CLIPPINGS

Coronavirus infections in the nervous system of children: A scoping review making the case for long-term neurodevelopmental surveillance (*Pediatric Neurol. 2021;117:47-63*)

This scoping review included 31 studies illustrating nervous system involvement by SARS-CoV-2 virus and 21 studies describing neurological involvement by other human coronaviruses. 31 SARS-CoV-2 articles (27 case reports and 4 case series) portrayed a wide spectrum of neurological manifestations in children involving both central nervous system (ADEM, encephalitis, seizures, stroke) as well the peripheral nervous system (GBS, transverse myelitis). Another group of children presenting with neurological manifestations with COVID-19 were those with MIS-C (multisystem inflammatory syndrome in children) which were described in 8 case reports. The authors found a wide variability in duration of follow-up and extent of evaluation amongst these studies. This study raises a rational concern that these children are at risk of long-term neurodevelopmental deficits which may not be apparent before discharge or during early follow-up. A comprehensive list of signs of potential neuro-developmental impairment across various age groups is also provided by the authors. As underscored by this article, there is a critical need for long-term neuro-developmental follow-up of these children by attaching them to developmental clinics under the collaborative care of pediatricians, pediatric neurologists and child psychologists.

A double-blind randomized, placebo-controlled clinical study of trofinetide in the treatment of fragile X syndrome (*Pediatric Neurol. 2020;110:30-41*)

Fragile X syndrome (FXS) is a neuro-developmental disorder characterised by >200 CGG repeats in the FMR1 gene. It has a significant prevalence of about 1 in 4000 males and 1 in 6000 females and there is no approved drug therapy for this disorder currently. This randomised controlled trial evaluated safety and tolerability of trofinetide in 72 adolescent and adult males with FXS. Trofinetide is an oral drug which is an analogue of amino-terminal tripeptide of insulin-like growth factor (IGF-1) which is postulated to improve symptoms of FXS by reducing neuro-inflammation, normalize dendritic morphology, reduce microglia activation and astrogliosis. Subjects were randomized to receive 35 mg/kg and 70 mg/kg trofinetide vs placebo BID for 28 days. Both doses were well tolerated and were found safe. Higher dose trofinetide was found to be efficacious in reducing key symptoms of FXS. As the duration of study was short and sample size was limited, larger trials are required to explore the efficacy of this potentially promising drug.

Clinical and imaging features of children with autoimmune encephalitis and MOG antibodies (*Neurol Neuroimmunol Neuroinflamm. 2020;7:e731*)

MOG abs (myelin oligodendrocyte glycoprotein antibodies) have been described typically in childhood central nervous system demyelinating disorders. Recently, these antibodies have been reported to be associated with autoimmune encephalitis (AE) with MRI features such as cortical and deep grey matter involvement in children and adults. This study describes a cohort of 10 children with AE and MOG abs. They presented at a median age of 8 years (range: 4-16 years) with encephalopathy (10/10) and a combination of headache, seizures and focal neurologic signs. Contrary to demyelinating disorders, none of the children had white matter involvement except juxta-cortical signal alterations in 6/10 children while all had cortical and deep grey matter involvement. Eight out of 10 children were treated with high dose intravenous methylprednisolone pulse therapy for 3-5 days and 1 child was given IV immunoglobulins. Nine out 10 children had favourable outcome (modified rankin scale 1) at 4 weeks except one child who had a residual focal deficit and had not received immunomodulation at the time of acute illness. This study highlights the crucial need of testing for MOG abs in all the children presenting with autoimmune encephalitis and prompt treatment with immunomodulation in such cases which is pivotal for a favourable outcome.

Pharmacological and neurosurgical interventions for individuals with cerebral palsy and dystonia: A systematic review update and meta-analysis (*Dev Med Child Neurol. 2021;dmcn.14874*)

This systematic review and meta-analysis is an update to the previous systematic review up to December 2015, with 19 new studies identified from January 2016 to May 2020. This review included a total of 46 studies comprising 915 participants. Awareness about the evidence on anti-dystonia measures is crucial for all pediatric medicine practitioners as it is a very common co-morbidity in children with cerebral palsy and other chronic neurological disorders.

Very low certainty evidence was found for clonidine, BoNT (botulinum toxin), ITB (intra-thecal baclofen) and DBS (deep brain stimulation) as anti-dystonia measures. Little to no effect on dystonia was found in randomized as well as non-randomized studies for trihexiphenidyl, one of the most commonly prescribed drug for dystonia. No studies evaluating benzodiazepines, gabapentin and medical cannabis were found during the review period. Evidence for levodopa was limited to a single randomized crossover trial. A new publication has suggested improvement in dystonia with clonidine. This study also highlights that both pharmacological and surgical measure should be exercised with caution as trihexiphenidyl, clonidine, BoNT, DBS and ITB may increase the adverse events.

Safety and efficacy of tocilizumab versus azathioprine in highly relapsing neuromyelitis optica spectrum disorder (TANGO): an open-label, multicentre, randomised, phase 2 trial (*Lancet Neurol. 2020;19:391-401*)

This multicentric, phase 2 trial explored the efficacy of intravenous tocilizumab (8 mg/kg every 4 weeks) as compared to oral

azathioprine (2-3 mg/kg/day), which is the standard therapy for long term immunosuppression for patients with neuromyelitis optica spectrum disorder (NMOSD). This study enrolled 118 adults (59 in each arm) who were evaluated for time to first relapse as the primary outcome measure. Median time to first relapse was longer for tocilizumab vs azathioprine (78.9 weeks vs 56.7 weeks, *P*=0.0026) in full analysis set. Eighty nine percent of patients in tocilizumab group remained relapse free at the end of the study as compared to 56% in the azathioprine group in the per-protocol analysis. This study highlighted tocilizumab as a safe and efficacious choice for long term immunosuppression for patient with NMOSD. These findings need to be validated in pediatric age group with an adequate sample size.

JUHI GUPTA
juhiguptadr@gmail.com