observed in 19(36.5%). When analyzing its development, MTS was clearly more frequent in brain lesions affecting the temporal lobe (p = 0.0001), with some etiologies such a remote cerebrovascular disease/brain injury (p = 0.001) or an acute CNS infection (p = 0.014), with higher EMSE scores (p = 0.011), and when LPDs were present (p = 0.002); furthermore, we observed a tendency in older patients (p = 0.089). After a multivariate analysis, the factors predicting the development of MTS were the presence of a lesion in temporal lobe (p = 0.003), and specific etiologies: a remote cerebrovascular lesion or traumatic brain injury (p = 0.002) and an acute CNS infection (p = 0.031). In 43 patients, an acute MRI was also performed, 19 (44.2%) showed changes related to SE in DWR and 30 (69.8%) in T2; when MRI acute changes were included in regression, the presence of a lesion in temporal lobe (p = 0.046) and a remote vascular or traumatic lesion (p = 0.016) remained as predictors of MTS, in addition to the finding of acute post-SE changes in DWR (p = 0.091).

Conclusion: In SE patients, the development of MTS was related with specific etiologies and the location of the brain insult.

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Prolonged Seizures in Children

Clodagh Mitchell[a], Libby Dickson[a], Paul Leonard[b], Celia Brand[b], Ailsa McLellan[b], Jay Shetty[b]
[a]*University Of Edinburgh, Edinburgh, United Kingdom*
[b]*Royal Hospital for Sick Children, Edinburgh, United Kingdom*

Background: Prolonged seizures (PS) in children carry significant risk of morbidity and mortality. Previous work has predominantly focused on status epilepticus ≥30min but a new ILAE definition has been produced following evidence that seizures ≥5min are associated with negative outcomes. There has been increasing effort by clinicians and epilepsy specialist nurses to manage PS effectively through benzodiazepines, education and training. This study aims to provide population-based data on children presenting with PS and their outcomes.

Methods: All children presenting to accident and emergency (A + E) between 2011-2017 from a Scottish Children's hospital were identified (capture-recapture method with multiple datasets). Data was collated from electronic health records; including patient demographics, clinical characteristics, acute seizure management and outcomes. This data can be used to study long-term outcomes, including educational outcome, through national data linkage systems.

Results: There were 666 children (1234 seizure episodes). These accounted for 0.38% (95% CI (0.34-0.42%)) of A + E admissions. Yearly prevalence rate was 0.8 per 1000 children. The median age was 3.65 years (range 0-20 years) and 54% of children were male (95% CI (53.1-60.7%)). The median seizure duration was 10 minutes (range 5 to 195 minutes). PS incidence increased at the extremes of socioeconomic status and relationship with distance from A + E can be determined. Seizure duration, mortality and requirement for ventilatory support decreased compared to historical data. Data highlighted children with epilepsy and those in specialist education as two particularly at risk groups for recurrent prolonged seizures. There was a lower likelihood of hospital admission where buccal midazolam was administered.

Conclusions: Adverse outcomes have decreased and the use of buccal midazolam is promising. Identifying high-risk groups provides opportunity for early intervention. This data forms the basis for extensive evaluation of acute seizure management and monitoring long-term outcomes.

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Long-term Safety and Efficacy of Add-on Cannabidiol (CBD) Treatment in Patients with Lennox Gastaut Syndrome in an Open-label Extension Trial (GWPCARE5)

Richard Chin[a], Anup Patel[b], Antonio Gil-Nagel[c], Wendy Mitchell[d], M. Scott Perry[e], Arie Weinstock[f], Lauren Whyte[g], Kevan VanLandingham[h]
[a]*Royal Hospital For Sick Children, Edinburgh, UK*
[b]*Nationwide Children's Hospital, Columbus, USA*
[c]*Hospital Ruber International, Madrid, Spain*
[d]*Children's Hospital Los Angeles, Los Angeles, USA*
[e]*Cook Children's Medical Center, Fort Worth, USA*
[f]*Oishei Children's Hospital, Buffalo, USA*
[g]*GW Research Ltd, Cambridge, UK*
[h]*Greenwich Biosciences, Inc., Carlsbad, USA*

Background: Lennox-Gastaut syndrome (LGS) is a rare epileptic encephalopathy that is often treatment-resistant. The efficacy of cannabidiol (CBD) was demonstrated with an acceptable safety profile in two Phase 3 randomised controlled trials (RCTs): GWPCARE3 (NCT02224560) and GWPCARE4 (NCT02224690). A second interim analysis of the open-label extension (OLE) of the two RCTs was conducted to assess long-term safety and efficacy of add-on CBD treatment in patients with LGS.

Methods: Patients who completed a 14-week, double-blind, randomised controlled trial (GWPCARE3/NCT02224560; GWPCARE4/NCT02224690) could enter this OLE trial (GWPCARE5/NCT02224573). Patients received GW Pharmaceuticals' formulation of plant-derived highly purified CBD in oral solution (100 mg/mL) for ≤3 years. Primary endpoint was safety. Secondary endpoints were drop and total seizure frequency, and Subject/Caregiver Global Impression of Change (S/CGIC).

Results: Overall, 99% (366/368) of eligible patients with LGS entered the OLE trial. Median follow up was 61 weeks (3 days to 87 weeks); 88 patients (24%) withdrew. Mean age: 16 years; 33% ≥18 years; 54% male. Baseline median seizure frequency/28 days: 80 drop seizures; 168 total seizures. During the extended follow up, adverse event (AE) incidence: 94%; serious AE incidence: 33%; 11% discontinued owing to AEs. Most common AEs (≥20%): diarrhoea, convulsion, somnolence, pyrexia, vomiting and decreased appetite. Forty-seven patients (13%) had elevations in liver transaminases >3× upper limit of normal; 35 (74%) were taking concomitant valproate. There were 5 deaths; none deemed treatment-related by the investigator(s). Median percentage reductions in seizure frequency (12-week windows over 72 weeks): 48–70% for drop seizures; 48–63% for total seizures. Approximately 88% of patients/caregivers reported an improvement in overall condition on the S/CGIC at Weeks 24 and 48.

Conclusions: Long-term add-on CBD treatment had a similar AE profile to that observed in the core studies at 14 weeks. Reductions in drop and total seizure frequency and improvements in overall condition were maintained through 72 weeks.

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Responsive Neurostimulation Therapy for Super-Refractory Autoimmune Epilepsy

Anteneh Feyissa[a], William Tatum[a], Jeffrey Britton[b]
[a]*Mayo Clinic, Jacksonville, United States*
[b]*Mayo Clinic, Rochester, United States*

Background: Immunotherapy remains the cornerstone for treatment of autoimmune epilepsy; however, some remain super-refractory despite immunotherapy and anti-seizure medications (ASMs).

Methods: Case-series study of two patients with super-refractory AE treated with bilateral hippocampal responsive neurostimulation (RNS).

Results: Case 1: A 37 year-old woman presented with frequent (5-8/day) focal seizures with flushing and disabling chest pain of 4 years. Seizures are refractory to intravenous methylprednisolone and immunoglobulin and 9 ASMs. Serum autoimmune epilepsy panel was positive for Glutamic acid decarboxylase 65 (GAD65) antibody (250mg/dL). Brain MRI showed left mesial temporal sclerosis (MTS) and fluorodeoxyglucose positron emission tomography (fdg-PET) showed bitemporal hypometabolism. Evaluation for occult malignancy was negative. Bilateral independent temporal seizures were recorded. She was treated with RNS utilizing bi-hippocampal electrodes. Right hippocampal onset seizures were aborted within 8 weeks, however left hippocampal onset seizures were only reduced by 25%. At 18 months, she continued to experience seizures, albeit at reduced frequency.

Case 2: A 39 year-old woman presented with frequent focal and bilateral tonic clonic seizures. CSF was inflammatory but neuroimmunology panel was negative. Seizures are refractory to intravenous methylprednisolone and immunoglobulin, plasma exchange, Rituximab, Cyclophosphamide, and Azathioprine, 11 ASMs, and vagus nerve stimulation therapy. Brain MRI showed bilateral MTS. Screening for occult was unrevealing. Bilateral independent temporal seizures were recorded, and she was implanted with bi-hippocampal RNS electrodes. Within 8 weeks, seizure frequency was reduced by over 50%. Further, the RNS data disclosed catamenial clustering and led to the initiation of progesterone. At 6 months follow-up, she reported significant seizure reduction.

Conclusions: RNS has a role in the treatment of super-refractory autoimmune epilepsy. RNS helps track seizure burden objectively and may inform anti-seizure medication optimization in this patient population.

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Updated Data on the Tocilizumab Treatment in New Onset Refractory Status Epilepticus

Hyoshin Son, Soon-Tae Lee, Hye-Rim Shin, Eun-Young Kim, Woo-Jin Lee, Kon Chu, Kyung-Il Park, Sang Kun Lee
Department of Neurology, Seoul National University Hospital, Seoul, South Korea

Background: New onset refractory status epilepticus (NORSE) is defined by new onset status epilepticus (SE), showing no response to at least 2 anti-epileptic drugs (AEDs) without evidence of other structural, toxic, or metabolic causes in patients who have been otherwise previously healthy. As no clear etiology has been established for NORSE, autoimmune or paraneoplastic causes account for the majority of NORSE cases with an identifiable cause. Even though immunotherapies including steroid, immunoglobulin, and rituximab have been tried to treat NORSE, approximately 60% of the patients had poor functional outcomes, suggesting need of the next line of immunotherapy. With updated data on the tocilizumab treatment in NORSE patients, we investigated the therapeutic potential of the tocilizumab, interleukin-6 receptor inhibitor, as new candidate of immunotherapy for NORSE.

Methods: In this study, updated data on two additional NORSE patients were analyzed to the previous data published. In a prospective cohort for autoimmune encephalitis since June 1, 2012, of which patients who have been admitted to Seoul National University, the patients who were diagnosed with NORSE with poor response to conventional immune therapy including steroid, immunoglobulin, and rituximab and treated with tocilizumab from August 2015 to November 2018 were subjected to further analysis.

Results: Compared to the previous data of 7 SE patients, 7 out of 9 SE patients showed cessation of SE with a median interval of 5 days from the initiation of treatment. According to our data, patients who responded to tocilizumab tended to show either clinical or electrophysiological improvement at most within the second cycle of treatment, which means early response to treatment. Two patients experienced infection as adverse event after tocilizumab treatment, and one patient on updated data showed no response to tocilizumab even after two cycles of treatment.

Conclusions: Tocilizumab treatment resulted in cessation of SE in 7 out of 9 patients according to our results. Therapeutic effects of tocilizumab on SE patients who do not show definite response to conventional immunotherapy are to be further studied with alternative immunologic pathway, and further prospective study with larger number of patients is warranted.

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Combination therapy of immunoglobulin, Rituximab, and Tocilizumab in treating acute autoimmune encephalitis

Woo-jin Lee, Han-Sang Lee, Hye-Rin Shin, Eun-Young Kim, Hyoshin Son, Yong-Won Shin, Hyeyeon Chang, Soon-Tae Lee, Kyung-Il Park, Kon Chu, Sang Kun Lee
Seoul National University Hospital, Seoul, South Korea

Background: A considerable portion of autoimmune encephalitis (AE) does not respond to conventional immunotherapies and subsequently have poor outcomes. Tocilizumab, an anti- interleukin-6 antibody, has some effect on treating AE refractory to first-line immunotherapies and Rituximab. We aimed to determine the efficacy of the combination therapy of immunoglobulin (±steroid), Rituximab, and Tocilizumab (IsRT) in treating acute AE over conventional treatment options.

Methods: This institutional cohort included seventy-nine consecutive patients with antibody-proven AE. Acute treatment regimens were categorized as IsRT, IsR, and Is. Patients' clinical severity was assessed at every two weeks for the first three months, at every month for the next