Conclusion: There was a significant increase in responder rate with increasing plasma exposure of CBD and 7-OH-CBD. Positive correlations with AUC were determined for several AEs for both CBD and 7-OH-CBD. Results suggest that the observed reduction in drop seizures and onset of certain AEs are related to CBD and 7-OH-CBD exposure.

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EPILEPSY IN CHILDHOOD 1

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019 | Prospective Video EEG Tracking of Infants with Tuberous Sclerosis Complex (TSC) in the First Year of Life


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Purpose: To describe the epileptogenesis in TSC patients by studying serial video EEG recordings in the first year of life in the multicentre, prospective EPISTOP project.

Method: According to the EPISTOP protocol, infants aged up to 4 months with TSC, but without previous seizures were included. Serial video EEG’s during sleep and wakefulness were performed every 4–6 weeks and were analysed using an unformed scoring system describing the frequency and distribution of epileptiform discharges focal (A), multifocal in one (B) or in two (C) hemispheres, and hypsarrhythmia (D).

Results: At 1 year, 92.5% (87/94) had had at least one abnormal EEG showing epileptiform discharges or (sub-) clinical seizures. Already 80% (75/94) had an abnormal EEG at 4 months. The mean age at the first abnormal EEG was 73 days (SD 70). In 27% the first abnormal EEG showed focal epileptiform discharges (A) and in 71% it was already multifocally disturbed (25% score B and 46% score C). Hypsarrhythmia (D) was never seen as a first abnormal EEG pattern. In 2% the first abnormal EEG showed no interictal discharges but only (sub-) clinical seizures. In 63% (55/87) this epileptic activity was seen for less than 1% of the time. Per EPISTOP protocol some patients received antiepileptic treatment after appearance of epileptiform abnormalities in absence of clinical seizures. 54% (51/94) developed clinical or subclinical seizures during the first year of life. 27 (29%) of the infants developed seizures without preceding EEG abnormalities. 10/23 (43%) of infants with focal epileptiform EEG abnormalities developed seizures, compared to 37/62 (60%) of infants with multifocal epileptiform EEG abnormalities.

Conclusion: At 4 months, 80% of the TSC infants already had an abnormal EEG recording with multifocal discharges in the majority. The score of the first abnormal EEG did not predict the occurrence of (sub-)clinical seizures.

020 | Dravet Syndrome, PCDH19-Related Epilepsy and SCN1A-Related Epilepsies: Early Differential Diagnosis

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Introduction: Our aim is to compare electroclinical profile at onset and at short-term evolution in order to identify features allowing an early differentiation between Dravet syndrome (DS), PCDH19-related epilepsy (PCDH19-E), and SCN1A-related epilepsies (SCN1A-E).

Method: We analysed electroclinical and neuropsychological data of 44 patients (19 DS, 13 PCDH19-E, and 12 SCN1A-E) longitudinally followed at the Neuropsychiatry of Verona. Data were collected into the Italian National Registry of these conditions (RESIDRAS).

Results: Mean age at seizure-onset was lowest in DS (4.6 months), while in SCN1A-E group was 8.5 months and in PCDH19-E patients 10 months. One quarter of SCN1A-E group and PCDH19-E began before 5 months, although the range extends to 18 months. Fever was more frequent at onset in PCDH19-E. Status Epilepticus at onset was often present in both DS (63%) and SCN1A-E (40%). Seizures in cluster were present at onset in PCDH19-E and SCN1A-E group. Seizure semiology was variable in SCN1A-E, mostly focal in PCDH19-E, and unilateral or generalized clonic seizure in 63% of DS. Interval between the first and second seizure was shorter in DS in comparison with the other groups, however at single-subject level a short interval is the rule in DS but also possible in PCDH19-E and SCN1A-E. Psychomotor development at onset was normal in the totality of DS, in 92% of PCDH19-E and 83% of SCN1A-E. Epilepsy features and neuropsychological outcome at 3 and 6 years of age further allows distinction between the three groups.
Conclusions: Patients with PCDH19-E can be relatively easily differentiated from DS, due to distinctive features at clinical onset and in the short-term evolution. For the same reasons an early identification of DS is also possible in the majority of DS. However, in some cases, patients with DS and SCN1A-E have overlapping early features and only the follow-up will allow differential diagnosis.

021 | Seizure Frequency, Overall Healthcare Resource Utilization, and all-Cause Mortality in Children with Epilepsy in the UK

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Purpose: To understand the association of seizure frequency with overall healthcare resource utilization (HCRU) and all-cause mortality in children with epilepsy.

Method: A retrospective cohort study was performed using The Health Improvement Network database, containing primary care data on over 15 million patients. Children with epilepsy ≥1 and < 18 years of age with a record of seizure frequency were included in mortality analyses from 2005 to 2015 and HCRU analyses from 2010 to 2015. The main outcomes included frequency of overall HCRU during the year following last reported seizure frequency and all-cause mortality (descriptive, negative binomial regression and Cox proportional hazards regression) from first record of seizure frequency. Covariates (demographics, comorbidities, diagnosis of epilepsy prior to vs. following index date, and number of antiepileptic drugs [AEDs]) were included if they altered the beta coefficient for seizure frequency by >10%.

Results: Data included 1273 patients with seizure frequency and HCRU records and 3,324 patients with seizure frequency and mortality records. Each category increase in seizure frequency (less than once-a-year, once-a-year, monthly, weekly, daily) related to 11% more visits to general practitioners (GPs), 35% more in-patient admissions, 15% more outpatient visits, and increased direct HCRU costs (24%). Eleven patients died during 12,490 patient-years follow-up. The unadjusted hazard ratio of mortality per higher category of seizure frequency was 2.56 (95% CI 1.52 to 4.31), but adjusted attenuated down to 2.11 (95% CI 1.24 to 3.60). The mean number of overall GP visits, GP face-to-face consultations, number of AEDs, in-patient admissions, accidents and emergency hospital visits per patient increased with increase in seizure frequency. Total healthcare cost increased by 24% with increase in seizure frequency.

Conclusion: Higher seizure frequency is associated with greater HCRU and mortality in children with epilepsy in the UK.

022 | Cannabidiol Treatment Effect and Adverse Events in Patients with Lennox-Gastaut Syndrome: Pooled Results from Two Trials


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Purpose: To assess efficacy and safety of add-on cannabidiol (CBD) in treatment-resistant Lennox-Gastaut syndrome (LGS).

Method: Data were pooled from two multicenter, double-blind, placebo (PBO)-controlled trials (GWPCARE3/NCT02224560; GWPCARE4/NCT02224690). Patients were randomized to PBO or a plant-derived pharmaceutical formulation of CBD oral solution at 10 (CBD10) or 20 mg/kg/day (CBD20) in two equally divided doses over a 2-week titration followed by a 12-week maintenance period. Median percent changes from baseline in monthly drop seizures were evaluated.

Results: Overall, 396 patients were randomized (73 CBD10; 162 CBD20; 161 PBO). Baseline demographic characteristics were evenly distributed. Median percent changes from baseline in drop seizure frequency CBD10 37% versus PBO 17% and CBD20 43% versus PBO 20% during the treatment period; CBD10 40% versus PBO 19% and CBD20 48% versus PBO 20% during the maintenance period. Greater reductions in monthly drop seizure frequency were evident during the titration period and each 4-week interval of the maintenance period for CBD versus PBO. Adverse events (AEs) were reported by CBD10 84%, CBD20 90%, and PBO 71%; onset was more common during titration versus maintenance periods. Many AEs resolved within 4 weeks of onset; most resolved within the 14-week study period. Elevated transaminases (>3x upper limit of normal) were reported in three CBD10, 31 CBD20, and one PBO patient, most receiving concomitant valproic acid; all resolved on discontinuation or dose adjustment.

Conclusion: In this pooled analysis of two randomized, controlled trials of add-on CBD treatment in patients with LGS, reductions in monthly drop seizure frequency were greater with both CBD doses than with PBO; this treatment...