

Perampanel effects on seizures and sleep quality in people with epilepsy: PER-SLEEP, a prospective multicenter study

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Objective

Preliminary studies suggested a potential beneficial effect of perampanel (PER) on sleep in people with epilepsy (PwE). The present multicenter study evaluated the clinical potential of the early use of PER in PwE on seizures and on sleep quality, insomnia, daytime sleepiness and circadian rhythm preferences, as well as on depressive symptoms and quality of life.

Methods

PwE starting PER as early add-on ASM were evaluated at baseline (T0) and after six months of treatment (T1) using standardized questionnaires: Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), Morningness–Eveningness Questionnaire (MEQ), and the Quality of Life in Epilepsy Inventory (QoLIE-31).

Results

74 PwE (44.6% male, mean age 42.41 ± 18.06 years) were included and 59 PwE completed the study. At T1, 45.76% (27/59) of PwE were seizure-free and a significant reduction in seizure frequency was found (10.80±20.72 vs. 5.93±16.77, p=0.002). At T1, a significant improvement in sleep quality (PSQI, 7.18±4.27 vs. 4.63±3.09, p=0.001) was evident, and particularly in sleep duration, efficiency and in the reduction of the use of sleeping medication. Insomnia symptoms (ISI, 8.15±6.23 vs. 5.32±5.25, p=0.002) and quality of life (QoLIE-31, 58.32±16.57 vs. 65.81±16.31, p=0.033), mainly social functioning and perceived well-being, also significantly improved. No significant changes were evident for daytime sleepiness, circadian preferences and depressive symptoms.

Table 2. Changes in Seizure Frequency, Sleep Parameters, Mood, and Quality of Life from Baseline to the Six-Month Follow-Up.

	Time	Mean	SD	ANCOVA
Mean number of seizures	Baseline	10.09	19.88	t=3.313, p=0.002
	6-month Follow-up	5.93	16.77	
Global PSQI	Baseline	7.18	4.27	F(1,53)=11.800, p=0.001
	6-month Follow-up	4.63	3.09	
C1. Subjective Sleep Quality	Baseline	1.22	0.83	F(1,53)=2.171, p=0.147
	6-month Follow-up	0.98	0.82	
C2. Sleep Latency	Baseline	1.24	1.07	F(1,53)=2.238, p=0.141
	6-month Follow-up	1.08	0.88	
C3. Sleep Duration	Baseline	0.93	0.93	F(1,53)=11.922, p=0.001
	6-month Follow-up	0.10	0.55	
C4. Sleep Efficiency	Baseline	1.07	1.08	F(1,53)=10.582, p=0.002
	6-month Follow-up	0.10	0.55	
C5. Sleep Disturbances	Baseline	1.24	0.57	F(1,53)=1.658, p=0.203
	6-month Follow-up	1.07	0.55	
C6. Sleeping Medication	Baseline	0.70	1.18	F(1,53)=5.068, p=0.029
	6-month Follow-up	0.42	1.00	
C7. Daytime Dysfunction	Baseline	0.77	0.96	F(1,53)=0.778, p=0.382
	6-month Follow-up	0.86	0.88	
ISI	Baseline	8.15	6.23	F(1,55)=10.076, p=0.002
	6-month Follow-up	5.32	5.25	
ESS	Baseline	6.49	3.93	F(1,53)=0.759, p=0.388
	6-month Follow-up	5.63	3.55	
MEQ	Baseline	54.66	9.90	F(1,53)=1.050, p=0.310
	6-month Follow-up	56.24	8.79	
NDDI-E	Baseline	11.32	4.13	F(1,53)=1.169, p=0.284
	6-month Follow-up	10.51	3.54	
Seizure worry (QoLIE-31)	Baseline	42.80	28.12	F(1,50)=1.068, p=0.306
	6-month Follow-up	52.14	24.03	
Overall quality of life (QoLIE-31)	Baseline	61.75	17.36	F(1,50)=4.533, p=0.038
	6-month Follow-up	69.24	19.59	
Emotional well-being (QoLIE-31)	Baseline	60.83	20.26	F(1,50)=1.753, p=0.191
	6-month Follow-up	64.88	19.82	
Energy/Fatigue (QoLIE-31)	Baseline	51.36	23.93	F(1,50)=3.284, p=0.076
	6-month Follow-up	58.21	18.18	
Cognitive Function (QoLIE-31)	Baseline	60.79	26.73	F(1,50)=2.391, p=0.128
	6-month Follow-up	69.17	25.17	
Medication effects (QoLIE-31)	Baseline	66.42	23.38	F(1,50)=0.082, p=0.776*
	6-month Follow-up	63.39	21.31	
Social Function (QoLIE-31)	Baseline	60.50	21.20	F(1,50)=5.309, p=0.025
	6-month Follow-up	71.02	21.13	
Overall score QoLIE-31	Baseline	58.32	16.57	F(1,50)=4.801, p=0.033
	6-month Follow-up	65.81	16.31	

Abbreviations: PSQI – Pittsburgh Sleep Quality Index; C – PSQI Component; ISI – Insomnia Severity Index; ESS – Epworth Sleepiness Scale; MEQ – Morningness–Eveningness Questionnaire; NDDI-E – Neurological Disorders Depression Inventory for Epilepsy; QoLIE-31 – Quality of Life in Epilepsy Inventory; Overall QoL – Overall Quality of Life; ANCOVA – Analysis of Covariance; SD – Standard Deviation.

Table 1. PwE Demographic and Clinical Characteristics obtained at Baseline.

	Whole Group (n = 74)	PwE who completed FU (n=59)	PwE who discontinued PER (n=15)
	Mean ± SD	Mean ± SD	Mean ± SD
Age in years	42.41 ± 18.06	39.69 ± 18.38	52.93 ± 12.30
Sex, n. (%)			
Males	33 (44.6%)	30 (50.8%)	3 (20.0%)
Females	41 (55.4%)	29 (49.2%)	12 (80.0%)
Age at Epilepsy Onset	27.08 ± 18.87	26.19 ± 18.26	30.86 ± 21.61
Epilepsy Type, n (%)			
Focal	43 (58.1%)	33 (55.9%)	10 (66.7%)
Generalized	13 (17.6%)	9 (15.3%)	3 (20.0%)
Focal and Generalized	16 (21.6%)	14 (23.7%)	2 (13.3%)
Unknown	2 (2.7%)	2 (3.4%)	0 (0.0%)
Aetiology of Epilepsy, n. (%)			
Structural	19 (25.7%)	16 (27.1%)	3 (20.0%)
Genetic	14 (18.9%)	10 (16.9%)	4 (26.7%)
Infectious	2 (2.7%)	2 (3.4%)	0 (0%)
Immune	3 (4.1%)	3 (5.1%)	0 (0%)
Unknown	36 (48.6%)	28 (47.5%)	8 (53.3%)
N° of previous ASM treatment, n. (%)			
0	48 (64.9%)	39 (66.1%)	9 (60.0%)
1	16 (21.6%)	13 (22.0%)	3 (20.0%)
2	5 (6.8%)	5 (8.5%)	0 (0%)
3	1 (1.4%)	0 (0%)	1 (6.7%)
4	3 (4.1%)	1 (1.7%)	2 (13.3%)
5	1 (1.4%)	1 (1.7%)	0 (0%)
N° of concomitant ASMs at the time of PER prescription, n. (%)			
1	56 (75.7%)	48 (81.4%)	8 (53.3%)
2	15 (20.3%)	9 (15.3%)	6 (40.0%)
3	3 (4.1%)	2 (3.4%)	1 (6.7%)
PER as add-on, n. (%)			
1 concomitant ASM	56 (75.7%)	48 (81.4%)	8 (53.3%)
2 or more concomitant ASM	18 (24.3%)	11 (18.6%)	7 (46.7%)
Mean number of seizures at baseline	10.90 ± 20.72	10.09 ± 19.88	14.54 ± 24.71

Abbreviations: PwE, people with epilepsy; ASM, anti-seizure medication; PER, Perampanel; NA, not-applied; SD, Standard Deviation

Bibliography

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Conclusions: Treatment with Perampanel, prescribed as early adjunctive therapy for epilepsy, significantly reduces seizures and is associated with an improvement in sleep quality, insomnia, and quality of life in people with epilepsy, without inducing excessive daytime sleepiness or worsening depressive symptoms.