PERAMPANEL IS EFFECTIVE AS ADD-ON THERAPY IN DRUG-RESISTANT TEMPORAL LOBE EPILEPSY WITH OR WITHOUT HIPPOCAMPAL SCLEROSIS

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Introduction: Perampanel (PER) is a novel orally active antiepileptic drug (AED), highly selective non-competitive antagonist of alpha-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptor and indicated for focal onset seizures, with or without secondarily generalization, and primary tonic-clonic seizures. Evidence based on mechanism of action and preclinical and clinical efficacy of PER, allows to suppose its use in add-on therapy for temporal lobe epilepsy (TLE), the most common type of focal epilepsy, with or without hippocampal sclerosis (HS). Aim of this study is to compare PER efficacy as add-on therapy in patients with a specific well-defined epileptic syndrome such as TLE, with or without HS, compared to patients affected by not-TLE epilepsy.

Materials and methods: Retrospective analysis of patients' clinical records with: age > 12years, drug-resistant focal epilepsy and treatment with PER as add-on therapy. Exclusion criteria were: status epilepticus, continuous partial epilepsy, concurrent untreated psychiatric disorders, psychogenic non-epileptic seizures, low treatment compliance and pregnancy. Patients were stratified on the basis of specific epileptic syndrome as TLE, extra-TLE or epileptic encephalopathy/multifocal epilepsy. The presence of HS was defined by 3Tesla magnetic resonance (MR).

Results: The study sample comprised 258patients with epilepsy, including 81(31.4%) with a TLE diagnosis. All patients recruited were started on once-daily add-on PER; an initial dose of 2mg was used and subsequently titrated from 2mg weekly, on the basis of clinical judgement, up to a maximum dose of 12mg daily. All participants were followed regularly at 3-months intervals for at least 12months. Seizures frequency (number of seizures/month) was assessed at baseline and during each outpatient visit. Following treatment with PER, a significantly higher number of patients in the TLE group achieved a seizures free status (19.8% vs 4.0%, $p < 0.0001$) or a major clinical response (MCR), namely all patients categorized as ≥ 50% improvement or seizure free (51.9% vs 24.3%, $p < 0.0001$). No significant differences between groups were found regarding PER dose, concomitant AEDs and measures of treatment safety. A significant higher percentage of patients with generalized seizures achieved MCR (40.38% vs 72.41% $p = 0.01$) compared with patients affected by focal seizures. After stratification for the presence of HS ($n = 39$, 48.15% of all TLE patients); the analysis revealed no significant difference between groups. Analysis with Kaplan-Meyer curves demonstrated a longer treatment survival in patients with TLE compared to those without TLE (20.9months; 95% CI, 19.6-22.3vs 18.5months, 95% CI, 17.4-19.5; log-rank $p = 0.01$).

Discussion and conclusions: Our retrospective data analysis found that perampanel add-on therapy was effective in seizures control and had longer treatment survival in TLE patients, without any influence from HS, compared to other epileptic encephalopathies/multifocal epilepsy. Despite the retrospective data collection and limited sample size, these findings support existing data on perampanel efficacy and may also suggest its greater effectiveness in the TLE.