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Research Article

Efficacy of Perampanel in Nocturnal Seizures in Adult Patients with Epilepsy

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Objective. Nocturnal seizures are usually underestimated and represent a major problem in adult patients with epilepsy. Our aim was to study the effectiveness of perampanel for the treatment of nocturnal seizures in adult patients with epilepsy. *Methods*. Observational study of a prospectively acquired sample of adult patients with focal and generalized epilepsy in which perampanel was started from January to October 2021 in a specialized epilepsy unit in a tertiary hospital. Demographic and clinical characteristics were recorded. All patients completed a follow-up period of at least 3 months. Seizure frequency during the 6-month period before the patient started treatment was obtained from medical records. Retention and responder rates (considered as a nocturnal seizure frequency reduction of ≥50%) and improvement of subjective sleep disturbances were analyzed as outcome measures. *Results*. Forty-eight patients were included (mean age 39.8 ± 17.4; 60.4% men), and 38 of them had a 6-month follow-up. Focal epilepsy was the most common diagnosis (81.3%), and most patients had a structural etiology (56.3%). Thirty-four (70.8%) patients had drug-resistant epilepsy. The mean nocturnal seizure frequency per month at baseline was 13.2 ± 35.9. Fifteen (31.3%) patients had subjective sleep disturbances at baseline, of which insomnia was the most frequent complaint (16.7%). Perampanel was started at a median dose of 4 mg/day (range = 2-14). At 3-month follow-up, the retention rate was 74.6%; 64.6% were considered responders (54.2% were seizure-free). Monthly nocturnal seizures decreased significantly at 3 months (8.2 ± 26.7 vs. 13.2 ± 35.9 seizures/month; $p = 0.044$) and 6 months (5.3 ± 18.2 vs. 13.2 ± 35.9 seizures/month; $p = 0.006$). Subjective sleep disturbances improved at 3-month follow-up (10.4% vs. 31.3%; $p = 0.002$) and 6-month follow-up (10.5% vs. 31.3%; $p = 0.022$). *Significance*. Perampanel can be a suitable treatment option in adult patients with both focal and generalized epilepsy with nocturnal seizures and can reduce the presence of sleep complaints.

1. Introduction

The relationship between sleep quality and epilepsy is well-known to have a bidirectional interplay. Interictal epileptiform activity and seizures occurring during sleep, particularly nocturnal seizures (NS), can disrupt sleep [1], and sleep disorders can lead to impaired seizure control [2, 3]. There is currently increasing evidence that NS represent a particularly important seizure type to consider in this setting [4, 5].

Patients with epilepsy are more vulnerable to the effects of sleep disruption than the healthy population [4]. Several studies have shown that in patients with epilepsy, the presence of active sleep disorders has a negative effect on mood and quality of life [5–7]. Fragmented sleep also has several

adverse effects, such as daytime sleepiness, as well as problems related to mood, cognition, and behavior [5–8].

NS can be present in any type of epilepsy [9] and are often unwitnessed [6]. In addition, they can be misdiagnosed as other sleep paroxysmal disorders. Most NS generate a brief awakening that disrupts the structure of sleep [10, 11]. When seizures occur during sleep, there is a marked reduction in the REM phase, an increase in stage 1 sleep, and a reduction in sleep efficiency [5].

In addition, antiseizure medications (ASMs) can affect the quality of sleep and can influence sleep architecture [12]. At the same time, it seems that the pharmacological control of seizures, especially NS, represents a fundamental strategy for the stabilization of sleep and, secondarily, the quality of life of patients with epilepsy [5].

Perampanel (PER) is an ASM that has been approved as adjuvant therapy for focal seizures, with or without secondary generalization, and in primary generalized tonic-clonic seizures for patients with idiopathic generalized epilepsy [13–16]. The main mechanism of action is inhibiting the α-amino-3-hydroxyl-5-methyl-4-isoxazolepropionic acid (AMPA) receptor [17]. Postdose drowsiness is among the most well-known adverse events of this drug, which is commonly minimized by taking the medication in a single daily dose before going to sleep. A recent study showed that an improvement in sleep architecture without increasing daytime sleepiness was observed after PER initiation in patients with refractory epilepsy [18].

The aim of this study was to establish the efficacy and safety of PER for the treatment of NS, as well as the potential improvement of subjective complaints regarding sleep in patients with epilepsy.

2. Material and Methods

2.1. Study Design and Participants. This is a prospective longitudinal analytical study following the guidelines of STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) for observational studies. Patients were included in the study if they had at least one NS in the six-month period prior to the baseline visit, had started PER according to clinical indications, and had already received at least 3 months of follow-up. Nocturnal seizures were considered as those seizures with hypermotor semiology or bilateral tonic-clonic seizures occurring during sleep. The patients were prospectively recruited between January and October 2021 in the Epilepsy Unit of Vall d'Hebron University Hospital. The project was approved by the local ethics committee (internal project: PR(AG)552020, post-authorization study: EPA(AG)14/2020(5607)) and authorized by the Spanish Agency for Medicines and Medical Devices (AEMPS). All patients were evaluated at baseline and during follow-up by an expert epileptologist. The type of epilepsy, etiology, and type of seizures were evaluated in each patient based on clinical and electroencephalographic (EEG) data, according to the 2017 International League Against Epilepsy (ILAE) classification [19]. Drug resistance was evaluated according to the 2010 ILAE Task Force [20], and patients who met the criteria for refractory epilepsy were categorized as drug-resistant.

Patients were excluded from the study if they did not wish to participate or had another condition potentially masking the results, such as obstructive sleep apnea or other sleep-related diseases. In those cases in which clinical history suggested those disorders, patients were referred to the sleep unit, and specific assessment was provided in order to confirm/discard such diagnosis prior to study initiation. In patients in whom a longer follow-up was available at the time of the analysis, clinical data were also collected at a 6-month follow-up. Clinical and demographic data, clinical characteristics of epilepsy (including seizure type, epilepsy etiology, and duration), and ASM history were collected at baseline from medical records.

PER was started at the baseline visit. At each visit, information was collected on the frequency of NS and total seizures (TS) (including daytime and NS), the type of seizures, and the dose of PER and other associated ASMs. Treatment-emergent adverse events (AEs) and their severity (categorized into 3 levels: transient, persistent, and leading to medication discontinuation) were also recorded. Responder (patients with a reduction in seizure frequency $\geq 50\%$), seizure freedom, and retention rates as well as AEs were analyzed as outcome measures during follow-up. In the case of PER withdrawal, the date and reason for discontinuation were recorded. Data related to subjective sleep complaints, such as insomnia, frequent arousals, nightmares, or daytime sleepiness, were also assessed and collected at each visit.

2.2. Statistical Analysis. Descriptive and frequency statistical analyses were obtained, and comparisons were performed with IBM SPSS Statistics 26.0. Categorical variables were reported as frequencies (percentages) and continuous variables as mean ± standard deviation (SD) or median (interquartile range (IQR)), as appropriate.

The Wilcoxon signed-rank test was performed to assess changes in total and nocturnal seizure frequencies at 3 and 6 months of follow-up. Changes in the proportion of sleep complaints during follow-up were assessed with the McNemar test.

Statistical significance in the comparisons with the rate of responders, seizure-free, AEs, and sleep complaints was assessed by Pearson's chi-square or Fisher's exact test for categorical variables and the Student t-test or Mann–Whitney U test for quantitative variables.

Retention rates during follow-up were analyzed with the Kaplan-Meier product limit method using the log-rank test to determine statistical significance between groups and simple Cox proportional-hazard models to establish associations with quantitative variables. Finally, a stepwise multiple Cox regression model was performed to identify factors independently associated with treatment discontinuation.

A p value < 0.05 was considered statistically significant.

3. Results

3.1. Demographic and Clinical Characteristics. Among 56 patients who met inclusion criteria, 2 patients refused to

participate in the study and a total of 54 patients with NS were initially recruited, with 6 lost-to-follow-up. Three-month follow-up was completed in 48 (88.8%) patients, and 38 (70.3%) patients were followed up until 6 months after PER initiation. Mean age was 39.8 ± 17.4 years, and 29 (60.4%) patients were men. The mean age at epilepsy onset was 22.5 ± 18.4 years. Thirty-nine (81.3%) patients had focal epilepsy, of which temporal lobe epilepsy was the most frequent type ($n = 25$, 64.1%), and 6 (12.5%) patients had idiopathic generalized epilepsy. The most common etiology was structural (56.3%), followed by unknown etiology (29.2%). Among the specific causes, malformations of cortical development (29.6%), mesial temporal sclerosis (29.6%), and tumors (18.5%) were the most frequent. A total of 32 (70.8%) patients had drug-resistant epilepsy. A detailed description of the baseline is shown in Table 1.

Before the initiation of PER, the median number of previously withdrawn ASMs was 1 (IQR 0-3), with levetiracetam and valproic acid being the most frequently discontinued medications prior to inclusion in the study (31.3% and 20.8%, respectively). The median number of active ASMs at the time of PER initiation was 2 (IQR 1.5-3), with levetiracetam (39.6%) and lacosamide (33.3%) being the most frequent concomitant medications.

At baseline, the mean monthly seizure frequency was 13.2 ± 35.9 for NS and 24.9 ± 53.9 for TS. Fifteen (31.3%) patients had subjective sleep complaints, reported as insomnia in 8 (16.7%) patients, poor sleep quality in 5 (10.4%), and nocturnal spasms and hypersomnia, each in 1 (2.1%) patient.

PER was started at a median dose of 4 mg daily (range 2-14 mg). During follow-up, the median dose was 4 mg (range 2-8 mg) at 3 months and 6 mg (range 4-10 mg) at 6 months.

3.2. Perampanel Efficacy: Response Rate, Retention Rate, and Treatment Discontinuation. At follow-up, a significant reduction in the frequency of NS was observed, both at 3 months (mean 8.2 ± 26.7 vs. 13.2 ± 35.9; $p = 0.044$) and at 6 months (mean 5.3 ± 18.2 vs. 13.2 ± 35.9; $p = 0.006$) (Figure 1(a)). Responder rates were 64.6% and 86.8% at 3 and 6 months of follow-up, respectively. A total of 26 (54.2%) and 29 (76.3%) patients were free of NS at 3 and 6 months, respectively. No clinical factors were associated with responder rates or nocturnal seizure freedom.

Regarding the global seizure frequency, a significant reduction in the frequency of TS was also observed at both 3 (mean 13.2 ± 8.2 vs. 24.9 ± 53.9; $p = 0.009$) and 6 (mean 10.9 ± 27.5 vs. 24.9 ± 53.9; $p = 0.020$) months of follow-up (Figure 1(b)). At the 3-month follow-up, 26 (54.2%) patients were considered responders, and 14 (29.2%) were seizure-free. At 6 months, 26 (64.8%) patients were considered responders, and 17 (44.7%) were seizure-free. Responders (TS) had fewer previous ASMs (median (IQR): 0 (0-2) vs. 2 (2-3); $p = 0.043$). Patients without drug-resistant epilepsy were more likely to be free of TS at 3 (50% vs. 20.6%; $p = 0.042$) and 6 months (75% vs. 30.8%; $p = 0.011$) of follow-up. No other clinical factors were associated with responder rates or global seizure freedom.

A significant reduction of daytime seizure frequency was also observed at 3 months (mean 5.0 vs. 11.7; $p = 0.046$), but not at 6 months (mean 5.6 vs. 11.7; $p = 0.227$). At 3-month follow-up, 38 (79.2%) patients were considered responders, and 31 (64.6%) were seizure-free. At 6 months, 31 (81.6%) were considered responders, and 24 (63.2%) were seizure-free.

The retention rate was 83.3% (standard error 5.4%) in the first month, 74.6% (standard error 6.3%) at 3 months, and 62.7% (standard error 7.2%) at 6 months (Figure 2). At 6 months, patients with drug-resistant epilepsy (72.3% vs. 39.2%; $p = 0.010$) and those with a higher number of previous ASMs (median (IQR): 3 (2-3) vs. 1 (1-2); $p < 0.001$) had a higher retention rate. The retention rate was also higher in patients who started PER at a dose of 4 mg compared to those

Table 1: Demographic and clinical baseline characteristics.

Variable	$N = 48$
Age, years (mean ± SD (range))	39.8 ± 17.4 (16-77)
Sex (male), *n* (%)	29 (60.4)
Age at epilepsy onset, years (mean ± SD (range))	22.5 ± 18.4 (0-77)
Epilepsy duration, years (mean ± SD (range))	17.3 ± 15.4 (0.5-63)
Epilepsy type, *n* (%)	
Focal	39 (81.3)
Generalized	6 (12.5)
Focal/generalized	1 (2.1)
Unknown	2 (4.2)
Focal localization ($n = 39$), *n* (%)	
Frontal	12 (30.8)
Occipital	1 (2.6)
Temporal	25 (64.1)
Undetermined	1 (2.6)
Syndrome, *n* (%)	
Focal epilepsy of unknown etiology	14 (29.2)
Focal epilepsy of structural etiology	29 (60.4)
Idiopathic generalized epilepsy	3 (6.3)
Juvenile myoclonic epilepsy	1 (2.1)
Other	1 (2.1)
Etiology, *n* (%)	
Unknown	14 (29.2)
Structural	27 (56.3)
Infectious	2 (4.2)
Genetics	5 (10.4)
Specific cause ($n = 27$), *n* (%)	
Vascular	3 (11.1)
Tumor	5 (18.5)
Mesial sclerosis	8 (29.6)
Malformation cortical development	8 (29.6)
Cavernoma/arteriovenous malformation	1 (3.7)
Postanoxic encephalopathy after cardiac arrest	1 (3.7)
Neonatal anoxia	1 (3.7)
Drug-resistant epilepsy, *n* (%)	37 (70.8)

CNS: central nervous system; SD: standard deviation.

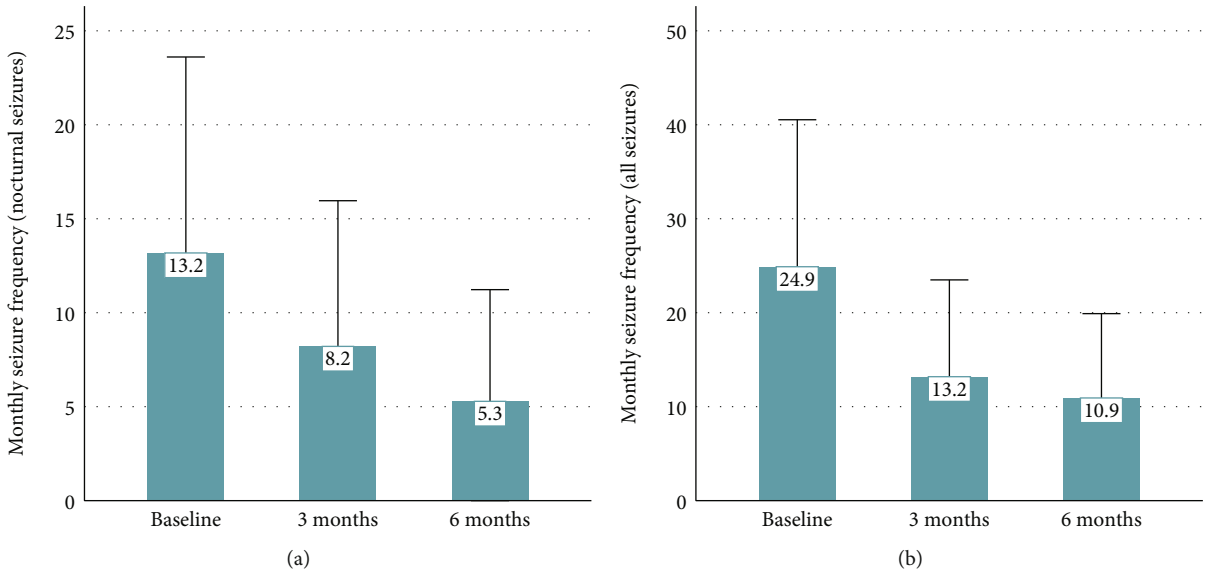

Figure 1: Frequency of (a) nocturnal seizures and (b) total seizures at baseline and during follow-up. Monthly seizure frequency is shown as the mean frequency of seizures at each visit. A significant reduction in nocturnal and total seizures was observed during follow-up.

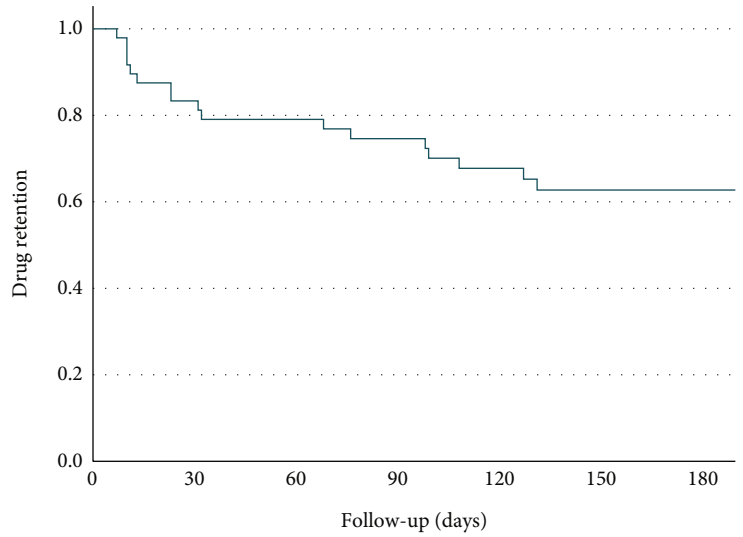

Figure 2: Kaplan-Meier representation of PER retention during follow-up.

who started at 2 mg daily (69.2% vs. 36.4%; $p = 0.007$). Patients with neurological comorbidities had a lower retention rate (33.3% vs. 67%; $p = 0.05$). Fewer concomitant ASMs (HR 0.27 (95% CI: 0.15-0.51); $p < 0.001$) and neurological comorbidities (HR 3.95 (95% CI: 1.15-13.57); $p = 0.029$) were independent predictors for treatment discontinuation.

PER was withdrawn in 17 (35.4%) patients during follow-up (mean time 51.6 ± 45.6 days; median 31; range 7-131). Treatment discontinuation occurred during the first 3 months in 13 patients (76.5%) and between the third and sixth months in 4 (23.5%) patients. The main reasons for withdrawal were AEs ($n = 10$, 58.8%), lack of efficacy ($n = 4$, 23.5%), and patient decision ($n = 3$, 17.6%).

3.3. Adverse Events. A total of 22 (45.8%) patients reported treatment-emergent AEs during the overall follow-up period. The most commonly reported AEs were drowsiness ($n = 18$, 37.6%), dizziness ($n = 11$, 23%), fatigue ($n = 4$, 8.4%), instability ($n = 3$, 6.2%), gastrointestinal symptoms ($n = 2$, 4.2%), and irritability ($n = 1$, 2.4%). In relation to the severity of symptoms, AEs were considered transient in 10 (20.8%) patients and remained stable in 2 (4.2%) patients. AEs leading to treatment discontinuation occurred in 10 (20.8%) patients. No clinical factors were associated with the occurrence of treatment-emergent AE.

3.4. Sleep Complaints. A statistically significant reduction of sleep complaints was observed during follow-up, at both 3 (10.4% vs. 31.3%, $p = 0.002$) and 6 months (10.5% vs. 31.3%, $p = 0.022$) (Figure 3). Specifically, from 15 patients with sleep complaints at baseline, 5 patients (10.4%) continue with these symptoms (insomnia in three patients,

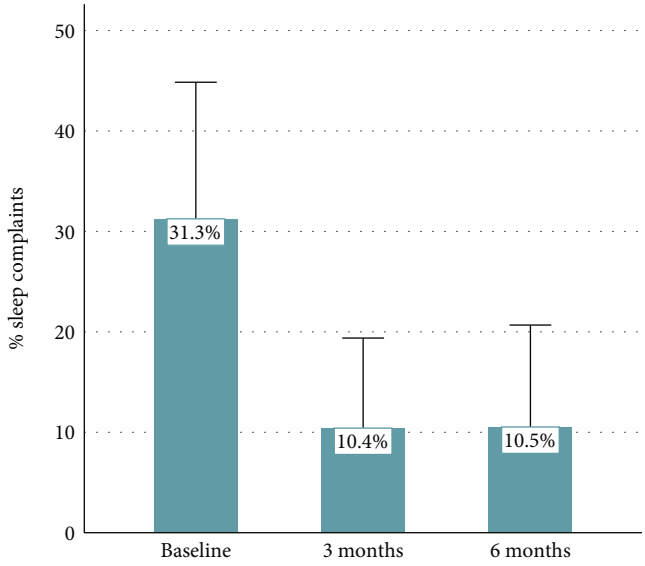

FIGURE 3: Frequency of sleep complaints at baseline and during follow-up. A significant reduction in sleep complaint frequency was observed during follow-up.

daytime sleepiness in two patients) at 3 months of follow-up and 4 patients (insomnia in all of them) at 6 months of follow-up. Patients with neurological comorbidities (50% vs. 5.9%; $p = 0.047$) and those without hypnotic medications (50% vs. 6.1%; $p = 0.050$) reported more sleep complaints at 6 months of follow-up. Patients reporting sleep complaints at some point during follow-up had a tendency towards a lower retention rate at 6 months (42.9% vs. 66.5%), although this difference was not statistically significant ($p = 0.160$).

4. Discussion

This is the first study designed to evaluate the efficacy and safety of PER in patients with focal and generalized epilepsy with nocturnal seizures, as well as the potential benefit in sleep complaints. Consistent with published PER data, we observed a reduction in overall seizures after PER initiation. The responder rate in terms of NS was above 80%, and the retention rate was over 60% at 6 months. As previously described, an improvement in sleep complaints was observed during follow-up.

Previous studies have assessed the effectiveness of ASMs for the treatment of NS, mainly based on the hypothesis that most epilepsies with seizures occurring only during sleep have a focal origin, particularly in frontal lobe epilepsy [21, 22]. Although nocturnal seizures are more typically reported in frontal lobe epilepsy, in our sample, temporal lobe epilepsy was the most common syndromic diagnosis. These results are probably influenced by the fact that temporal lobe epilepsy is the most common type of focal epilepsy in adults, particularly when selecting patients with difficult-to-control seizures who require adjunctive treatments, and especially considering nonmesial temporal lobe or "temporal plus" epilepsies. Oxcarbazepine, topiramate, or lacosamide are some of the ASMs that have proved to be effective treatments in NS [23, 24]. In line with our results, a recent study showed the efficacy of PER in patients with sleep-related focal epilepsy with hypermotor seizures and found a potential benefit by reducing the number of nocturnal seizures in patients with drug-resistant epilepsy [25]. In addition, the AMPA receptor has a wide distribution in the central nervous system and plays an important role in neuronal synchronization and propagation of seizures [26, 27]. Due to its mechanism of action, PER could be considered a potential agent for the treatment of generalized seizures. Although previous evidence is mainly focused on focal epilepsy, our study supports the hypothesis that PER is an effective treatment for patients with NS in focal and generalized epilepsies [25].

A significant reduction in global seizure frequency was also observed in our sample, along with a reduction of NS. This could be the result of an additional benefit of better seizure control during sleep, which may avoid sleep fragmentation and improve sleep quality. However, when we analyzed diurnal seizures in detail, we observed a reduction of diurnal seizure frequency but only was statistically significant at 3 months of follow-up. This could explain the particular benefit of low-dose PER in the treatment of nocturnal seizures, and it is possible that higher doses may be required for long-term control of diurnal seizures.

Most (70.8%) patients included in our sample had drug-resistant epilepsy with a high seizure frequency of both NS and TS, as well as a median of 2 concomitant ASMs at the time of initiating PER. The data is consistent with previous reports indicating that focal, sleep-related epilepsy is usually refractory to medical treatment [28, 29]. In this study, 6 patients with generalized epilepsy and nocturnal seizures were included. We are aware that nocturnal seizures are not the most typical seizure types in generalized epilepsy, and we believe that there is likely an overrepresentation of drug-resistant generalized epilepsy in our sample, and those patients represent particularly difficult-to-control epilepsy that required polytherapy and addiction to adjunctive therapies.

Furthermore, the retention rate was higher in refractory patients with a higher number of concomitant ASMs, thus highlighting the benefit of the treatment in this particularly difficult-to-treat epilepsy population. However, alternative therapeutic options are limited in this subtype of patients with epilepsy, which can overestimate retention rates, and so, these results should be interpreted with caution. On the other hand, we observed greater retention in patients who started the medication at a dose of 4 mg compared to 2 mg. These results should be interpreted with caution since it is likely that the 2 mg dose was preferred for more complicated patients with greater drug resistance and medication load, in which poorer tolerability was expected, and this could explain the higher discontinuation rates. Furthermore, the responder rate was higher in patients who had fewer prior ASMs. Although this effect can be presumably achieved with different new therapeutic interventions in "drug-naïve" patients, our results could indicate a benefit of the drug in the first attempts to optimize the control of NS, even before they can be strictly considered drug-resistant.

AEs were reported in nearly half the patients included in our study. This proportion was lower than others described

in previous postcommercialization analyses [30–32]; this result could be due to the relatively lower PER doses used in our patients. However, a recent study, which includes a large number of patients, found similar data to our results [33]. In addition, the majority of AEs were transient and did not lead to treatment discontinuation. Nevertheless, AEs represented one of the main reasons for treatment discontinuation, which were more likely to occur within the first 3 months after PER initiation. In our study, no patient had serious psychiatric symptoms, possibly because of the relatively low doses used and the probable exclusion of some patients at risk of developing such adverse events.

More than 30% of the patients included in our study had subjective sleep complaints at baseline, which improved significantly during follow-up. The influence of PER on different stages of sleep has been assessed in a recent study, where doses between 4 and 8 mg were found to exert a protective effect for seizures by improving sleep architecture [18]. Another study concluded that adjunctive PER may improve the global quality of sleep in patients with focal epilepsy without increasing daytime sleepiness [34]. Based on the previous results of the influence of PER on sleep regulation and the results obtained in our study, it could be assumed that PER could exert a beneficial effect on sleep quality in patients with epilepsy by reducing the presence of subjective sleep complaints.

The observational design and the relatively small sample size could have prevented us from identifying clinically relevant associations. Due to the observational design of the study, the frequency of nocturnal seizures at baseline was somewhat low to draw definite conclusions about the response rate of the drug in this small subgroup of patients. However, based on the importance of this type of seizure, larger studies are of interest to help give more consistency to our results. We also take into account that the nocturnal and diurnal seizure frequency was collected through the anamnesis performed at each visit, which did not allow for providing a semiological classification of seizures and could represent a major limitation of our study since some seizures could be underrepresented. NS counting can be difficult in these cases and some of them are likely to be unnoticed, and our results should be interpreted cautiously to avoid wrong interpretations in this matter. In addition, data related to subjective sleep complaints were collected from the medical records, so the absence of standardized scores to evaluate sleep quality may have introduced a bias in the interpretation of sleep complaints. Another limitation of the study is the limited follow-up time of 3 and 6 months, and concomitant ASMs were not controlled as confounding factors, although in this period, low doses of PER also achieved good results in terms of seizure control. However, long-term prognosis is difficult to predict, particularly for patients with a low seizure frequency at baseline, and future studies with a longer follow-up period are needed to corroborate our results. Finally, video-EEG and polygraphic records before and after treatment initiation could help quantify the number of NS, as self-reported seizure counts may underestimate the actual seizure frequency, as well as to rule out the presence of concomitant undetected obstructive sleep apnea or other sleep disorders. Since baseline values of nocturnal seizure frequency were very low in some patients, we have used the mean frequency (instead of median) to represent a greater visual impact of our results. Nonetheless, the study is based on routine clinical practice, which reflects the real-world experience with PER in the management of nocturnal seizures and sleep complaints in patients with epilepsy. However, future studies including larger samples are needed to compare the effects of different ASMs on NS and sleep disturbances.

5. Conclusion

Perampanel is a suitable option in patients with focal and generalized epilepsy who have NS and offers a potential benefit in the reduction of seizure frequency and improving subjective sleep complaints.

Abbreviations

AEs: Adverse events
AEMPS: Spanish Agency for Medicines and Medical Devices
AMPA: α-Amino-3-hydroxyl-5-methyl-4-isoxazolepropionic acid
ASMs: Antiseizure medications
CNS: Central nervous system
EEG: Electroencephalogram
ILAE: International League Against Epilepsy
IQR: Interquartile range
NS: Nocturnal seizures
PER: Perampanel
SD: Standard deviation
STROBE: STrengthening the Reporting of OBservational studies in Epidemiology
TS: Total seizures.

Data Availability

After publication, anonymized data supporting the findings of this study are available from the corresponding author upon reasonable request from any qualified investigator.

Additional Points

Key Points Box. (i) Clinical data were collected from real-world experience in patients with epilepsy with nocturnal seizures treated with perampanel. (ii) Perampanel was started at a median dose of 4 mg/day, and the responder rate was 64.6% at 6 months (54.2% free of nocturnal seizures). (iii) Retention rate was 74.6% and 62.7% at 3 and 6 months, respectively. (iv) Subjective sleep complaints improved significantly during follow-up (10.5% vs. 31.3%, $p = 0.022$). (v) Adverse events were reported by 45.8% of patients, of which 45.5% were transient and 45.5% led to treatment discontinuation.

Ethical Approval

We confirm that we have read the journal's position on issues concerning ethical publication and affirm that this report is consistent with those guidelines.

Disclosure

Eisai Inc. was not involved in the study design, the collection, analysis, or interpretation of the data gathered, the writing of the report, or the decision to submit the article for publication. This work was presented at the 14th European Epilepsy Congress, which took place in Geneva in July 2022. The abstract is published as platform session #443 in the Congress Abstracts document (page 43) (link: https://www.epilepsycongress.org/wp-content/uploads/2022/07/EEC2022-Congress-Abstracts-U.pdf).

Conflicts of Interest

S. López-Maza declares travel support from Eisai Inc. A. Gifreu declares research funding from UCB Pharma and Bial Pharmaceutical. E. Fonseca declares research funding and honoraria from UCB Pharma, Laboratorios Esteve, Eisai Inc., Bial Pharmaceutical, GW Pharmaceuticals, Angelini Pharma, and Sanofi Genzyme. Manuel Quintana has received honoraria from UCB Pharma, Eisai Inc., Sanofi, GW Pharmaceuticals, Neuraxpharm Spain, and Pierre Fabre Ibérica. E. Santamarina has received research funding and speaker fees from UCB Pharma, Bial Pharmaceutical, Eisai Inc., Arvelle, and Laboratorios Esteve. L. Abraira has received research funding and speaker fees from UCB Pharma, Bial Pharmaceutical, Eisai Inc., Sanofi Genzyme, and Laboratorios Esteve. D. Campos declares research funding from UCB Pharma. M. Toledo declares research funding and speaker fees from UCB Pharma, GW Pharmaceuticals, Bial Pharmaceutical, Eisai Inc., Sanofi, Arvelle, and Laboratorios Esteve.

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