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Sleep-Related Effects of Brivaracetam Monotherapy in Epilepsy: Insights from a Prospective Study

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ABSTRACT

Objective: To evaluate sleep-related effects in patients with epilepsy newly initiated on brivaracetam (BRV) monotherapy in a tertiary care hospital in South India.
Methods: In this prospective analytical study, 46 patients aged ≥12 years with newly diagnosed epilepsy were enrolled. Patients received BRV monotherapy (50–100 mg twice daily; pediatric dose: 0.75–1.5 mg/kg twice daily). Sleep-related adverse events were recorded, and patients were assessed at baseline and one month using the Epworth Sleepiness Scale – Indian version (ESS-I), Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), and a one-month sleep log. Paired t-tests and McNemar's exact test were used to compare baseline and follow-up measures.
Results: The mean age was 37.8 ± 11.9 years; 47.8% were male. The majority had generalized epilepsy (69.6%) and duration of epilepsy <1 year (78.2%). Mean total sleep duration increased from 7.6 ± 1.5 hours to 8.1 ± 1.6 hours ($p = 0.005$). ESS-I scores increased (2.1 ± 2.5 to 3.4 ± 4.2, $p = 0.007$), indicating mild increases in daytime sleepiness. ISI and PSQI scores showed non-significant improvements. Proportion of patients with total sleep duration >10 hours/day increased from 4.3% to 17.4% ($p = 0.031$). Daytime sleep >1 hour/day increased from 6.5% to 21.7% ($p = 0.002$). No patients discontinued BRV due to adverse effects.
Conclusion: BRV monotherapy is associated with mild increases in daytime sleepiness and sleep duration without serious adverse events. BRV appears safe and well-tolerated in newly diagnosed epilepsy, with manageable effects on sleep. Larger studies with long-term follow-up are needed.

Keywords*: Brivaracetam, epilepsy, sleep, monotherapy, ESS, PSQI, ISI*

Introduction

Epilepsy is a common neurological disorder affecting approximately 50 million people worldwide [1]. Sleep disturbances are frequent in epilepsy and may exacerbate seizure frequency and reduce quality of life [2–5]. Antiepileptic drugs (AEDs) can influence sleep architecture, cognition, and behavior [6–8].

Brivaracetam (BRV) is a selective high-affinity ligand of synaptic vesicle protein 2A (SV2A) and has shown efficacy in focal epilepsy, both as adjunctive therapy and in limited monotherapy studies [9–15]. While somnolence and fatigue are reported adverse events in adjunctive therapy, data on sleep-related effects in BRV monotherapy are limited [11–14,23]. The primary objective of this study was to assess sleep-related outcomes and adverse events among patients with epilepsy newly initiated on BRV monotherapy at a tertiary care hospital in South India. Secondary objectives included evaluating changes in cognitive, behavioral, and sleep parameters and documenting any dose adjustments or drug withdrawals.

Methods

Study Design and Setting

A prospective analytical study was conducted in the neurology outpatient department of a tertiary care hospital in South India over two months after obtaining Institutional Ethics Committee approval.

Participants

Inclusion criteria:

- Patients ≥12 years with newly diagnosed epilepsy started on BRV monotherapy
- Written informed consent

Exclusion criteria:

- Severe neurological or psychiatric comorbidities (e.g., autism, cerebral palsy, severe depression)
- Severe organ disease or substance abuse
- Children <12 years

Treatment

BRV was initiated at 50 mg twice daily, up-titrated to 100 mg twice daily based on response (maximum 200 mg/day). Pediatric dosing was 0.75–1.5 mg/kg twice daily.

Data Collection

Demographics, seizure type, duration of epilepsy, aura, and baseline cognitive complaints were recorded. Sleep outcomes were assessed using:

- Epworth Sleepiness Scale – Indian version (ESS-I) [16,17]
- Pittsburgh Sleep Quality Index (PSQI) [18]
- Insomnia Severity Index (ISI) [19]
- One-month sleep log

Adverse events were recorded, including drug discontinuation or dose modification.

Statistical Analysis

Continuous variables were expressed as mean ± SD; categorical variables as n (%). Pre- and post-treatment comparisons were performed using paired t-tests for continuous variables and McNemar's exact test for categorical variables. Analysis was performed using SPSS v24.

Results

Demographic and Clinical Characteristics

A total of 46 patients were enrolled in the study. The mean age of participants was 37.8 ± 11.9 years, with 22 (47.8%) males. Over half of the cohort (56.5%) had attained a college education. The majority of patients (78.2%) had a duration of epilepsy of less than one year, and generalized epilepsy was more common than focal epilepsy (69.6% vs. 30.4%). Aura was reported in 7 patients (13%).

Treatment Characteristics

The mean initial dose of brivaracetam was 90.2 ± 19.8 mg/day, and the maximum dose achieved during the one-month follow-up was 96.7 ± 30.2 mg/day. Dose escalation was required in 7 patients (13%), while 3 patients (6.5%) required dose reduction due to tolerability. No patients discontinued the drug due to adverse events, indicating good overall tolerability.

Sleep Parameters

Total Sleep Duration: The mean total sleep duration per day increased significantly from 7.6 ± 1.5 hours at baseline to 8.1 ± 1.6 hours at one-month follow-up (mean difference +0.5 hours, $t = 2.9$, $p = 0.005$).

Daytime Sleepiness: The ESS-I score increased from 2.1 ± 2.5 at baseline to 3.4 ± 4.2 at follow-up (mean difference +1.3, $t = 2.8$, $p = 0.007$), suggesting a mild increase in daytime sleepiness after initiation of brivaracetam. At baseline, only 2 patients (4.3%) had ESS-I scores >10, compared to 7 patients (15.2%) at follow-up (absolute difference 10.9%, 95% CI: 3.1–18.7; $p = 0.063$).

Insomnia and Sleep Quality: The Insomnia Severity Index (ISI) decreased slightly from 6.3 ± 4.9 to 5.6 ± 3.9 (mean difference -0.7, $t = 1.4$, $p = 0.162$), while the PSQI global score decreased from 4.2 ± 4.1 to 3.8 ± 3.4 (mean difference -0.4, $t = 1.4$, $p = 0.160$), indicating no statistically significant change in insomnia or sleep quality.

Categorical Sleep Changes: The proportion of patients with total sleep duration >10 hours/day increased from 2 (4.3%) at baseline to 8 (17.4%) at follow-up (absolute difference 13%, 95% CI: 2.1–23.9; $p = 0.031$). Similarly, daytime sleep duration exceeding 1 hour/day increased from 3 patients (6.5%) to 10 patients (21.7%) (absolute difference 15.2%, 95% CI: 6.4–24.0; $p = 0.002$).

Overall, while brivaracetam monotherapy led to modest increases in total sleep duration and daytime sleep, no patient discontinued the drug due to sleep-related adverse events.

Table 1. Baseline demographic and clinical characteristics of patients with epilepsy initiated on brivaracetam monotherapy (n = 46)

Variable	n (%) / Mean ± SD
Age, years	37.8 ± 11.9
Male	22 (47.8)
College educated	26 (56.5)
Duration of epilepsy <1 year	36 (78.2)
Duration of epilepsy >1 year	10 (21.7)
Generalized epilepsy	32 (69.6)
Focal epilepsy	14 (30.4)
Presence of aura	7 (13.0)

SD = Standard Deviation

Table 2. Treatment characteristics of brivaracetam monotherapy among study participants (n = 46)

Treatment Variable	n (%) / Mean ± SD
Initial dose (mg/day)	90.2 ± 19.8
Maximum dose achieved (mg/day)	96.7 ± 30.2
Dose escalation required	7 (13)
Dose reduction required	3 (6.5)
Drug withdrawal due to adverse effects	0 (0)

Table 3. Comparison of sleep parameters before and after initiation of brivaracetam monotherapy

Variable	Baseline (Mean ± SD)	Follow-up (Mean ± SD)	Mean difference	t (df)	p value[1]
Total sleep duration per day (hrs)	7.6 ± 1.5	8.1 ± 1.6	+0.5	2.9 (45)	0.005
Insomnia Severity Index (ISI) – total score	6.3 ± 4.9	5.6 ± 3.9	-0.7	1.4 (45)	0.162
ESS-I score	2.1 ± 2.5	3.4 ± 4.2	+1.3	2.8 (45)	0.007
PSQI global score	4.2 ± 4.1	3.8 ± 3.4	-0.4	1.4 (45)	0.160

[1] Paired t-test; SD = Standard Deviation; ESS-I = Epworth Sleepiness Scale – Indian version; PSQI = Pittsburgh Sleep Quality Index

Table 4. Categorical sleep parameters before and after brivaracetam monotherapy

Variable	Baseline n (%)	Follow-up n (%)	Absolute difference % (95% CI)	p value[1]
ESS-I score >10				
Absent	44 (95.7)	39 (84.8)	10.9 (3.1–18.7)	0.0625
Present	2 (4.3)	7 (15.2)		
Total sleep duration >10 hrs/day				
Absent	44 (95.7)	38 (82.6)	13.0 (2.1–23.9)	0.0313
Present	2 (4.3)	8 (17.4)		
Daytime sleep duration >1 hr/day				

Variable	Baseline n (%)	Follow-up n (%)	Absolute difference % (95% CI)	p value[1]
Absent	43 (93.5)	36 (78.3)	15.2 (6.4–24.0)	0.002
Present	3 (6.5)	10 (21.7)		

[1] McNemar exact test; ESS-I = Epworth Sleepiness Scale – Indian version

Discussion

This study indicates that BRV monotherapy in patients with epilepsy is associated with modest increases in total sleep duration and mild daytime sleepiness, without serious adverse events. The observed rise in ESS-I scores suggests a subtle increase in subjective daytime sleepiness, consistent with prior reports of somnolence in adjunctive BRV studies [11–14,23]. Importantly, no participants required discontinuation of therapy, highlighting the favorable tolerability of BRV.

Our findings are in line with previous research indicating that SV2A ligands, including BRV, can induce sedation while generally preserving daily functioning [9–10,24]. Unlike some older antiepileptic drugs such as benzodiazepines or valproate, BRV's selective binding to SV2A likely limits cognitive and behavioral adverse effects, a feature that may contribute to its suitability as monotherapy [7,25].

The modest increase in daytime napping observed in this study may represent a compensatory response to mild sleepiness rather than a clinically concerning effect. Notably, PSQI and ISI scores showed non-significant changes, suggesting that overall sleep quality and insomnia symptoms remained largely unaffected. Taken together, these results indicate that while BRV may produce mild sedation, it does not appear to negatively impact overall sleep architecture or quality, supporting its use in patients for whom preservation of cognitive function and daily alertness is a priority.

Strengths and Limitations: Strengths include the prospective design, use of validated sleep scales, and consecutive sampling. Limitations are the small sample size, short follow-up (1 month), and reliance on self-reported sleep measures. Future studies should include polysomnography and longer-term follow-up.

Conclusion

BRV monotherapy is well-tolerated in newly diagnosed epilepsy, with mild increases in daytime sleepiness and total sleep duration, but no serious adverse events. These findings support its safety profile and tolerability in clinical practice. Longitudinal studies with larger cohorts are warranted.

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