting symptoms were sleep problems (8 individuals; 36%), gait problems (8;36%), bulbar dysfunction (3;14%), chorea (2;9%) and cognitive dysfunction (1;5%). After analyzing of the clinical features, 4 clinical syndromes were recognized. (1) a sleep disorder with parasomnia and sleep breathing difficulty (8,36%); (2) a bulbar syndrome including dysphagia, sialorrhea, stridor, or acute respiratory insufficiency (6,27%); (3) a syndrome resembling progressive supranuclear palsy (PSP-like) (5,23%); and (4) cognitive decline with/out chorea (3,14%). Eventually all the patients developed sleep related problems such as insomnia, parasomnia, sleep apnea or excessive daytime sleepiness. Association with HLA- DRB1*10:01 and HLA-DQB1*05:01 was demonstrated in 13/15 (87%) patients, while the prevalence of DRB1*10:01 allele was 36 times that of the general population. 16 patients had paired serum and CSF sample in which 14 had antibodies in both, and the remaining 2 only demonstrated serum IgLON5 and both had PSP-Like syndrome. 20 patients had IgG1 and IgG 4 antibodies.

Conclusion: Patients with IgLON5 disease present with sleep disorder preceded or accompanied by bulbar symptoms, gait problems, oculomotility problems, and, less frequently, cognitive decline and chorea. IgG4 subclass were prevalent than IgG1 and there is a strong association with the HLA-DRB1*10:01 allele.

Randomized controlled trial of deutetrabenazine for tardive dyskinesia: The ARM-TD study.
Hubert H. Fernandez, MD, Stewart A. et al.
Neurology. 2017 May 23;88(21):2003-2010. doi: 10.1212/WNL.0000000000003960. Epub 2017 Apr 26.

Tardive Dyskinesia (TD) is a disabling consequence of long-term use of dopamine antagonists. In more than 80% of patients, TD is irreversible even if the culprit drug is discontinued. There are limited therapeutic options for TD and tetrabenazine off label use is not conclusively recommended.

This was a randomized, double blinded, multi-center study aimed at determining the efficacy and safety of deutetrabenazine in TD.

117 patients with TD were randomized either to deutetrabenazine or placebo and the primary end point was reduction of Abnormal Involuntary Movement Score (AIMS) from baseline to week 12. Deutetrabenazine significantly reduced the AIMS score by 12 weeks. Both deutetrabenazine and placebo group did show low rates of psychiatric adverse effects such as anxiety (3.4% vs 6.8%), depression (1.7% vs 1.7%), and suicidal ideation (0% vs 1.7%). In addition no parkinsonism was noted as measured by Unified Parkinson Disease Scale (UPDRS) motor subscale.

Conclusion: Deutetrabenazine was well tolerated and significantly reduced abnormal movements in TD and this study provides class 1 evidence that deutetrabenazine effectively reduces AIMS score in TD.

Tenecteplase in ischemic stroke offers improved recanalization: Analysis of 2 trials.
Bivard A, Huang X, Levi CR et al.
Stroke. 2015 Sep;46(9):2541-8. doi: 10.1161/STROKEAHA.115.010180. Epub 2015 Aug 4.

Pooled clinical and imaging data from 2 phase 2 randomized trials comparing tenecteplase with alteplase allowed CT angiography (CTA) scans to be assessed centrally for occlusion status at baseline and at 24 hours post thrombolysis using the modified thrombolysis in cerebral infarction (TICI) scale. Twenty-four-hour poststroke NIH Stroke Scale (NIHSS) and 90-day modified Rankin Scale (mRS) scores were also compared between treatment groups using linear regression to generate odds ratios (ORs).
From 146 pooled patients, 69 had a TICI 0/1 occlusion overall at baseline. Tenecteplase-treated patients with a complete vessel occlusion had greater complete recanalization rates at 24 hours (71% for tenecteplase vs 43% for alteplase, $p < 0.001$). Patients with a TICI 0/1 occlusion who were treated with tenecteplase also showed greater early clinical improvement (median NIHSS change with tenecteplase was 9, interquartile range [IQR] 6, alteplase 1, IQR 1, $p = 0.001$) and higher rates of favorable 90-day outcomes (mRS 0-1 of tenecteplase compared with alteplase, OR 4.82, 95% confidence interval 1.02-7.84, $p = 0.05$).

Conclusion: Tenecteplase may offer greater recanalization efficacy compared to alteplase, possibly exaggerated in patients with complete vessel occlusions on baseline CTA.

Risks and benefits of clopidogrel–aspirin in minor stroke or TIA: Time course analysis of CHANCE
Pan Y, Jing J, Chen W, Meng X, Li H, et al.
Neurology. 2017 May 16;88(20):1906-1911. doi: 10.1212/WNL.0000000000003941. Epub 2017 Apr 19.

Data were derived from the Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events (CHANCE) trial. The primary outcome was a new ischemic stroke. Safety outcomes included any bleeding and moderate to severe bleeding. Time course analyses were performed for the outcomes of both stroke and bleeding. Results: A total of 204 new ischemic strokes occurred in the clopidogrel–aspirin group [145 (71.1%), 13 (6.4%), and 12 (5.9%) at the first, second, and third week, respectively], vs 295 in the aspirin alone group [223 (75.6%), 19 (6.4%), and 8 (2.7%) at the first, second, and third week, respectively]. A total of 23 (38.3%), 15 (25.0%), and 9 (15.0%) of 60 bleeding cases in the clopidogrel–aspirin group vs 15 (36.6%), 8 (19.5%), and 3 (7.3%) of 41 in the aspirin alone group occurred at the first, second, and third week, respectively. Clopidogrel–aspirin treatment numerically reduced the risk of ischemic stroke within the first 2 weeks. From the 10th day, the number of any bleeding cases caused by dual antiplatelets outweighed that of new stroke reduced by dual antiplatelets.

Conclusion: Clopidogrel–aspirin treatment may have a benefit of reducing stroke risk outweighing the potential risk of increased bleeding especially within the first 2 weeks compared with aspirin alone in patients with minor stroke or TIA.

Sri Lankan Corner
Studies by Sri Lankan researchers published in indexed international journals

Viral aetiologies of acute encephalitis in a hospital-based South Asian population
Lohitharajah J, Malavige N, Arambepola C, Wanigasinghe J, Gamage R, Gunaratne P, Ratnayake P, Chang T.
BMC Infect Dis. 2017 Apr 24;17(1):303. doi: 10.1186/s12879-017-2403-z.

This was a cross-sectional study conducted among 99 patients with encephalitis/meningoencephalitis admitted to 2 tertiary-care hospitals in Colombo. Cerebrospinal fluid and serum were tested for conventional and emerging encephalitogenic viruses. Specific nucleic acid amplification and antibody assays were used to identify viruses. Plaque reduction neutralization test was done to confirm the diagnosis of West Nile virus (WNV).

A viral aetiology was identified in only 27.3%. These included dengue virus (40.7%), Japanese encephalitis virus (25.9%), varicella zoster virus, WNV and probable Epstein Barr virus (11.1% each). None were positive for herpes simplex viruses or cytomegalovirus. Screening for bacterial aetiologies was negative for all patients. There were no distinguishable clinical or laboratory findings between the different viral aetiologies. The case fatality rate was 7%, which was higher among patients with an identified viral aetiology.

Conclusion: A viral aetiology was identified in only about a quarter of patients with encephalitis. Dengue virus accounted for the majority.