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EDITORIAL

Dear Colleagues,

We are publishing the first issue of our journal in 2026. In this issue, you will find a review article on the efficacy of vigabatrin, a drug no longer produced in our country, in infantile epileptic spasms. Unfortunately, every year, some drugs that have proven effective and play an important role in the treatment of epilepsy are discontinued, leaving us physicians and our patients in a difficult situation. I wanted to bring this problem to the forefront through this article. When it comes to human health, capitalism and the pursuit of profit must be kept under control, and the industry must also adhere to the ethical rules that many of us are bound by. The irresponsible withdrawal of a drug from the market should not be allowed.

In this issue and previous issues, studies on the psychological and emotional burden and social impacts of epilepsy on both patients and their caregivers have been frequently published. In this issue, a study on physical activity and epilepsy and another study on overprotection of individuals with epilepsy are particularly noteworthy. Archives of Epilepsy can be highlighted as a journal focusing on the socio-psychological aspects of epilepsy among journals publishing in the field of epilepsy.

I wish you pleasant reading.

S. Naz Yeni, M.D., Prof.
Editor-in-Chief

Archives of Epilepsy

Review

Efficacy of Vigabatrin Oral Suspension in Infantile Epileptic Spasms Syndrome: A Systematic Review

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Infantile epileptic spasms syndrome is a rare and severe epilepsy syndrome in infants. It is identified by clusters of spasms, developmental regression, and hypsarrhythmia. Although there are many different therapeutic options that include the use of vigabatrin (VGB) along with hormonal treatments, the best approach has still not reached a consensus. In this regard, a systematic review of oral suspension VGB is warranted to evaluate efficacy, safety, and its effects on different subpopulations of patients. A systematic review was conducted in accordance with the PRISMA 2020 guidelines (Oxford, UK). Randomized controlled trials, cohort studies, and retrospective analyses conducted in children aged 2 months to 2 years with infantile spasms were selected. Data on spasm cessation, electroencephalography (EEG) normalization, adverse events, and other treatment-specific outcomes were extracted. Bias was assessed through ROBINS-I tool (Cochrane, UK) and Cochrane RoB 2.0 tool (Cochrane, UK). Six studies (34 to 377 participants) from 1999 to 2022 were included. Mean age ranged between 5 and 13.5 months, and male predominance was present. Spasm cessation rates with VGB monotherapy were between 11% and 78%, whereas hormonal therapies reached up to 75%. The response rates for combination therapies that included VGB with hormones stood at 71.5%. The EEG normalization achieved the highest rate of 75% with cosyntropin monotherapy. The VGB had lower rates. Adverse event rates ranged from 0% to 86%, and adverse severe events, including visual field defects, occurred in as many as 19% of participants. Hormonal therapies were associated with irritability and weight gain, and some adverse effects that seemed mitigated by combination therapy. Hormonal therapies were not found to be noticeably better than VGB monotherapy, but combination therapies added better outcomes while maintaining balance between efficacy and safety. Tailored treatment strategy is critical, and further research is required.

Keywords: Infantile epileptic spasms syndrome, vigabatrin, hypsarrhythmia, combination therapy, hormonal treatments, spasm cessation, EEG normalization, adverse events

INTRODUCTION

Infantile epileptic spasms syndrome (IESS), previously referred to as infantile spasms (IS) or West syndrome, represents a severe developmental and epileptic encephalopathy of infancy. This syndrome is characterized by clusters of epileptic spasms, a chaotic interictal electroencephalography (EEG) pattern often described as hypsarrhythmia, and developmental arrest or regression.[1] The incidence is estimated at 0.25 to 0.6 per 1,000 live births, with onset typically within the first year of life, peaking around 4 to 7 months.[2]

IESS is associated with poor neurodevelopmental outcomes when left untreated, often leading to intellectual disability, refractory epilepsy, and severe developmental impairments. Etiologies are diverse, encompassing structural, genetic, metabolic, and acquired causes. Accurate classification by both electroclinical features and etiology is central to diagnosis and management, as emphasized by the International League Against Epilepsy classification system.[3,4]

IESS is resistant to conventional antiseizure drugs and presents some significant challenges in management. The treatment landscape remains very hormonal, dominated by either adrenocorticotropic hormone (ACTH) or oral corticosteroids, and the gamma-aminobutyric acid (GABA)-modulating agent vigabatrin (VGB).[5] Though hormonal therapies are generally considered the first-line treatments for asymptomatic IESS, VGB has become the treatment of choice in IS related to tuberous sclerosis complex (TSC). VGB exerts its effects by

inhibiting GABA transaminase, which increases the levels of the inhibitory neurotransmitter GABA in the brain.[6] This mechanism is especially effective in countering spasms, particularly in etiologies with structural anomalies or TSC.[7]

The introduction of VGB in the 1990s represents a landmark advance in the management of IESS. Its effectiveness has been shown to be effective in both monotherapy and adjunctive therapy. Investigations have shown that VGB results in a spasm cessation rate ranging from 50% to 70%, particularly in the first weeks of treatment.[8-10] Though highly clinically useful, the drug's long-term safety profile still raises concerns, including retinal toxicity and the risk of visual field defects, such that this drug's risk-benefit ratio remains under continued study.[10-12] Furthermore, questions abound about optimal dosing, the duration of therapy, and relative efficacy against other treatments at diverse etiological subgroups.

Despite the many decades of research, the choice of first-line therapy for IS continues to be contentious, as preferences for treatment are very often based on etiology, experience, and available healthcare resources. Most of the past studies have been primarily interested in short-term outcomes such as spasm cessation and EEG normalization, while giving little importance to long-term neurodevelopmental and seizure-free outcomes. Additionally, heterogeneity in study designs, patients studied, and outcome measures has made the synthesis of generalizable and robust conclusions problematic. Based on the evident gaps, this systematic review focuses on the effectiveness of oral VGB suspension for the treatment of IS and aims to present a comprehensive assessment of the therapeutic outcomes, safety profile, and role of VGB in the management of IESS.

MAIN POINTS

- **Treatment efficacy varies by therapy type and subpopulation**
  - Vigabatrin (VGB) monotherapy showed a wide range of spasm cessation rates, from 11% to 78% in the included studies.
  - Hormonal therapies (like cosyntropin or corticosteroids) demonstrated high cessation rates, reaching up to 75% , and were associated with the highest rates of electroencephalography normalization (75% with cosyntropin monotherapy).
  - Combination therapy (VGB with hormones) was found to have better response rates, reaching 71.5%, and may offer a better balance between efficacy and safety.
  - Etiology is critical: VGB is the treatment of choice and particularly effective for infantile spasms (IS) associated with tuberous sclerosis complex, often exceeding the response of hormonal therapy in this subgroup.
- **Safety profile highlights the risk of visual defects with VGB**
  - Adverse event rates ranged broadly from 0% in tightly controlled settings to 86% in broader clinical applications.
  - VGB is primarily associated with side effects such as lethargy, drowsiness, and the severe adverse event of visual field defects (in as many as 19% of cases in the abstract).
  - Hormonal therapies are mainly associated with irritability and weight gain.
  - Combination therapies may mitigate some risks, but visual field toxicity remains a concern for VGB.
- **A tailored treatment strategy is recommended**
  - The review concludes that hormonal therapies were not found to be noticeably better than VGB monotherapy overall, but combination therapies added better outcomes.
  - The optimal choice of first-line therapy for IS remains contentious and should be an individualized, tailored treatment strategy based on the patient's underlying etiology, safety considerations, and response to therapy.
  - Given the findings, the recommendation is to consider hormonal therapies first-line, but VGB-inclusive combination therapy is a viable alternative if hormonal treatments are ineffective or contraindicated.

METHODS

Inclusion and Exclusion Criteria

Studies were included if they: (1) involved patients aged between 2 months and 2 years with IS, (2) evaluated the efficacy of VGB, either as monotherapy or in combination with other drugs, (3) were designed to have measurable endpoints such as cessation of spasms, EEG normalization, or adverse events (4) were either randomized controlled trials (RCTs), cohort studies, or case-control studies, and (5) were published in a peer-reviewed journal in the English language. The exclusion criteria were for studies that addressed any of the following areas: (1) where VGB had not been evaluated per se, (2) conducted on patients with disorders apart from IESS, (3) lacked quantitative data on efficacy or safety, (4) were a review article, editorial or letter without original data or sources, or (5) duplicated data or overlapped patient cohorts.

Review Design

The PECOS framework was created in compliance with the reporting guidelines of PRISMA 2020 (University of Oxford, UK; University of Sydney, Australia)[13] to ensure systematic identification and evaluation of relevant studies. The population (P) consists of children between the ages of 2 months and 2 years, diagnosed with IS. The exposure (E) was oral VGB suspension administration. The comparator (C) includes other therapies like ACTH, corticosteroids, or placebo. The outcomes (O) were spasm cessation, EEG normalization, and adverse event rates. The study design (S) included RCTs, cohort studies, and case-control studies.

Database Search Protocol

The comprehensive search strategy was implemented on six databases: PubMed, Embase, Cochrane Library, Scopus, Web of Science, and ClinicalTrials.gov. An exact and sensitive search was carried out using Boolean operators and MeSH keywords. Terms related to "infantile spasms", "VGB", "oral suspension", "treatment outcomes", and "adverse events" were used in the search (Table 1). Variations of the keywords and synonyms were considered to capture all relevant literature. Filters for age group, study design, and language were applied where appropriate.

Data Extraction Protocol

Data were extracted with a standardised protocol to make it uniform and accurate. The extracted items include the following: title of the study, names of authors, year of publication, design of study, sample size, number of patients, including age, gender, and comorbid conditions, information on the intervention, including dosage of VGB, treatment duration, comparison treatments, and outcome measures, which include spasm resolution, EEG return to normal, side effects, and a statistical summary that includes confidence

Table 1. Search strings utilised across the assessed databases

Database	Search string
PubMed	("infantile epileptic spasms syndrome"[MeSH] or "West Syndrome") and ("vigabatrin"[MeSH] of "gamma-aminobutyric acid transaminase inhibitor") and ("oral suspension" or "administration and dosage") and ("treatment outcomes").
Embase	("infantile epileptic spasms syndrome"/exp or "West syndrome") and ("vigabatrin"/exp or "gaba transaminase inhibitor") and ("oral suspension" or "dose regimen") and ("efficacy" or "safety").
Cochrane Library	("infantile epileptic spasms syndrome" or "West syndrome") and ("vigabatrin" or "gamma-aminobutyric acid transaminase inhibitor") and ("oral suspension") and ("randomized controlled trial" or "observational study").
Scopus	TITLE-ABS-KEY ("infantile epileptic spasms syndrome" or "West syndrome") and TITLE-ABS-KEY ("vigabatrin") and TITLE-ABS-KEY ("oral suspension") and TITLE-ABS-KEY ("spasm cessation" or "EEG normalization").
Web of Science	("infantile epileptic spasms syndrome" or "West syndrome") and ("vigabatrin" or "gamma-aminobutyric acid transaminase inhibitor") and ("oral suspension") and ("efficacy" or "adverse events").
ClinicalTrials.gov	("infantile epileptic spasms syndrome" and "vigabatrin" and "oral suspension" and "adverse events") and (phase 2 or phase 3).

EEG: Electroencephalography, MeSH: Medical Subject Headings

intervals (CI) and p-values. Two reviewers independently extracted the data, and any discrepancy was resolved by discussion or referral to a third reviewer. This approach reduced the error, increasing the reliability of the extracted data.

Risk of Bias Protocol

Risk of bias was assessed for included studies in the ROBINS-I tool (Cochrane, UK)[14] for non-randomized studies and the RoB 2.0 tool (Cochrane, UK)[15] for RCTs. ROBINS-I (Cochrane, UK) domains included confounding, selection of participants, classification of interventions, and outcome measurement. RoB 2.0 (Cochrane, UK) evaluated the process of randomization, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selective reporting. Every domain was rated low, moderate, serious, or a critical risk of bias.

RESULTS

A total of 374 records were identified from the database search, and no records were obtained from the registers (Figure 1). After the removal of 43 duplicate entries, 331 records were screened for relevance. No records were excluded in the initial screening phase. Of these, 331 full-text reports were sought, of which 34 could not be retrieved. Thereafter, 297 full-text reports were assessed for eligibility. Of these, 291 reports were excluded on the grounds that 62 failed to satisfy the PECOS criteria, 74 were literature reviews, 58 concentrated on adult populations, 48 were case reports, and 49 were editorials. Finally, six studies[16-21] were included in the systematic review, and there were no further reports of newly included studies.

Geographic Distribution and Temporal Context

The studies included in this review were conducted in different regions and time periods, highlighting the global efforts to investigate the treatment of IS (Table 2). Research was conducted in the United Kingdom (UK)/Netherlands,[16] Australia,[17] Pakistan,[18] the USA,[19] and multinational collaborations across the UK, Australia, Germany, and Switzerland.[21] The studies ranged in publication years from 1999[16] to 2022[17,19] reflecting evolving approaches and advancements in the understanding of IS treatment.

Study Designs and Sample Sizes

Most studies were RCTs, consisting of controlled comparisons between VGB and other treatments.[16,19-21] Two were retrospective,

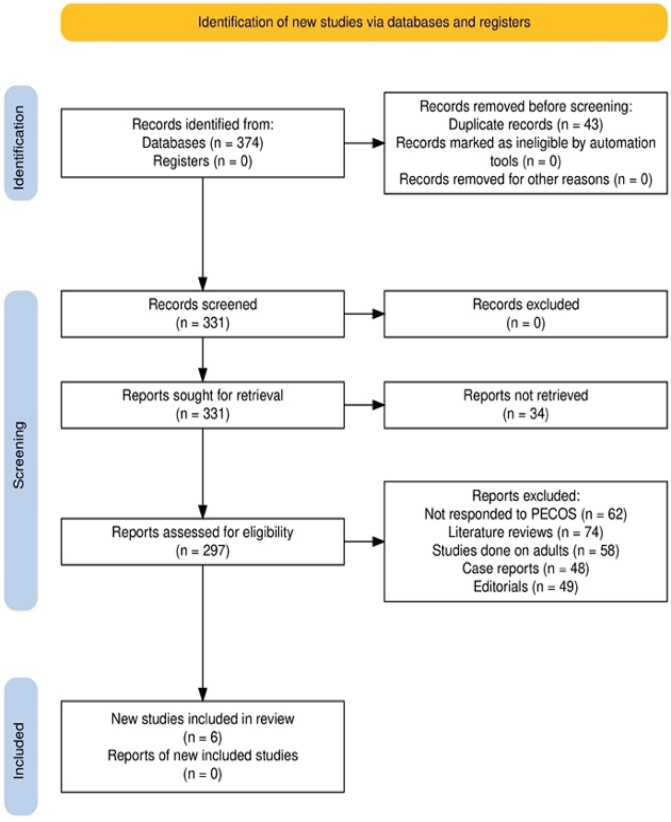

Figure 1. PRISMA study selection process for this review

based on real-world data from clinical records.[17,18] Sample sizes were highly variable, from 34 participants[19] to 377[21] with smaller studies made detailed therapeutic observations possible, while larger studies allow for greater generalisability.

Participant Characteristics

The mean age at spasm onset ranged considerably, and thus the populations involved were heterogeneous. The lowest mean age recorded was 5±1.4 months,[18] while the highest was at 13.5 months, a median value.[16] All the studies demonstrated a predominance of males in their patient demographics. Males represented between 53%.17 to 64.7%[19] of all cases. This trend in patient demographics has been observed to fit previous reports of a slightly higher prevalence of IS in male infants.

Table 2. Demographic variables assessed

Author ID	Year	Location	Study design	Sample size	Mean age (in years)	Male/female ratio	Follow-up period
Appleton et al.[16]	1999	UK/Netherlands	RCT	40	13.5 months (median)	60% male	24 weeks
Dzau et al.[17]	2022	Australia	Retrospective	151	8.2±1.3 months	53% male	42 days
Ibrahim et al.[18]	2010	Pakistan	Retrospective	56	5±1.4 months	62.5% male	6 months
Knupp et al.[19]	2022	USA	RCT	34	6 months (mean)	64.7% male	2 weeks
Lux et al.[20]	2004	UK	RCT	107	6.2±1.5 months	58% male	14 days
O'Callaghan et al.[21]	2017	UK/Australia/ Germany/Switzerland	RCT	377	7±2.3 months	Not reported	42 days

RCT: Randomized controlled trial

Duration of Follow-up

Follow-up durations ranging from a minimum of 2 weeks[19] to as much as 42 days.[17,21] Long-duration follow-ups helped evaluate in greater depth not only treatment efficacy but also side effects, while shorter-duration follow-ups primarily reflected immediate treatment results in the form of cessation of spasms and EEG normalization.

Types of Treatment and Dose Intervals

The studies assessed different treatment modalities: for example, VGB as monotherapy, hormonal treatments like prednisolone or cosyntropin (Table 3). The dosages for VGB varied from 12.5 mg/kg/day[18] to 150 mg/kg/day.[16,17,20,21] The hormonal treatments, such as cosyntropin, have been used at similar dosages across all the studies, which can be useful for comparison.

Response Rates

Spasm cessation rates with VGB monotherapy exhibited a broad range, spanning from 11% in some real-world clinical settings to as high as 78% in controlled trials, suggesting variability in response based on patient characteristics and study design.[16,19] In contrast, hormonal therapies demonstrated cessation rates reaching up to 75%[20] though these rates were not consistently superior to those of VGB across all populations. Notably, in cases of IESS associated with TSC, VGB was reported to be particularly effective, with a response rate exceeding that of hormonal therapy.[21-34] While combination therapy incorporating both VGB and hormonal treatments demonstrated improved response rates, these findings underscore the need to tailor treatment selection based on etiology and individual patient response. This approach avoids assuming the universal superiority of hormonal interventions.[18,21]

EEG Normalization

EEG normalization was another important secondary measure in most of the studies. The highest normalization rates were reported with cosyntropin monotherapy, where 75% of patients had resolution of hypsarrhythmia.[19] Similarly, hormonal therapies had normalization rates of 68% in some populations.[20] On the other hand, VGB monotherapy had lower normalization rates, which is consistent with its relatively lower efficacy in achieving complete spasm control.

Adverse Event Rates

Adverse events were seen within all treatment groups. For example, the rate has ranged from 0% for tightly controlled settings[16] to 86% for a broader clinical application.[19] Severe adverse events were less common: the rates were 12% in those on hormonal therapy and 9% in those who received VGB in one comparison.[17] The comparison of combination therapies with VGB monotherapy revealed relatively lower rates of severe adverse events.[21]

Types of Adverse Events

The adverse events varied depending on the treatment. VGB was mainly associated with lethargy, drowsiness, and visual field defects[18,19,21] while hormonal therapies were mainly associated with irritability and weight gain.[20] Combination therapies mitigated some of these risks, except that visual field toxicity remained an issue for VGB.[21]

Etiology and Subpopulations

The studies targeted diverse IESS subpopulations. Some studies targeted newly diagnosed IESS with classic hypsarrhythmia[16] while others excluded tuberous sclerosis to assess non-TSC IS.[17,20] Such distinctions are critical because the etiology of IESS significantly influences the treatment response. For example, VGB is highly effective in IESS associated with tuberous sclerosis but is less effective in other forms of IESS.[21]

Quality Levels Observed

Among the RCTs, most studies had a low risk of bias in multiple domains (Figure 2). However, there were specific concerns regarding the randomization process (D1) in Appleton et al.[16] and O'Callaghan et al.[21] as well as selective reporting (D3) in Lux et al.[20] Appleton et al.[16] and O'Callaghan et al.[21] also had some concerns about deviations from intended interventions (D4). Altogether, RCTs scored a low risk of bias, which ensures strong methodological quality, although with minor limitations in isolated domains.[16,19-21]

Table 3. Efficacy of VGB observed across the included papers

Author ID	Groups assessed	Vigabatrin dosage (mg/kg/day)	Duration of therapy (weeks)	Response rate (% cessation of spasms)	EEG normalization rate (%)	Adverse event rate (%)	Adverse event type(s)	Concurrent therapies	Study population characteristics (etiology/genotype of IESS)	Conclusion assessed
Appleton et al.[16]	VGB vs. placebo	50-150 mg/kg/day	5 days	78% (95% CI: 55-89%)	Not reported	0%	None reported	None	Newly diagnosed IESS, classic hypsarrhythmia	VGB effective, recommended as first-line
Dzau et al.[17]	PNL40, PNL60, VGB	100-150 mg/kg/day	42 days	PNL60: 63%, VGB: 45% (P=0.01)	EEG normalization: not significant	Severe effects: 12% (PNL), 9% (VGB)	Hospitalization, irritability	Sequential hormone therapy	Non-tuberous sclerosis IESS	Hormone escalation effective in non-responders
Ibrahim et al.[18]	VGB vs. ACTH	12.5-150 mg/kg/day	6 weeks	55.3% (ACTH: 50%)	Partial EEG improvement: 32%	Relapse: ACTH 55%, VGB 33%	Drowsiness, lethargy	ACTH second-line	Symptomatic/ idiopathic IESS	VGB preferred for first-line
Knupp et al.[19]	Cosyntropin, VGB, cosyntropin+VGB	Not specified	2 weeks	Cosyntropin: 75%, VGB: 11%, combination: 38% (p<0.01)	Hypsarrhythmia resolved: 75% (cosyntropin)	Adverse events: 86%, serious: 19%	Special interest: 42% (no significant differences)	None	New-onset IESS with hypsarrhythmia	Cosyntropin more effective than VGB for short-term outcomes
Lux et al.[20]	Hormones vs. VGB	100-150 mg/kg/day	14 days	VGB: 54%, hormones: 73% (p=0.043)	Hypsarrhythmia resolution: 68% (hormones)	Adverse effects: 55% (hormones)	Irritability, weight gain	Prednisolone, tetracosactide	Severe IESS excluding tuberous sclerosis	Hormones superior, recommend short duration
O'Callaghan et al.[21]	Hormones vs. hormones+VGB	100-150 mg/kg/day	42 days	Combination: 71.5%, hormones: 56.5% (p=0.002)	Electro-clinical improvement: 60% (combination)	Adverse effects: 18% (VGB)	Visual field defects	Hormonal therapy+VGB	Severe IESS without tuberous sclerosis	Combination superior, caution in toxicity

VGB: Vigabatrin, PNL: Peripheral nasal limit, ACTH: Adrenocorticotropic hormone, CI: Confidence interval, EEG: Electroencephalography, IESS: Infantile epileptic spasms syndrome

The cohort studies showed more variation in bias levels (Figure 3). The risk of bias for Dzau et al.[17] was low across many domains, but the authors had noted moderate concerns in the classification of interventions (D6). On the other hand, Ibrahim et al.[18] had moderate bias in many key domains such as confounding (D1), selection of participants (D2), and classification of interventions (D3). However, most of the other domains presented with low bias, thereby making the overall risk of bias for this study moderate.[17,18]

DISCUSSION

Mechanism of Action and Therapeutic Profile of VGB

VGB is associated with its antiepileptogenic properties due to an irreversible inhibition of the GABA catabolizing enzyme breakdown called transaminase, thus raising central nervous system inhibitory neurotransmitter GABA levels.[22] Other scientific research has shown that VGB can interfere with the glutamate-glutamine cycle between neurons and the central nervous system astrocyte cells, which contributes to its therapeutic effect in this patient population.[23] Early investigations conducted in 1983 showed that VGB is both an effective and tolerated drug among adult patients diagnosed with refractory epilepsy.[24] In 1989, its application extended to a refractory form of IESS, predominantly as add-on therapy, and proved highly efficacious, especially among TSC cases.[25-27] Several studies over the years assessed VGB's safety and efficacy profile for its use as the IESS treatment.[25-29] However, such studies also brought into view severe adverse effects associated with its use. According to a meta-analysis, VGB was related to retinal toxicity in 29% of the patients [95% confidence interval (CI): 7-69%] visual field defects were noted in 28% of patients (95% CI: 4-78%) and magnetic resonance imaging abnormalities in 21% of patients (95% CI: 15-29%).[30] Despite these risks, the therapeutic efficacy of VGB in IESS remains well established. VGB was approved by the United States Food and Drug Administration in 2009 for use as monotherapy in IESS and as adjunctive therapy for refractory complex partial seizures.[31]

Thematic Findings Across the Review

The included studies showed important patterns and differences in the efficacy and safety of VGB and hormonal therapies in the treatment of IESS, with varying degrees of similarity and divergence among the studies. The conclusions drawn from the studies by Appleton et al.[16] and Ibrahim et al.[18] which show similar results, show indicate that VGB monotherapy can achieve

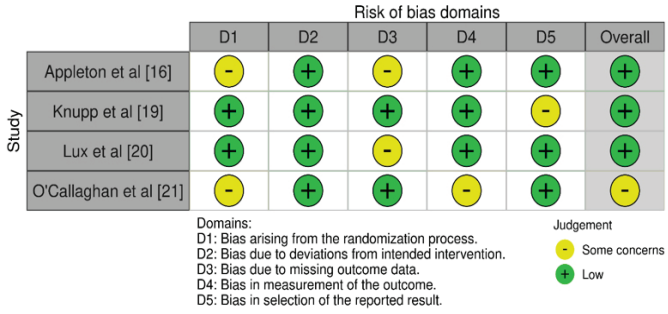

Figure 2. Bias assessed across the RCTs
RCTs: Randomized controlled trials

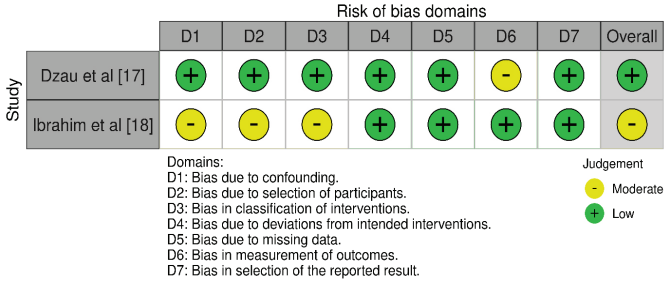

Figure 3. Bias assessed across the cohort studies

medium success as a first-line therapy, especially in newly diagnosed IESS cases. Both studies found a good rate of response to VGB; Appleton et al.[16] found a 78% spasm cessation rate, while the similar study by Ibrahim et al.[18] reported 55.3%, an observation which might be associated with the study population as well as the follow-up time.

The results by Knupp et al.[19] and Lux et al.[20] are quite similar. However, although they differ in the degree of superiority, a cosyntropin response is 75% in the former, while hormonal therapy was 73% in the latter as reported by Lux et al.[20] Both studies highlighted that VGB monotherapy was ineffective in non-TSC-associated IESS, as evidenced by its low response rates of 11% and 54%, respectively.

Dzau et al.[17] and O'Callaghan et al.[21] reported combination therapies. Both studies reported that the effects of combination therapies were better than hormones alone, but the magnitude of effect differed between the two studies. O'Callaghan et al.[21] documented a higher rate of response at 71.5% for combinations as compared to 56.5% for hormone therapy alone, while Dzau et al.[17] mentioned a minimal effect with insignificant differences in the rate of normalization of EEG.

Another area of distinction was adverse event profiles. Appleton et al.[16] had no adverse events, whereas in the study by Knupp et al.[19] 86% of patients experienced adverse events. Safety profiles of combination therapies studied in O'Callaghan et al.[21] were more favorable than the monotherapy with VGB, as reported in Dzau et al.[17] in which severe adverse effects, including hospitalization, occurred in 9% of cases.

Alignment with Previous Reviews

The efficacy of hormonal monotherapy in IESS has been well-documented, particularly in non-TSC-associated cases; however, recent meta-analyses challenge the notion that it is universally superior to VGB.[32,33] While hormonal therapies, including ACTH and corticosteroids, have shown robust response rates, several studies indicate that VGB is at least equally effective and, in some cases, superior, particularly when considering long-term neurodevelopmental outcomes and EEG normalization.[34,35] Additionally, the variability in study designs and patient demographics has contributed to inconsistencies in reported efficacy, making it imperative to interpret these findings with caution. The optimal treatment approach should therefore be individualized, incorporating factors such as etiology, safety considerations, and patient response to therapy.[19,22]

Our results are somewhat different from those of Xu et al.[33] who found no significant difference in spasm cessation rates between hormonal monotherapy and combination therapy (hormones+VGB) in two RCTs. In contrast, our review suggested that combination therapies could improve outcomes in some cases, though this finding requires cautious interpretation due to variability across studies.

Similar to our results, response rates to VGB have been much higher in patients with TSC-associated IESS, as reported by Prezioso et al.[34] The spasm cessation rate of 67% across observational studies and 88% in RCTs, in TSC patients, closely coincides with the higher efficacy of VGB in such a subgroup, as determined in our review. However, both reviews pointed out limitations because of high heterogeneity and low levels of evidence, thus requiring further robust studies to strengthen therapeutic recommendations.

Both our review and the results of Golec et al.[35] pointed out potential safety issues with VGB treatment, especially visual field defects and neuroimaging abnormalities. This only underscores the necessity to closely monitor the long-term safety of VGB. Our review did suggest that combination therapies may reduce some adverse effects, but Golec et al.[35] raised broader safety concerns, which limit the general use of VGB restricting its use only to specific indications like TSC-associated IESS.

Our review provided a world view of IESS management, whereas Sahu et al.[36] highlighted the unique epidemiological and clinical challenges in South Asia. Both analyses commented on an increased male-to-female ratio in IESS presentations, which is consistent with more general epidemiological trends. Additionally, Sahu et al.[36] pointed out other regional barriers: these include the lack of availability of ACTH and VGB, and more resource-specific strategies are of utmost importance, which cannot be the prime focus in our review.

Study Limitations

This study had several limitations due to the variability in study designs, sample sizes, and follow-up durations among the included studies. The heterogeneity among the patients' demographics (such as mean age at spasm onset and male-to-female ratios) may have resulted in confounding factors limiting the generalizability of the findings. Variability in treatment protocols, particularly dosages

and durations of VGB and hormonal therapies, complicated direct comparisons between studies. The inconsistent reporting of secondary outcomes, such as EEG normalization rates and long-term neurodevelopmental outcomes, limited the ability to draw definitive conclusions about the overall efficacy of VGB. Adverse event rates were sometimes reported inconsistently and some did not provide adequate descriptions of the safety profile, which made it challenging to thoroughly assess the risk-benefit ratio of VGB monotherapy or combination therapies.

Recommendations and Clinical Implications

Hormonal therapies should be considered the first-line of treatment for IS, because of their efficacy in spasm cessation and EEG normalization. If hormonal treatments alone prove to be ineffective or are contraindicated, combination therapy with VGB should be considered a viable alternative. Future clinical trials should ensure that all treatment protocols standardize the dosage and duration to allow for more comparisons. Long-term follow-up studies are also required to evaluate the effects of these treatments on neurodevelopmental outcomes and seizure recurrence. Adverse events should be systematically monitored and reported to provide a clearer understanding of the safety profiles of these treatments, particularly the retinal toxicity associated with VGB. Tailored approaches that account for the underlying etiology and patient-specific characteristics should guide clinical decision-making.

CONCLUSION

This review highlights the complexities in selecting optimal therapy for IS, as the comparative efficacy of VGB and hormonal treatments remains dependent on patient-specific factors, particularly etiology. While hormonal therapies have long been considered first-line treatments, recent meta-analyses indicate that VGB exhibits comparable, if not superior, efficacy in certain subgroups, especially in IESS cases linked to TSC. Moreover, EEG normalization and long-term neurodevelopmental outcomes may not always favor hormonal monotherapy over VGB. Combination therapies incorporating both VGB and hormonal agents have demonstrated promising outcomes, though their superiority over individual therapies requires further investigation. Given these findings, treatment decisions should be made on a case-by-case basis, weighing efficacy, safety profiles, and individual patient response rather than assuming a universal advantage of hormonal therapy.

Footnotes

Authorship Contributions

Surgical and Medical Practices: V.K.S., R.R., Concept: V.K.S., Design: V.T., Data Collection or Processing: R.R., Analysis or Interpretation: V.T., Literature Search: R.J., Writing: R.J.

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REFERENCES

1. Kotulska K, Kwiatkowski DJ, Curatolo P, et al. Prevention of epilepsy in infants with tuberous sclerosis complex in the EPISTOP trial. *Ann Neurol.* 2021;89(2):304-314. [Crossref]
2. Auvin S, Dozières-Puyravel B, Avbersek A, et al. Radiprodil, a NR2B negative allosteric modulator, from bench to bedside in infantile spasm syndrome. *Ann Clin Transl Neurol.* 2020;7(3):343-352. [Crossref]
3. Elterman RD, Shields WD, Mansfield KA, Nakagawa J; US Infantile Spasms Vigabatrin Study Group. Randomized trial of vigabatrin in patients with infantile spasms. *Neurology.* 2001;57(8):1416-1421. [Crossref]
4. Macdonald-Laurs E, Dzau W, Warren AEL, et al. Identification and treatment of surgically-remediable causes of infantile epileptic spasms syndrome. *Expert Rev Neurother.* 2024;24(7):661-680. [Crossref]
5. Zuberi SM, Wirrell E, Yozawitz E, et al. ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: position statement by the ILAE task force on nosology and definitions. *Epilepsia.* 2022;63(6):1349-1397. [Crossref]
6. Askalan R, Mackay M, Brian J, et al. Prospective preliminary analysis of the development of autism and epilepsy in children with infantile spasms. *J Child Neurol.* 2003;18(3):165-170. [Crossref]
7. Mirabella G, Morong S, Buncic JR, et al. Contrast sensitivity is reduced in children with infantile spasms. *Invest Ophthalmol Vis Sci.* 2007;48(8):3610-3615. [Crossref]
8. Darke K, Edwards SW, Hancock E, et al. Developmental and epilepsy outcomes at age 4 years in the UKISS trial comparing hormonal treatments to vigabatrin for infantile spasms: a multi-centre randomised trial. *Arch Dis Child.* 2010;95(5):382-386. [Crossref]
9. Buoni S, Zannolli R, Strambi M, Fois A. Combined treatment with vigabatrin and topiramate in West syndrome. *J Child Neurol.* 2004;19(5):385-386. [Crossref]
10. Snyder HE, Jain P, RamachandranNair R, Jones KC, Whitney R. Genetic advancements in infantile epileptic spasms syndrome and opportunities for precision medicine. *Genes (Basel).* 2024;15(3):266. [Crossref]
11. Gaily E, Liukkonen E, Paetau R, Rekola R, Granström ML. Infantile spasms: diagnosis and assessment of treatment response by video-EEG. *Dev Med Child Neurol.* 2001;43(10):658-667. [Crossref]
12. Tolbert D, Reid S, Harris S, Bekersky I. Vigabatrin lacks proarrhythmic potential: results from a thorough QT/QTc study in healthy volunteers. *Clin Ther.* 2017;39(8):1639-1648. [Crossref]
13. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71. [Crossref]
14. Igelström E, Campbell M, Craig P, Katikireddi SV. Cochrane's risk of bias tool for non-randomized studies (ROBINS-I) is frequently misapplied: a methodological systematic review. *J Clin Epidemiol.* 2021;140:22-32. [Crossref]
15. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ.* 2019;366:l4898. [Crossref]
16. Appleton RE, Peters AC, Mumford JP, Shaw DE. Randomised, placebo-controlled study of vigabatrin as first-line treatment of infantile spasms. *Epilepsia.* 1999;40(11):1627-1633. [Crossref]
17. Dzau W, Cheng S, Snell P, et al. Response to sequential treatment with prednisolone and vigabatrin in infantile spasms. *J Paediatr Child Health.* 2022;58(12):2197-2202. [Crossref]
18. Ibrahim S, Gulab S, Ishaque S, Saleem T. Clinical profile and treatment of infantile spasms using vigabatrin and ACTH--a developing country perspective. *BMC Pediatr.* 2010;10:1. [Crossref]
19. Knupp KG, Coryell J, Singh RK, et al. Comparison of cosyntropin, vigabatrin, and combination therapy in new-onset infantile spasms in a prospective randomized trial. *J Child Neurol.* 2022;37(3):186-193. [Crossref]
20. Lux AL, Edwards SW, Hancock E, et al. The United Kingdom Infantile Spasms Study comparing vigabatrin with prednisolone or tetracosactide

at 14 days: a multicentre, randomised controlled trial. *Lancet.* 2004;364(9447):1773-1778. [Crossref]

21. O'Callaghan FJ, Edwards SW, Alber FD, et al. Safety and effectiveness of hormonal treatment versus hormonal treatment with vigabatrin for infantile spasms (ICISS): a randomised, multicentre, open-label trial. *Lancet Neurol.* 2017;16(1):33-42. [Crossref]
22. Bhalla S, Skjei K. Fulminant vigabatrin toxicity during combination therapy with adrenocorticotropic hormone for infantile spasms: three cases and review of the literature. *Epilepsia.* 2020;61(10):e159-e164. [Crossref]
23. Singh A, Hadjinicolaou A, Peters JM, Salussolia CL. Treatment-resistant epilepsy and tuberous sclerosis complex: treatment, maintenance, and future directions. *Neuropsychiatr Dis Treat.* 2023;19:733-748. [Crossref]
24. Velíšek L, Velíšková J. Modeling epileptic spasms during infancy: are we heading for the treatment yet? *Pharmacol Ther.* 2020;212:107578. [Crossref]
25. Barrett KT, Choudhary A, Charkhand B, Scantlebury MH. Animal models in epileptic spasms and the development of novel treatment options. *J Clin Neurophysiol.* 2022;39(7):529-537. [Crossref]
26. Chopra SS. Infantile spasms and west syndrome - a clinician's perspective. *Indian J Pediatr.* 2020;87(12):1040-1046. [Crossref]
27. de Saint Martin A, Napuri S, Nguyen S. Tuberous sclerosis complex and epilepsy in infancy: prevention and early diagnosis. *Arch Pediatr.* 2022;29(5S):5S8-5S13. [Crossref]
28. Kats DJ, Roche KJ, Skotko BG. Epileptic spasms in individuals with down syndrome: a review of the current literature. *Epilepsia Open.* 2020;5(3):344-353. [Crossref]
29. Zhong L, Liu C, Lin L. Infantile spasms caused by NEXMIF mutation: a case report and literature review. *Appl Neuropsychol Child.* 2023;12(4):380-385. [Crossref]
30. Biswas A, Yossofzai O, Vincent A, Go C, Widjaja E. Vigabatrin-related adverse events for the treatment of epileptic spasms: systematic review and meta-analysis. *Expert Rev Neurother.* 2020;20(12):1315-1324. [Crossref]
31. Willmore LJ, Abelson MB, Ben-Menachem E, Pellock JM, Shields WD. Vigabatrin: 2008 update. *Epilepsia.* 2009;50(2):163-173. [Crossref]
32. Riikonen R. Infantile spasms: outcome in clinical studies. *Pediatr Neurol.* 2020;108:54-64. [Crossref]
33. Xu Z, Gong P, Jiao X, et al. Efficacy of vigabatrin in the treatment of infantile epileptic spasms syndrome: a systematic review and meta-analysis. *Epilepsia Open.* 2023;8(2):268-277. [Crossref]
34. Prezioso G, Chiarelli F, Matricardi S. Efficacy and safety of vigabatrin in patients with tuberous sclerosis complex and infantile epileptic spasm syndrome: a systematic review. *Expert Rev Neurother.* 2023;23(7):661-671.s. [Crossref]
35. Golec W, Sołowiej E, Strzelecka J, Jurkiewicz E, Jóźwiak S. Vigabatrin - new data on indications and safety in paediatric epilepsy. *Neurol Neurochir Pol.* 2021;55(5):429-439. [Crossref]
36. Sahu JK, Madaan P, Prakash K. The landscape of infantile epileptic spasms syndrome in South Asia: peculiarities, challenges, and way forward. *Lancet Reg Health Southeast Asia.* 2023;12:100170. [Crossref]

Post-traumatic Epilepsies: Prophylactic Antiseizure Medications Are Futile

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Abstract

Objective: Post-traumatic epilepsy (PTE) is a significant sequela of traumatic brain injury (TBI), with a high incidence of drug-resistant epilepsy. The role of prophylactic antiseizure medications (ASM) remains controversial. This study investigates the demographic, clinical, radiological, and electrophysiological characteristics of PTE and evaluates the impact of ASM use.

Methods: We retrospectively analyzed patients diagnosed with PTE at İstanbul University, İstanbul Faculty of Medicine Hospital (1994-2024). Clinical characteristics, imaging findings, electroencephalography results, and ASM use were assessed. Statistical analyses were conducted to explore correlations between trauma severity, epilepsy latency, and ASM efficacy.

Results: There were 67 patients diagnosed with PTE, 73% of whom were male. Severe TBI (bone fracture, hemorrhage, or loss of consciousness >24 hours) was observed in 60% of patients. Bilateral magnetic resonance imagining (MRI) lesions were significantly associated with shorter epilepsy latency ($p<0.01$). Drug-resistant epilepsy was more common in severe TBI cases ($p<0.03$) and patients with longer periods of unconsciousness. ASM use did not influence epilepsy latency or seizure frequency. Three patients exhibited psychogenic non-epileptic seizures.

Conclusion: ASM fails to prevent epileptogenesis and should not be routinely prescribed for seizure prophylaxis in patients with TBI. Trauma severity is a critical predictor of epilepsy onset and drug resistance. The presence of bilateral MRI lesions warrants closer monitoring. Given the complex consequences of TBI, these patients should be closely monitored by multidisciplinary teams.

Keywords: Trauma, antiseizure medications, psychogenic non-epileptic seizures, lesional epilepsy, drug-resistant epilepsy

INTRODUCTION

Traumatic brain injury (TBI) is one of the most common causes of epilepsy, documented as early as the 1700 BC Babylonian papyri.[1] The TBI group accounts for 20% of the cases of symptomatic epilepsy patients referred to a specialist epilepsy center, whereas 5 to 6% of the whole epilepsy cases are expected to arise due to trauma.[2,3] Post-traumatic seizures are strongly associated with poor functional outcomes and increased mortality.[4]

Seizures encountered following trauma are roughly divided into two groups: early seizures, which occur within the first 14 days post-trauma, and late seizures, which are more significant for the development of epilepsy and occur well after the first 14 days, either following TBI itself or during hospitalization. Up to 80% of the seizures arise within the first year. The pathophysiological basis of the seizures is believed to be associated with blood-brain barrier disruption and brain injury in the early period, while in the late period, excitotoxicity due to the accumulation of free radicals and glutamate plays a role.[5,6]

Trauma severity, which is an important determinant, is classified as mild (loss of consciousness for less than 30 minutes without skull fracture), moderate (loss of consciousness lasting no more than 24 hours regardless of the presence of a skull fracture), and severe (loss of consciousness exceeding 24 hours accompanied by skull fracture, contusion, or hematoma).[3] The predisposition to develop epilepsy after severe trauma, i.e., post-traumatic epilepsy (PTE), has been reported to be as high as 40-50%.

PTE is defined by a tendency to experience recurrent and unprovoked seizures in the long term due to the effects of trauma. Male gender, advanced age (over the age of 65), prior alcohol abuse, history of post-traumatic amnesia, focal neurological signs, presence and duration of loss of consciousness at the initial trauma, and possibly early seizures are associated with a greater risk for developing PTE.[7,8] Imaging

may be another important guide, as findings such as skull fracture, especially a depressed one, penetrating trauma, midline shift, brain contusion and hemorrhage are associated with an increased risk.[7,9]

The benefit of using antiseizure medications (ASM) in a prophylactic manner cannot be demonstrated in the long-term prognosis. Although some studies suggest a possible prophylactic effect of ASM such as levetiracetam and phenytoin in early seizures, further research is necessary to confirm their efficacy.[10] Another study shows levetiracetam may be a better alternative for mechanically ventilated pediatric patients.[11] However, a great number of studies, in addition to a recent guideline by the Neurocritical Care Society, have demonstrated important points. First, there was no significant reduction in the number of early seizures with ASM use versus no ASM or placebo, challenging the tendency to prescribe ASMs for early seizure prophylaxis.[12,13] Secondly, there was no significant effect of ASM for preventing late seizures, hence dashing the hopes on a true anti "epileptic" effect of ASM in such cases. Thirdly, patients receiving ASM had experienced side effects due to the therapy. Eventually, the final outcome was not improved by the ASM, with randomized trials, showing neutral effects on mortality and possibly worse overall epileptogenic effects, neurologic and cognitive outcomes, though the latter may be reversible upon drug discontinuation.[14,15] This has led to the recommendation of "either prophylactic ASM (initiated during index hospitalization) or no ASM could be used in patients hospitalized with moderate-severe TBI" and if it is initiated, it should be used for a short duration, i.e. ≤7 days in this guideline.[16]

Although the current literature suggests otherwise, a tendency to prescribe ASM to trauma patients persists and even creeps into some local guidelines, leading to unnecessary use of ASM, resulting in futile side effects and increasing economic costs.[17,18] The lack of consensus on the duration of such treatment strategies further deepens this dilemma.

This study aims to define the demographic, clinical, radiological, and electrophysiological characteristics of PTE patients followed up in our tertiary center, as well as to reveal the course and prognosis of the disease with specific attention to the use of ASM.

METHODS

Patients diagnosed with PTE at the İstanbul University, İstanbul Faculty of Medicine Epilepsy Unit between 1994 and 2024 were included in the study. Patients were excluded if they had a history of epilepsy or other factors that may explain their epilepsy etiology. Clinical characteristics, imaging, electroencephalography (EEG) findings, antiseizure drug use, and clinical progression were retrospectively analyzed.

MAIN POINTS

- Trauma is one of the leading causes of epilepsy.
- Prophylactic antiseizure medications use does not significantly reduce epilepsy latency, severity, or seizure frequency.
- Coexistence of psychogenic seizures highlights the need to address psychological trauma alongside physical injury.
- Bilateral magnetic resonance imagining lesions are associated with shorter latency to epilepsy onset and are often seen in severe traumatic brain injurys.
- Epilepsy surgery is a viable option and should be considered in drug-resistant patients.

The severity of head trauma was classified as mild (loss of consciousness less than 30 minutes without skull fracture), moderate (loss of consciousness less than 24 hours regardless of skull fracture), or severe (presence of skull fracture, cerebral contusion, or hematoma with loss of consciousness more than 24 hours).[3] Patients whose seizures persisted despite the use of at least two appropriately chosen, and adequately dosed ASM were defined as having drug-resistant epilepsy.

This study was approved by the İstanbul University Clinical Research Ethics Committee (approval no: 2025/214, date: 28.04.2025).

Statistical Analysis

Statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics used to summarize the data included frequencies and percentages for categorical variables, and median and interquartile ranges (IQR) for non-normally distributed continuous variables. The chi-square test was used to compare categorical values, and the Mann-Whitney U and Kruskal-Wallis tests were utilized since the data distribution was not normal within categories, according to the Shapiro-Wilk test. Following significant chi-square test results, Cramér's V was employed to determine the effect size and strength of association between the nominal variables.

RESULTS

There were 67 patients fulfilling the diagnosis of PTE with their data available. The demographic findings and data are summed up in Table 1. Among the included patients, 73% (n=49) were male, and 27% (n=18) were female. The median patient age was 54.50 (IQR: 40.75-62.50). Severe trauma (bone fracture, hemorrhage, or loss of consciousness for more than one day) was observed in 60% of patients. The median latency for epilepsy onset post-TBI was 24 months (IQR, 6-96 months). The median age at trauma occurrence was 18 years (IQR, 8-31 years). The trauma was encountered during childhood in 28 patients (44%). Acute symptomatic seizures were present in only three of the patients.

Unconsciousness after trauma was reported in 25.4% of the patients (n=17). The presence of unconsciousness was associated with neither age at trauma nor the epilepsy latency. Refractoriness of epilepsy was not associated with the presence of unconsciousness either. The duration of the unconsciousness showed a significant correlation with the refractoriness ($p<0.029$, $\varphi c=0.718$).

A family history of epilepsy was present in seven patients (11%). Focal seizures with impaired awareness were observed in 61% of the patients, while 60% experienced focal-onset seizures evolving into bilateral tonic-clonic seizures. Regarding seizure frequency, 45% of the patients had monthly seizures, 23% had yearly seizures, 22% had weekly seizures, 5% experienced daily seizures, and only 5% of the patients were seizure-free. Psychogenic non-epileptic seizures coexisted in three patients. Status epilepticus history was noted in eight patients (12%). None of these patients experienced status epilepticus at the time of trauma. One patient experienced his first seizure manifested as status epilepticus.

Brain magnetic resonance imagining (MRI) findings showed trauma-related sequelae, most commonly multifocal (48%), followed by frontal (34%), temporal (9%), and parietal (7%) lobes. There were no cases with isolated occipital involvement, and isolated infratentorial involvement was observed in only 1 patient. Lesion lateralization was most commonly observed on the left side (42%), followed by right-sided lesions (36%) and bilateral lesions (22%). MRI findings were normal in seven patients (11%).

Table 1. Demographic and clinical details of the patients

	% (n)
Gender	
Female	27% (18)
Male	73% (49)
Age (median, IQR)	54 (40-62)
Trauma severity	
Mild	15% (10)
Moderate	25% (16)
Severe	60% (39)
Unconsciousness period	
Unknown	66% (44)
None	2% (1)
Minutes	3% (2)
Days	10% (7)
Weeks	10% (7)
Months	9% (6)
Family history of epilepsy	11% (7)
Trauma recurrence	17% (11)
Epilepsy latency (month, median, IQR)	24 (6-96)
Antiseizure medication	
Carbamazepine	46% (29)
Levetiracetam	30% (19)
Phenytoin	22% (14)
Prophylactic antiseizure medication	16% (9)
Seizure types	
Focal motor, aware	8% (5)
Focal motor with impaired awareness	61% (41)
Focal to bilateral tonic-clonic seizure	60% (39)
Seizure frequency	
Daily	5% (3)
Weekly	22% (13)
Monthly	45% (27)
Yearly	23% (14)
Seizure-free	5% (3)
Neurological examination	
Motor findings	25% (15)
Speech abnormalities	16% (10)
Cognitive problems	28% (17)

IQR: Interquartile range

EEG findings are summed up in Table 2. EEG showed background slowing in 72.1% of cases and approximately one third of these patients had moderate to severe slowing (21.3%). Focal epileptiform activity was observed in 57% of the patients, most commonly in the frontal and temporal regions. EEG was normal in eleven patients (18%). Non-convulsive status epilepticus was detected in two patients. Cramér's V test revealed a significant medium-sized correlation between the lateralization of EEG and MRI findings as expected ($p<0.001$, $\varphi c=0.405$).

As for the epilepsy treatment, the most commonly preferred ASMs were carbamazepine and levetiracetam, with carbamazepine prescribed for 46% of patients and levetiracetam for 30%. Drugresistance was observed in 37% of patients.

Table 2. Radiological end electrophysiological characteristics of the patients

	% (n)
MRI localizations	
Frontal	34% (19)
Temporal	9% (5)
Parietal	7% (4)
Occipital	-
Infratentorial	2% (1)
Multifocal	48% (27)
MRI lateralizations	
Left	42% (23)
Right	36% (20)
Bilateral	22% (12)
EEG background activity	
Normal	28% (17)
Slow-mild	54% (33)
Slow-moderate/severe	21% (13)
EEG lateralization	
None-normal	18% (11)
Left	33% (20)
Right	23% (14)
Bilateral	20% (12)
EEG focal findings-slowing	57% (35)
Frontal	48% (29)
Temporal	42% (28)
Central	12% (8)
Parietal	12% (8)
Occipital	0% (0)
EEG focal findings-epileptiform	57% (35)
Frontal	36% (22)
Temporal	31% (19)
Central	10% (6)
Parietal	8% (5)
Occipital	0% (0)

MRI: Magnetic resonance imagining, EEG: Electroencephalography

Prophylactic ASM was initiated in 16% (n=9) of the patients. All of these patients had a history of moderate or severe trauma. Seven underwent surgical interventions, and ASMs were initiated during post-operative intensive care follow-up in the absence of seizures. Among patients who received prophylactic ASM, the median epilepsy latency was 12 months (IQR: 4-90 months). The most commonly prescribed ASMs were levetiracetam, carbamazepine, and phenytoin. None of the patients remained seizure-free. Four patients met the criteria for drug-resistant epilepsy despite the use of two appropriately selected and adequately dosed ASMs. No significant differences were found between those who used prophylactic ASM and those who did not in terms of epilepsy latency, seizure frequency, or drug resistance ($p>0.58$).

Latency, seizure frequency, and drug-resistant epilepsy rates were similar between those with childhood trauma and those with adulthood trauma ($p>0.17$). Drug-resistant epilepsy was significantly more common in patients with severe TBI ($p<0.03$). Patients with bilateral MRI lesions had a shorter epilepsy latency ($p<0.01$). MRI lateralization showed a consistent correlation with trauma severity: bilateral lesions were expected in more severe cases, while milder TBIs were more likely to have normal MRIs ($p<0.001$, $\varphi c=0.458$).

DISCUSSION

This study further emphasized that the prophylactic use of ASM does not contribute to the latency or severity of developing epilepsy. Bilateral traumatic involvement causes hastier epileptogenesis and earlier seizures. The severity of the trauma and longer periods of unconsciousness are risk factors for drug-resistant epilepsy. Coexistence of psychogenic seizures reminds the clinician that trauma is a multifaceted event exceeding mere physical damage. Therefore, a multidisciplinary approach may be required in such cases.

The risk factors described in the literature for PTE include male sex, existence of focal neurological signs, duration of unconsciousness, and fixed imaging findings, all of which were found to be more common in our PTE cohort, consistent with the literature.[7-9] It is also well known that the risk of seizures and epilepsy increases in proportion to the severity of TBI.[19] Our study shows that drug-resistant epilepsy is more common in patients with a history of severe trauma in a cohort of PTE patients, highlighting that trauma severity is associated not only with the development of epilepsy but also with the development of drug resistance.

EEG findings were consistent with the imaging as expected. No correlation was found between lesion localization on brain MRI and seizure occurrences. However, the presence of bilateral MRI lesions is significant, as it warrants a shorter latency to epilepsy onset. This is believed to be due to the severity of the TBI because more severe TBIs are more likely to cause bilateral, multifocal involvement in the brain parenchyma, leading to prominent neuroinflammation and remodeling.[20] This is an important, albeit overlooked aspect of the PTEs. In the current era, bits and pieces of the underlying neuroinflammatory process are addressed, but we are far from grasping the totality of cellular and neuroinflammatory interactions that ultimately give way to epileptogenesis following TBIs.[21] The lack of biomarkers capable of foreseeing which patient is undergoing the epileptogenesis process after such insult is another important limitation for such studies, resulting in either studies conducted retrospectively or the recruitment of every patient with TBI, leading to unjustifiably high budgets and a waste of resources.

Our study showed that prophylactic use of ASM does not contribute to the latency of the developing epilepsy or severity of the seizures. This is well in line with the previous literature, suggesting that avoiding the prescription of ASM to TBI patients without seizures could be more beneficial, as they do not provide anti-epileptic effects do not stop the epileptogenesis process.[12,13,16,22,23] Although there have been some positive effects of pharmacological and cellular interventions on animal models, sadly, the attempt to translate these findings into clinical implications has failed.[24] Giving TBI patients ASM can lead to unwanted side effects, worsen cognitive outcomes, and cause unnecessary economic burden. Even if prophylactic treatment is initiated, early discontinuation should be planned promptly.[16]

Another overlooked aspect is the complex nature of trauma itself, transcending the physical harm aspect. The coexistence of psychogenic seizures in this cohort suggests that psychological trauma may also be a contributing factor. As these patients are mostly followed up by a team of doctors and physiotherapists due to their complex injuries and their aftermath, psychiatric aspects should not be overlooked, and psychiatric evaluation should be considered an essential part of the evaluation and follow-up plan for these patients.[25]

Study Limitations

The main limitation of this study is the number of patients included; however, since this cohort is diagnosed, treated, and followed up comprehensively from a single center, the insights gained are still quite valuable due to the rather standardized management and approach in addition to the chance to capture nuances. As traumatic encephalomalacia is not a typical lesion considered resectable, our detailed examination allows us to identify cases that could significantly benefit from epilepsy surgery. Summary of a case from this cohort that has undergone resection is presented in Figure 1.

CONCLUSION

In conclusion, this study contributes valuable insights into the clinical, radiological, and electrophysiological features of PTE. It reinforces that ASM are not beneficial as prophylactic agents. TBI severity not only influences epilepsy development, but also it affects the likelihood of drug resistance, and the psychiatric aspect of the trauma should not be overlooked. Given the limitations of current treatment strategies, a shift towards individualized, biomarker-driven approaches and a broader neuropsychiatric perspective in patient management is warranted.

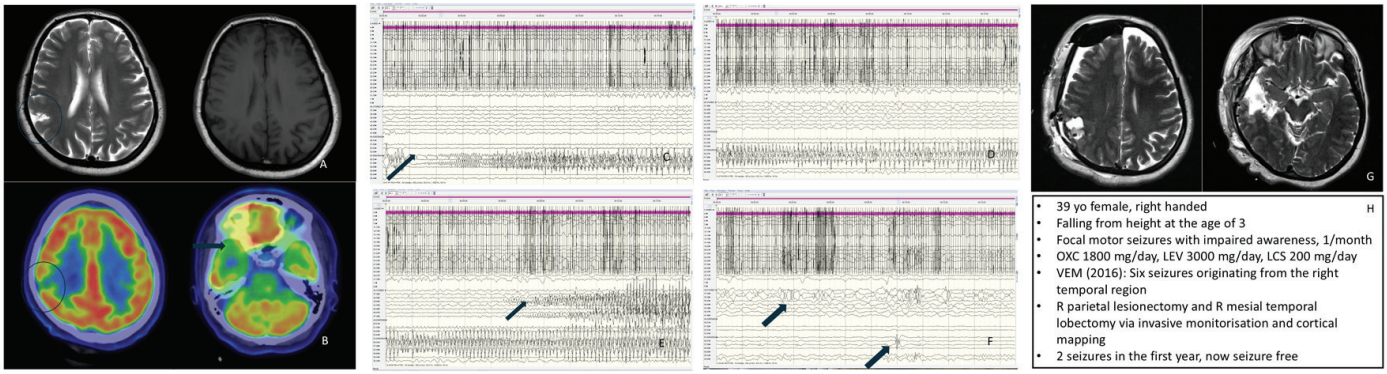

Figure 1. A short case snippet. A) Pre-operative brain MRI showing a T2 hyperintense and T1 hypointense lesion in the right parietal region. B) Brain PET imaging revealing hypometabolism in the right parietal region and pronounced bilateral mesial temporal hypometabolism, more prominent on the right. C,D,E) A seizure originating from the right temporal region electrodes, spreading to the grid electrodes, and becoming generalized during invasive monitoring. F) Invasive EEG monitoring during the interictal period showing independent sharp wave discharges in the right temporal electrodes and the grid electrodes over the parietal lesion. G) Post-operative brain MRI showing encephalomalacic areas consistent with right parietal lesionectomy and right temporal lobectomy. H) short case summary
MRI: Magnetic resonance imagining, EEG: Electroencephalography, PET: Positron emission tomography, yo: Years old, OXC: Oxcarbazepine, LEV: Levetiracetam, LCS: Lacosamide, VEM: Video EEG monitoring, R: Right

Ethics

Ethics Committee Approval: This study was approved by the İstanbul University Clinical Research Ethics Committee (approval no: 2025/214, date: 28.04.2025).

Informed Consent: Retrospective study.

Footnotes

Author Contributions

Surgical and Medical Practices: Ö.K., A.D.E., O.A., F.U., N.B., Concept: O.A., N.B., Design: O.A., N.B., Data Collection or Processing: Ö.K., O.A., F.U., N.B., Analysis or Interpretation: Ö.K., A.D.E., F.U., N.B., Literature Search: Ö.K., A.D.E., Writing: Ö.K., A.D.E., F.U., N.B.

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REFERENCES

1. Magiorkinis E, Sidiropoulou K, Diamantis A. Hallmarks in the history of epilepsy: epilepsy in antiquity. *Epilepsy Behav.* 2010;17(1):103-108. [Crossref]
2. Christensen J, Pedersen MG, Pedersen CB, Sidenius P, Olsen J, Vestergaard M. Long-term risk of epilepsy after traumatic brain injury in children and young adults: a population-based cohort study. *Lancet.* 2009;373(9669):1105-1110. [Crossref]
3. Lowenstein DH. Epilepsy after head injury: an overview. *Epilepsia.* 2009;50(Suppl 2):4-9. [Crossref]
4. Englander J, Bushnik T, Wright JM, Jamison L, Duong TT. Mortality in late post-traumatic seizures. *J Neurotrauma.* 2009;26(9):1471-1477. [Crossref]
5. Agrawal A, Timothy J, Pandit L, Manju M. Post-traumatic epilepsy: an overview. *Clin Neurol Neurosurg.* 2006;108(5):433-439. [Crossref]
6. Hunt RF, Boychuk JA, Smith BN. Neural circuit mechanisms of post-traumatic epilepsy. *Front Cell Neurosci.* 2013;7:89. [Crossref]
7. Xu T, Yu X, Ou S, et al. Risk factors for posttraumatic epilepsy: a systematic review and meta-analysis. *Epilepsy Behav.* 2017;67:1-6. [Crossref]
8. Annegers JF, Coan SP. The risks of epilepsy after traumatic brain injury. *Seizure.* 2000;9(7):453-457. [Crossref]
9. Zasler N, Katz DI, Zafonte RD, editors. Brain injury medicine: principles and practice. 3rd ed. New York: Springer Publishing Company; 2021. [Crossref]
10. Angriman F, Taran S, Angeloni N, Devion C, Lee JW, Adhikari NKJ. Antiseizure medications in adult patients with traumatic brain injury: a systematic review and bayesian network meta-analysis. *Crit Care Explor.* 2024;6(10):e1160. [Crossref]
11. Haque KD, Grinspan ZM, Mauer E, Nellis ME. Early use of antiseizure medication in mechanically ventilated traumatic brain injury cases: a retrospective pediatric health information system database study. *Pediatr Crit Care Med.* 2021;22(1):90-100. [Crossref]
12. Vespa PM, Nuwer MR, Nenov V, et al. Increased incidence and impact of nonconvulsive and convulsive seizures after traumatic brain injury as detected by continuous electroencephalographic monitoring. *J Neurosurg.* 1999;91(5):750-760. [Crossref]
13. Patanwala AE, Kurita A, Truong E. Low-dose levetiracetam for seizure prophylaxis after traumatic brain injury. *Brain Inj.* 2016;30(2):156-158. [Crossref]
14. Pingue V, Mele C, Biscuola S, Nardone A, Bagnato S, Franciotta D. Impact of seizures and their prophylaxis with antiepileptic drugs on rehabilitation course of patients with traumatic or hemorrhagic brain injury. *Front Neurol.* 2022;13:1060008. [Crossref]
15. Dikmen SS, Temkin NR, Miller B, Machamer J, Winn HR. Neurobehavioral effects of phenytoin prophylaxis of posttraumatic seizures. *JAMA.* 1991;265(10):1271-1277. [Crossref]
16. Frontera JA, Gilmore EJ, Johnson EL, et al. Guidelines for seizure prophylaxis in adults hospitalized with moderate-severe traumatic brain injury: a clinical practice guideline for health care professionals from the Neurocritical Care Society. *Neurocrit Care.* 2024;40(3):819-844. [Crossref]
17. McGovern Medical School, Department of Surgery. Post-traumatic seizure prophylaxis in patients with traumatic brain injury clinical practice guideline. [Crossref]
18. North Bristol NHS Trust Intensive Care Unit. Antiepileptics for severe traumatic brain injury guideline for adult patients. 2014. [Crossref]
19. Zimmermann LL, Martin RM, Girgis F. Treatment options for posttraumatic epilepsy. *Curr Opin Neurol.* 2017;30(6):580-586. [Crossref]
20. Mukherjee S, Arisi GM, Mims K, Hollingsworth G, O'Neil K, Shapiro LA. Neuroinflammatory mechanisms of post-traumatic epilepsy. *J Neuroinflammation.* 2020;17(1):193. [Crossref]

21. Sun L, Shan W, Yang H, Liu R, Wu J, Wang Q. The role of neuroinflammation in post-traumatic epilepsy. *Front Neurol.* 2021;12:646152. **[Crossref]**
22. Szaflarski JP, Nazzal Y, Dreer LE. Post-traumatic epilepsy: current and emerging treatment options. *Neuropsychiatr Dis Treat.* 2014;10:1469-1477. **[Crossref]**
23. Temkin NR. Preventing and treating posttraumatic seizures: the human experience. *Epilepsia.* 2009;50(Suppl 2):10-13. **[Crossref]**
24. Pitkänen A, Immonen RJ, Gröhn OH, Kharatishvili I. From traumatic brain injury to posttraumatic epilepsy: what animal models tell us about the process and treatment options. *Epilepsia.* 2009;50(Suppl 2):21-29. **[Crossref]**
25. Mazzini L, Cossa FM, Angelino E, Campini R, Pastore I, Monaco F. Posttraumatic epilepsy: neuroradiologic and neuropsychological assessment of long-term outcome. *Epilepsia.* 2003;44(4):569-574. **[Crossref]**

Detection Rates of Interictal Epileptiform Discharges in Epilepsy Patients: A Comparison of Routine, 1-3 Hours Daytime, and Whole-night EEG Recordings

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Abstract

Objective: The detection rate of interictal epileptiform discharges (IEDs) varies among electroencephalography (EEG) recordings in patients with epilepsy. This study aimed to compare the yield of IED detection across three recording protocols of varying durations routinely used at our center: routine 20-30 minutes EEG, 1-3 hours daytime video-EEG (vEEG), and whole-night (8-12 hours) vEEG.

Methods: The EEG reports of adult patients treated at the Dokuz Eylül University Hospital epilepsy outpatient clinic between 2006 and 2024 were retrospectively reviewed. Patients older than 18 years who had undergone at least one routine EEG, one 1-3 hours daytime vEEG, and one whole-night vEEG on separate occasions were included. The detection rates of IEDs across the three modalities, along with patients' clinical characteristics, were analyzed.

Results: Seventy-three patients (43 women and 30 men) were included in the study. For the initial EEG, the IED detection rate was 17.8% for routine EEG, 45.2% for 1-3 hours daytime vEEG, and 46.6% for whole-night vEEG. The routine EEG detection rate was significantly lower (p=0.001). With repeated examinations, the yield of routine EEG increased to 41.1%, daytime vEEG to 52.1%, and whole night vEEG to 56.2%; with no significant difference between the modalities (p=0.099).

Conclusion: Although IED detection was highest with whole-night vEEG, daytime 1-3 hours vEEG recordings that included sleep achieved a comparable yield and may be preferred to reduce laboratory workload. The recording duration can be individualized according to the laboratory resources and patient preferences.

Keywords: Electroencephalography, interictal epileptiform discharges, recording duration

INTRODUCTION

Electroencephalography (EEG) is extensively used for the diagnosis and monitoring of epilepsy, with the primary objective of capturing interictal epileptiform discharges (IEDs). However, IEDs are not consistently detectable in every EEG recording.

The reported detection rate of IEDs in the initial routine 20-30 minutes EEG ranges from 28% to 53% in patients with epilepsy.[1-3] In instances where IEDs are not identified, routine EEG may be repeated. Conducting routine EEG three times can increase the detection rate to 77%.[2] Alternatively, longer recording durations may have been required. Extending the routine EEG to 45 min has been demonstrated to enhance the yield of IEDs.[4] Ambulatory EEG or whole-night video-EEG (vEEG) can also be used. In patients experiencing a single unprovoked seizure, 24-hour vEEG detects IEDs in 44-57% of cases.[5,6] Comparative studies between ambulatory 24-h EEG and the first two routine EEGs have indicated a higher sensitivity for ambulatory 24-h EEG.[7,8]

In our center, in addition to routine EEG, we used daytime 1-3 hours vEEG and 8- to 12-hour whole-night vEEG to detect IEDs. In this study, we analyzed the IED detection rates in recordings conducted at various times and durations in patients with epilepsy. We also compared the relative performance of repeated routine EEG, daytime 1-3 hours vEEG, and whole-night vEEG.

METHODS

EEG recordings of patients who were followed up in the epilepsy outpatient clinic of Dokuz Eylül University Hospital between 2006 and 2024 were reviewed retrospectively. Adult patients (≥18 years) who underwent at least one routine EEG, one 1-3 hours daytime vEEG,

and one whole-night vEEG on separate occasions were included in the study. Patients who did not have results from any of these three modalities were excluded. Additionally, repeated EEGs of patients in these three modalities were examined. A comparison was made between the initial and cumulative EEG IED detection rates. The purposes of the EEG recordings were classified as follows: diagnosis and follow-up. The diagnostic EEG included the diagnosis of epilepsy and classification of epilepsy syndromes. Follow-up EEG was conducted for various reasons, including changes in seizure frequency and assessment prior to withdrawal of anti-seizure medication (ASM).

Routine EEGs were obtained in the outpatient setting with the patient seated comfortably for 20-30 min. Daytime 1-3 hours and whole-night vEEG recordings were performed with the patient lying on a bed in a quiet, dark room. Whole-night vEEG lasted 8-12 hours. All the EEGs used the international 10-20 electrode system. The recordings were evaluated by a clinical neurophysiologist or a clinical neurophysiology resident.

Demographic data, ASMs at the time of the last visits, brain magnetic resonance imaging (MRI), and seizure frequencies for the last year were recorded. If the brain MRI could not be accessed from the records, it was classified as unknown; if available, it was classified as normal or abnormal.

Recordings were examined for the presence of IEDs, defined as spikes, spike-and-wave discharges, sharp waves, temporal intermittent rhythmic delta activity, and generalized spike-and-wave discharges. The IEDs were classified as generalized, focal, or multifocal. The localization of focal IEDs was recorded.

This study was approved by the Dokuz Eylül University Non-Interventional Research Ethics Committee (approval no: 2025/02-05, date: 15.01.2025).

Statistical Analysis

Statistical analyses were performed using IBM SPSS version 23 (Inc., Armonk, NY, USA). Normality was assessed using the Shapiro-Wilk test. Associations between independent categorical variables were analyzed using the Yates corrected χ^2 test, Fisher's exact test with Monte Carlo correction, or Pearson's χ^2 test with pairwise comparisons using the Bonferroni corrected Z test. Cochran's Q test was used for dependent categorical variables. The Mann-Whitney U test was used to compare non-normally distributed continuous variables between the two groups. The results for categorical variables are presented as frequency (percentage); continuous variables are presented as mean±standard deviation and median (minimum-maximum). Statistical significance was set at $p<0.05$.

MAIN POINTS

- This study evaluated the interictal epileptiform discharge (IED) detection rates across routine electroencephalography (EEG), 1-3 hours daytime video-EEG (vEEG), and whole-night vEEG in adult patients with epilepsy.
- Seventy-three patients who underwent all three EEG modalities on separate occasions were retrospectively included.
- Routine EEG had a significantly lower initial IED detection rate (17.8%) compared to daytime vEEG (45.2%) and whole-night vEEG (46.6%).
- Repeated recordings increased detection rates across all modalities, eliminating statistically significant differences.
- Daytime vEEG with sleep achieved a detection yield comparable to whole-night vEEG and may offer a practical alternative to reduce laboratory burden.

RESULTS

In total, 73 patients (43 women, 30 men) were analysed. Their clinical and EEG characteristics are summarised in Table 1. The ASMs used are shown in Figure 1. In this study, a total of 195 EEGs were analyzed. Of these, 36 EEGs were conducted for diagnostic purposes and 159 were performed for follow-up assessments. Nineteen routine EEGs, 8 daytime vEEGs lasting 1-3 hours, and 9 whole-night vEEGs were performed for diagnostic purposes. With repeated EEG recordings, the average number of routine EEGs was 2.8; the number of 1-3 hours daytime vEEGs was 1.6; and the number of whole-night vEEGs was 1.5.

In the initial recording, the detection rates of IEDs were 17.8% for routine EEG, 45.2% for daytime 1-3-h vEEG, and 46.6% for whole-night vEEG. Notably, routine EEG was significantly less effective than the other two vEEG modalities (p=0.001).

With repeated recordings, the IED yield of routine EEG increased to 30.2% on the second, 36.9% on the third, and 41.1% on the fourth study. For daytime 1-3 hours vEEG the yield increased to 50.6% on the second and 52.1% on the fourth recording. For whole-night vEEG, the second recording yielded 56.2%, with no further increase thereafter (Figure 2). Across repeated examinations, there was no significant difference in IED detection among the three modalities (p=0.099).

Table 1. Demographic and clinical characteristics of the patients

Age (years)	37.27±12.6 (20-69)
Epilepsy duration (years)	16.4±6.3 (6-31)
Number of routine EEGs	2.8±1.7 (1-7)
Number of 1-3 hours daytime EEGs	1.56±0.7 (1-4)
Number of whole-night EEGs	1.45±0.9 (1-6)
Cranial MRI, n (%)	
Normal	16 (21)
Abnormal	25 (34.2)
Unknown	32 (44.8)
Seizure frequency per year, n (%)	
≤1	44 (60.3)
2-6	8 (11)
7-12	5 (6.8)
≥13	16 (21.9)
ASM use, n (%)	
Yes	65 (89)
No	8 (11)
Number of ASMs, n (%)	
1	29 (39.7)
2	25 (34.2)
>2	11 (26.1)

ASM: Anti-seizure medication, MRI: Magnetic resonance imaging, EEG: Electroencephalography

IEDs were detected by at least one of the three modalities in 78.1% of the patients, whereas 21.9% showed no IEDs on any study. The proportions of generalised and focal IEDs detected by the three modalities were similar (p=0.49, p=0.38, p=0.73) (Figure 3).

IED detection on any routine EEG, daytime 1-3 hours or whole-night vEEG was not significantly related to ASM use, last year seizure frequency, or MRI abnormalities (Table 2).

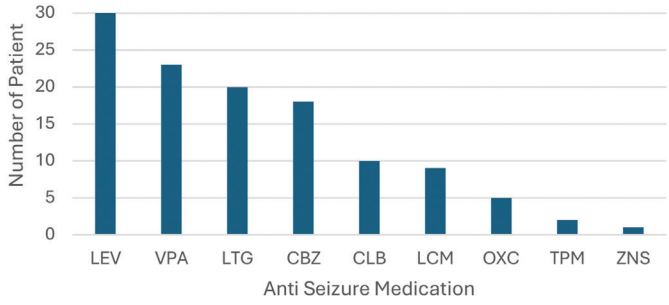

Figure 1. Antiseizure medications used by the patients
CBZ: Carbamazepine, CLB: Clobazam, LCM: Lacosamide, LEV: Levetiracetam, LTG: Lamotrigine, OXC: Oxcarbazepine, TPM: Topiramate, VPA: Valproic acid, ZNS: Zonisamide

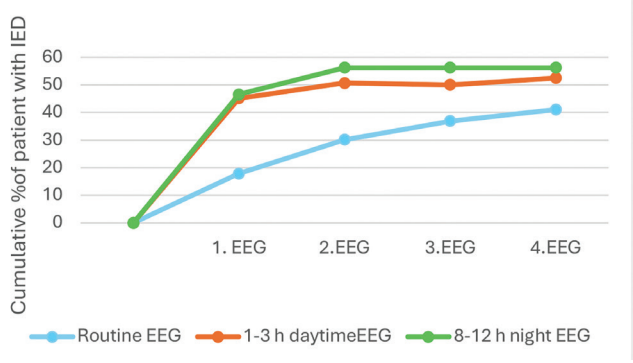

Figure 2. IED detection rates in repeated routine EEG, 1-3 hours daytime vEEG, and whole-night vEEG
IED: Interictal epileptiform discharge, EEG: Electroencephalography, vEEG: Video-electroencephalography

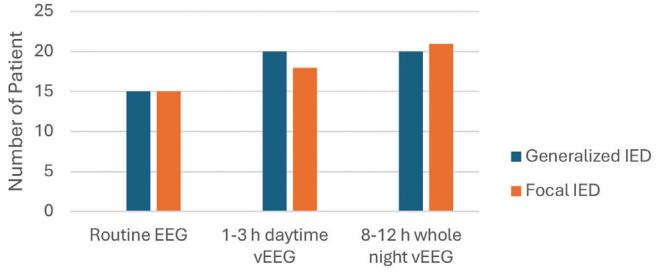

Figure 3. Detection rates of generalized and focal IEDs in routine, 1-3 hours daytime vEEG, and whole-night vEEG
IED: Interictal epileptiform discharge, EEG: Electroencephalography, vEEG: Video-electroencephalography

DISCUSSION

The detection of IEDs on EEG is crucial for effective management of epilepsy. This study demonstrates that both daytime 1-3 hours vEEG and whole-night vEEG recordings identify a greater number of IEDs than the first routine EEG. However, four or more routine EEGs achieved an IED yield comparable to that of longer recordings.

The probability of detecting IEDs increases with recording duration. Extending routine EEG to 45-60 min has been reported to provide an additional yield.[4,9] The benefit may relate not only to a longer duration but also to the inclusion of sleep, which facilitates IED generation.[10] A study investigating the frequency of IED detection by extending the duration of routine EEG to 60 minutes, found that IEDs occurring after 30 minutes were more prevalent in those who slept after the first 30 min.[4] As sleep state was not systematically documented for routine EEGs, we could not analyze its effect.

Although the whole-night vEEG group, with durations of 8-12 hours, had higher IED detection rates than the daytime vEEG group, the difference was not statistically significant. In our study, EEG recordings were conducted at the same location, which was slightly dark and quiet, for both 1-3 hours and a whole night. This environment facilitated the patients' capacity to fall asleep during the 1-3 hours daytime EEG sessions. As a result, the absence of a statistically significant difference between the 1-3 hours daytime and whole-night vEEG recordings may be attributed to the inclusion of sleep in the 1-3 hours vEEG. A study reported that the detection rate of IEDs in patients with epilepsy was similar in 30-60 minutes sleep deprivation EEGs compared to 24-hour ambulatory EEGs.[11] This study and our findings suggest that sleep is as crucial as the extension of EEG duration for the detection of IEDs. An EEG recording of at least one hour that includes sleep may be effective in detecting IEDs.

Conversely, prior research has indicated that extended recording durations improve the detection rate of IED. A study involving whole-night EEG on patients with epilepsy reported an IED detection rate of 57.4%.[12] Detection rates ranging from 74% to 89% within 24 hours[13,14] and from 88% to 95% within 48 hours[11,13] were observed. Therefore, recordings lasting 24 to 48 hours may be considered when it is necessary to enhance the likelihood of IED detection.

Previous studies have reported IED detection rates of 28-53% in a single routine EEG, increasing to 59-77% with repeated routine EEGs.[1-3] In our study, IED detection rates also increased with repeated routine EEGs. On initial examination, both 1-3 hours daytime vEEG, and whole-night vEEG were superior to routine EEG. However, performing video EEG on all patients instead of routine EEG is impractical. Therefore, the choice of EEG modality should be based on the clinical and laboratory conditions.

When the three methods were collectively evaluated, the overall detection rate of IEDs was superior to that of each method individually. Considering that sleep duration is longest in whole-night vEEG, this discrepancy may reflect the variable nature of IED occurrence.[15] Consequently, even in long-term EEG recordings in which no IED is detected, EEG repetition should not be avoided.

Table 2. Association between clinical features and IED detection (n, %)

	Routine EEG IED+	p	1-3 hours daytime vEEG IED+	p	8-12 hours whole night vEEG IED+	p
Sex						
Female	18 (60)	1.0	24 (63)	0.60	23 (56)	0.76
Male	12 (40)		14 (37)		18 (44)	
Epilepsy type						
Generalised	15 (30)	0.67	20 (53)	0.40	20 (49)	0.30
Focal	15 (30)		18 (47)		21 (51)	
ASM use (last visit)						
Yes	26 (87)	0.44	32 (84)	0.43	36 (88)	1
No	4 (13)		6 (16)		5 (12)	
Seizure frequency (/last year)						
<1	16 (53)	0.41	20 (52)	0.34	21 (51)	0.09
2-6	5 (17)		5 (13)		4(10)	
7-12	3 (10)		4 (11)		5 (12)	
>12	6 (20)		9 (24)		11 (27)	
Cranial MRI						
Normal	5 (17)	0.66	7 (18)	0.29	11 (27)	0.26
Abnormal	11 (37)		11 (29)		11 (27)	
Unknown	14 (46)		20 (53)		19 (46)	

ASM: Antiseizure medication, EEG: Electroencephalography, IED: Interictal epileptiform discharge, MRI: Magnetic resonance imaging, vEEG: Video electroencephalography

Study Limitations

The limitations of our study include the retrospective analysis of patients with varying clinical features in an epilepsy outpatient clinic. The indications for EEG varied; some patients underwent evaluation prior to the discontinuation of ASMs, while others experienced an increased frequency of seizures. Most patients used ASMs, which may have influenced the detection of IEDs. Some ASMs are known to affect the occurrence of IEDs;[16] possibly contributing to a lower IED detection rate in repeated routine EEGs as reported in the literature. However, our study did not find any relationship between ASM use and IED detection. The rate of IED detection increases in EEGs performed within the first 24-hour after a seizure.[12] Nevertheless, due to inadequate documentation, our study did not specify the duration between the last seizure and the performance of the EEG. Another limitation is the lack of documentation of sleep status in routine EEGs.

CONCLUSION

In conclusion, our findings suggest that with four or more repeated routine EEGs, the IED detection rate can approach that of 1-3 hours daytime vEEG and whole-night vEEG. Daytime vEEG of 1-3 hours, including sleep, and a whole-night vEEG, is similar for detecting IEDs. The duration of EEG recording should be determined based on patient and physician preferences as well as EEG laboratory conditions.

Ethics

Ethics Committee Approval: This study was approved by the Dokuz Eylül University Non-Interventional Research Ethics Committee (approval no: 2025/02-05, date: 15.01.2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: İ.Ö., B.B., Design: İ.Ö., Data Collection or Processing: İ.Ş.Ö., L.Ç., Analysis or Interpretation: İ.Ş.Ö., A.Y.E., Literature Search: İ.Ş.Ö., L.Ç., Writing: İ.Ş.Ö., A.Y.E., B.B.

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REFERENCES

1. Salinsky M, Kanter R, Dasheiff RM. Effectiveness of multiple EEGs in supporting the diagnosis of epilepsy: an operational curve. *Epilepsia*. 1987;28(4):331-334. [Crossref]
2. Baldin E, Hauser WA, Buchhalter JR, Hesdorffer DC, Ottman R. Yield of epileptiform electroencephalogram abnormalities in incident unprovoked seizures: a population-based study. *Epilepsia*. 2014;55(9):1389-1398. [Crossref]
3. Doppelbauer A, Zeitlhofer J, Zifko U, Baumgartner C, Mayr N, Deecke L. Occurrence of epileptiform activity in the routine EEG of epileptic patients. *Acta Neurol Scand*. 1993;87(5):345-352. [Crossref]
4. Burkholder DB, Britton JW, Rajasekaran V, et al. Routine vs extended outpatient EEG for the detection of interictal epileptiform discharges. *Neurology*. 2016;86(16):1524-1530. [Crossref]
5. Chen T, Si Y, Chen D, et al. The value of 24-hour video-EEG in evaluating recurrence risk following a first unprovoked seizure: a prospective study. *Seizure*. 2016;40:46-51. [Crossref]
6. Haddad N, Melikyan G, Alarcon G, et al. 24-hour video EEG in the evaluation of the first unprovoked seizure. *Clin Neurophysiol Pract*. 2021;6:123-128. [Crossref]
7. Keezer MR, Simard-Tremblay E, Veilleux M. The diagnostic accuracy of prolonged ambulatory versus routine EEG. *Clin EEG Neurosci*. 2016;47(2):157-161. [Crossref]

8. Hernandez-Ronquillo L, Thorpe L, Feng C, et al. Diagnostic accuracy of ambulatory EEG vs routine EEG in patients with first single unprovoked seizure. *Neurol Clin Pract*. 2023;13(3):e200160. **[Crossref]**
9. Tutkavul K, Çetinkaya Y. Optimum recording time of routine electroencephalogram for adults with epilepsy*. *Turk J Med Sci*. 2019;49(2):635-638. **[Crossref]**
10. Ferrillo F, Beelke M, Nobili L. Sleep EEG synchronization mechanisms and activation of interictal epileptic spikes. *Clin Neurophysiol*. 2000;111(Suppl 2):S65-S73. **[Crossref]**
11. Liporace J, Tatum W 4th, Morris GL 3rd, French J. Clinical utility of sleep-deprived versus computer-assisted ambulatory 16-channel EEG in epilepsy patients: a multi-center study. *Epilepsy Res*. 1998;32(3):357-362. **[Crossref]**
12. Xing Y, Wang J, Yin X, Fan Z, Luan S, Sun F. Optimizing electroencephalogram duration for efficient detection of epileptiform abnormalities in diverse patient groups: a retrospective study. *BMC Neurol*. 2024;24(1):285. **[Crossref]**
13. Werhahn KJ, Hartl E, Hamann K, Breimhorst M, Noachtar S. Latency of interictal epileptiform discharges in long-term EEG recordings in epilepsy patients. *Seizure*. 2015;29:20-25. **[Crossref]**
14. Narayanan JT, Labar DR, Schaul N. Latency to first spike in the EEG of epilepsy patients. *Seizure*. 2008;17(1):34-41. **[Crossref]**
15. Baud MO, Schindler K, Rao VR. Under-sampling in epilepsy: limitations of conventional EEG. *Clin Neurophysiol Pract*. 2020;6:41-49. **[Crossref]**
16. Guida M, Iudice A, Bonanni E, Giorgi FS. Effects of antiepileptic drugs on interictal epileptiform discharges in focal epilepsies: an update on current evidence. *Expert Rev Neurother*. 2015;15(8):947-959. **[Crossref]**

Archives of Epilepsy

Original Article

The Effect of Levetiracetam Monotherapy on Complete Blood Count Values and Inflammatory Markers in Long- and Short-term Treatment

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Abstract

Objective: This study aimed to this study was to determine the effect of levetiracetam (LEV) monotherapy on complete blood count parameters and inflammatory markers at six and 12 months in children with epilepsy.

Methods: Files from 66 patients with epilepsy who were on LEV monotherapy were examined. Age, sex, and type of epilepsy, electroencephalography and cranial magnetic resonance imaging results at presentation, and complete blood count data at the start of treatment and at six and 12 months were recorded from the patients' files. Neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and red cell distribution width/lymphocyte ratio (RDW/LYM) values were calculated from complete blood counts and used as inflammatory markers.

Results: The mean age of 66 patients was 10.18±4.88 years. The patients were equally distributed by gender. A comparison of complete blood parameters in patients receiving LEV monotherapy at baseline and at six and 12 months revealed a significant decrease in RDW values at 12 months ($p<0.05$), with no significant differences in other hematological parameters ($p>0.05$). Also, no significant differences were observed in inflammatory markers (NLR, MLR, PLR, and the RDW/LYM ratio) calculated from complete blood count parameters ($p>0.05$).

Conclusion: Use of LEV altered multiple complete blood count parameters. In addition, NLR, MLR, PLR, and the RDW/LYM ratio, recognized inflammatory markers, also changed during LEV therapy.

Keywords: Epilepsy, levetiracetam, complete blood count, inflammatory markers

INTRODUCTION

Epilepsy is the most common neurological disorder in childhood, characterized by seizures.[1] Antiseizure medications (ASMs) are used to reduce the frequency and severity of such seizures. Since epilepsy frequently requires lifelong treatment, the objective, in addition to seizure control, is to protect patients as much as possible from treatment-related side effects and to enable them to maintain a good quality of life.[2] The evaluation and follow-up of potential side effects associated with treatment are therefore essential.

ASMs have broad adverse effects across multiple organ systems. One such system is the hematological system.[3] Studies have shown that they can cause side effects, including thrombocytopenia, leukopenia, leukocytosis, neutropenia, pancytopenia, pure red cell aplasia, aplastic anemia, macrocytosis, megaloblastic anemia, and bone marrow depression.[4-6]

Levetiracetam (LEV) is a new-generation ASM that has been frequently employed in recent years and is effective for secondary generalized tonic-clonic, focal, myoclonic, and primary generalized tonic-clonic seizures.[7] However, studies of the potential hematological side effects of LEV therapy are limited, and their results are inconsistent. Some studies investigating the side effects of LEV therapy have reported that, in addition to its systemic side effects, it can result in an unexplained increase in infections, such as pharyngitis and rhinitis.[8-11]

Various biomarkers are currently employed for the etiological and early diagnosis of infectious diseases, and for disease severity and response to treatment. White blood cell (WBC), neutrophil (NEU), platelet (PLT), red blood cell distribution width (RDW), lymphocyte (LYM), monocyte, and basophil values and parameters calculated from complete blood counts [the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and RDW/LYM] can be used as systemic inflammatory markers.[12]

Limited numbers of studies have investigated the effects of LEV therapy on complete blood count parameters, and none have investigated the potential effects on inflammatory markers obtained from complete blood counts. This study aimed to determine the effect of LEV monotherapy on complete blood count parameters and on inflammatory markers derived from those counts at six and 12 months in children with epilepsy.

METHODS

Study Design

Patients aged 0-18 years who were diagnosed with epilepsy based on International League Against Epilepsy diagnostic criteria and who received LEV monotherapy at the Balıkesir University Faculty of Medicine, Pediatric Neurology Clinic, Türkiye, between 01.08.2019 and 01.08.2022 were retrospectively included in the study. Patients with chronic diseases (liver disease, kidney disease, thyroid disease, or hematological disorder) who were using other drugs, who had a history of infection or antibiotic use in the previous two weeks, or who had missing file data were excluded.

There is no standardization concerning the follow-up of patients with epilepsy under treatment, although in our clinic and in the light of our patient numbers we follow-up our stable patients at three-month intervals. We also evaluate the hematological parameters of our patients every six months. However, we can also perform these follow-ups and evaluations more frequently, depending on clinical manifestations and symptoms.

Age, sex, type of epilepsy, electroencephalography (EEG) and cranial magnetic resonance imaging (MRI) results at presentation, and complete blood count data at the start of treatment and at six and 12 months were recorded from the patients' files in this study. NLR, MLR, PLR, and RDW/LYM ratio values were calculated from complete blood counts as inflammatory markers.

MAIN POINTS

- A limited number of studies have investigated the effects of levetiracetam (LEV) therapy on complete blood count parameters, and none have investigated the potential effects of LEV therapy on inflammatory markers obtained from complete blood counts.
- LEV use altered various complete blood count parameters. In addition, neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and red cell distribution width (RDW)/lymphocyte ratio values, recognized inflammatory markers, also changed with LEV therapy.
- We observed no clinical change in our patients. This finding indicates that attention to RDW values is required in patients using LEV. As with all drugs, it is important for patient safety that side effects of LEV use are reported to the relevant pharmacovigilance units.

Pre-treatment complete blood count parameters and inflammatory markers measured at 6 and 12 months of treatment were subjected to statistical comparisons. Approval from the Balıkesir University Clinical Research Ethics Committee was obtained prior to commencement (approval no: 2022/98, date: 07.09.2022).

Statistical Analysis

Statistical analyses were performed using SPSS version 19.0. Categorical variables were presented as frequencies (n) and percentages (%), and complete blood count parameters and inflammatory markers were presented as mean±standard deviation. Statistical analysis was performed using a Bonferroni-corrected repeated-measures analysis of variance. P-values <0.05 were considered statistically significant.

RESULTS

Sixty-six patients with a mean age of 10.18±4.88 years (1-18) were included in the analysis. The patients were equally distributed by gender (n=33, 50%). The patients were diagnosed with focal epilepsy, generalized epilepsy, or epilepsy of unknown cause and were receiving LEV monotherapy at doses of 20-25 mg/kg, administered as syrup (68.2%) or tablet (31.8%) forms. MRI and EEG findings at the start of treatment are shown in Table 1.

No differences by gender or pharmaceutical form were observed in complete blood count parameters at baseline, six months, or 12 months of treatment ($p>0.05$). A comparison of complete blood parameters in patients receiving LEV monotherapy at the beginning of treatment and after six and 12 months revealed a significant decrease in RDW values at 12 months ($p<0.05$), but no significant difference in other hematological parameters ($p>0.05$) (Table 2). No statistically significant differences were observed when we compared inflammatory markers (NLR, MLR, PLR, and the RDW/LYM ratio) calculated from complete blood count parameters ($p>0.05$) (Table 3).

Table 1. Demographic characteristics of patients using levetiracetam

Age	**1-18 (10.18±4.88)**
Gender	**n (%)**
Male	33 (50%)
Female	33 (50%)
Seizure type	**n (%)**
Focal	28 (42.4%)
Generalized	32 (48.5%)
Unknown	6 (9.1%)
MRI	**n (%)**
Normal	46 (69.7%)
Abnormal	20 (30.3%)
EEG	**n (%)**
Epileptiform	43 (65.2%)
Normal	18 (27.3%)
Abnormal	5 (7.6%)
Drug pharmaceutical form	**n (%)**
Syrup	45 (68.2%)
Tablet	21 (31.8%)

EEG: Electroencephalogram, MRI: Magnetic resonance imaging

Table 2. Complete blood count parameters of patients using levetiracetam

Complete blood count parameters	Before treatment	6th month of treatment	12th month of treatment	p
WBC (10^3/uL)	7.81±2.63	7.67±2.68	7.34±2.11	p=0.409
RBC (10^6/uL)	4.67±0.48	4.69±0.38	4.63±0.54	p=0.533
HB (g/dL)	12.50±1.82	12.88±1.01	12.83±1.11	p=0.357
HCT (%)	37.91±3.30	38.10±3.11	36.93±6.93	p=0.375
MCV (fL)	80.98±5.63	81.37±5.35	81.57±5.41	p=0.643
MCH (pg)	27.08±2.27	27.52±1.87	27.58±2.11	p=0.337
MCHC (g/dL)	33.41±0.85	33.81±0.75	33.77±1.03	p=0.085
RDW (%)	13.92±1.26	13.63±1.06	13.40±0.90*	p=0.013
PLT (10^3/uL)	301.77±88.12	297.06±83.55	303.53±84.39	p=0.803
PDW (%)	16.33±1.21	16.49±0.63	16.47±0.43	p=0.537
PCT (%)	0.24±0.06	0.25±0.10	0.25±0.05	p=0.924
NEU (10^6/uL)	4.14±2.14	3.92±2.61	3.61±1.59	p=0.367
LYM (10^3/uL)	2.76±1.42	3.14±1.67	2.90±1.30	p=0.409
MON(10^3/uL)	0.59±0.24	0.59±0.22	0.62±0.36	p=0.186
EOS (10^3/uL)	0.19±0.19	0.19±0.20	0.20±0.21	p=0.976
BAS (10^3/uL)	0.03±0.05	0.03±0.06	0.03±0.06	p=0.876
NEU%	52.28±14.50	48.02±14.38	48.69±12.67	p=0.196
LYM%	36.45±13.21	40.87±13.10	39.64±11.86	p=0.191
MON%	7.79±2.72	7.87±2.27	8.24±2.57	p=0.370
EOS%	2.75±2.86	2.65±2.55	2.63±2.69	p=0.929
BAS%	0.64±0.43	0.61±0.63	0.58±0.37	p=0.244

Compared with pre-treatment values; *: p<0.05, WBC: White blood cell, HB: Hemoglobin, HCT: Hematocrit, RDW: Red blood cell distribution width, PLT: Platelet, MPV: Mean platelet volume, NEU: Neutrophil, LYM: Lymphocyte, MON: Monocyte, EOS: Eosinophil, BAS: Basophil, RBC: Red blood cell, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, PDW: Platelet distribution width, PCT: Plateletcrit

Table 3. Inflammatory markers of patients using levetiracetam

Complete blood count parameters	Before treatment	6th month of treatment	12th month of treatment	p
NLR	1.89±1.50	1.53±1.16	1.48±0.95	p=0.277
MLR	0.25±0.15	0.21±0.08	0.24±0.16	p=0.364
PLR	129.47±61.94	112.33±47.69	117.22±41.31	p=0.533
RDW/LYM	6.27±3.88	5.27±2.07	5.42±2.14	p=0.065

NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, MLR: Monocyte to lymphocyte ratio, RDW/LYM: Red cell distribution width/lymphocyte ratio

DISCUSSION

Epilepsy is a severe neurological disorder frequently encountered in childhood, and one that often requires lifelong treatment.[1] ASMs can give rise to various systemic side effects, including hematological ones.[13,14] While the mechanisms underlying the hematological side effects of ASMs are not yet fully understood, various mechanisms have been proposed, such as direct toxic effects of the drugs, increased levels of toxic metabolites and homocysteine, decreased folic acid levels, and direct effects of the drugs on cells. The observation that side effects, such as neutropenia, typically emerge within the first two weeks after medication exposure and resolve within the first few days after drug discontinuation suggests that immunological mechanisms may also contribute to the pathophysiology.[13] Potential pharmacokinetic and pharmacodynamic drug interactions may also affect the emergence of hematological side effects.

LEV is a new-generation ASM.[7] It is widely used in children due to its broad spectrum of effects, low side-effect profile, and ease of administration.[15-17] Preparations containing LEV are available under various trade names and in tablet, oral solution, and infusion forms. We consider both patient age and preference when prescribing medications in our clinic. We may encounter patients and parents who prefer the liquid formulation at ages when tablets can be used. We also have patients whom we initially start on tablets but subsequently switch to the syrup formulation because of poor adherence. In this study, our patients were diagnosed with focal, generalized, or unknown epilepsy and were receiving LEV monotherapy in syrup (68.2%) and tablet (31.8%) forms.

The most frequently reported side effects among patients receiving LEV therapy are somnolence, asthenia, and dizziness.[8] Few studies have examined the LEV therapy on hematological parameters. Some of these studies have reported that LEV use produces changes in complete blood count parameters and even side effects

such as anemia and pancytopenia.[17-24] Similar to other ASMs, the mechanism underlying the hematological changes reported with LEV use remains unclear. A potential association has been reported between pancytopenia and bone marrow aplasia, and between anemia and folic acid deficiency.[25] It has been suggested that immune mechanisms may play a role in the development of thrombocytopenia[26] and that synaptic vesicle protein 2A, regarded as the site of action of LEV, is associated with PLT expression.[27]

Some studies evaluating the side effects of LEV therapy have reported an unexplained increase in the incidence of infections, such as pharyngitis and rhinitis.[8-11] The reason for that increase is still unknown. Some complete blood count parameters are known to be associated with systemic inflammation. WBC counts and their subtypes, including LYMs, as markers of the immune system, are known to play a role in inflammation. PLTs are also involved in blood clotting during various inflammatory events. PLT distribution width, in addition to PLT counts, is used to estimate PLT function and activation.[28,29]

Cohort studies have also shown an association between RDW, a complete blood count parameter, and inflammatory processes.[30] The NLR, PLR, MLR, and the RDW/LYM ratio have recently emerged as predictors of systemic inflammation and as novel markers correlated with prognosis.[12,31-33] These markers are easily obtained and calculated from complete blood counts and are relatively inexpensive.

Studies investigating the hematological effects of ASMs have focused on changes in cell numbers in complete blood counts, and very few have included an evaluation of inflammatory markers. The number of studies examining changes in cell counts from complete blood counts in patients treated with LEV is also quite low. Studies have shown that NEU and leukocyte counts were within normal ranges in patients using LEV who developed infection;[17] however, no previous studies have evaluated the effects of LEV on inflammatory markers (NLR, MLR, PLR, and RDW/LYM ratios). The present study compared inflammatory markers, calculated from complete blood count parameters, at baseline and after six and 12 months of treatment in patients receiving LEV monotherapy. When we compared complete blood parameters in patients receiving LEV monotherapy at the beginning of treatment and after 6 and 12 months, we observed a significant decrease in RDW values after 12 months ($p<0.05$). However, there were no significant differences in other hematological parameters ($p>0.05$; Table 2). Also, No significant differences were observed when we compared inflammatory markers (NLR, MLR, PLR, RDW/LYM ratio) calculated from complete blood count parameters ($p>0.05$; Table 3).

Study Limitations

In our clinic, we initiate our patients on the lowest recommended daily therapeutic dose specified in the drug prospectus (20 mg/kg/day). However, we may raise this to as much as 40 mg/kg/day, depending on the response to treatment. This study evaluated changes in hematological parameters and inflammatory markers at 6 and 12 months of treatment in a limited number of patients receiving 20-25 mg/kg/day LEV monotherapy. The drug dosage and duration may affect the patient's response to treatment and may also influence the occurrence of adverse effects. Further prospective studies, including more patients and using LEV for different durations, especially at higher doses, are needed to examine the relationship between LEV treatment and inflammatory markers, a finding revealed for the first time in this study.

CONCLUSION

This research represents one of the few studies to evaluate potential changes in complete blood count parameters in association with LEV therapy. This study is important because it investigates, for the first time in the literature, the relationship between LEV therapy and the inflammatory parameters NLR, MLR, PLR, and the RDW/LYM ratio, and demonstrates that RDW values, which have been linked to inflammatory processes, can change in response to LEV therapy.

Differences among study results evaluating complete blood count parameters suggest that treatment duration and drug dosage may influence the observed effects. The present study evaluated, in a limited number of patients receiving 20-25 mg LEV monotherapy, changes in hematological parameters and inflammatory markers at six and 12 months. The changes in inflammatory markers associated with LEV use, first reported in this study, should be examined in further studies evaluating different dosages, treatment durations and larger patient cohorts.

Although we observed no clinical change in our patients, the findings indicate that monitoring RDW values is warranted in patients using LEV. As with all drugs, it is important in terms of patient safety for side-effects of LEV use to be reported to the relevant pharmacovigilance units.

Ethics

Ethics Committee Approval: Approval from the Balıkesir University Clinical Research Ethics Committee was obtained prior to commencement (approval no: 2022/98, date: 07.09.2022).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.A., Concept: O.K., H.A., Design: O.K., Data Collection or Processing: H.A., Analysis or Interpretation: O.K., Literature Search: O.K., H.A., Writing: O.K., H.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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REFERENCES

1. Reilly C, Atkinson P, Das KB, et al. Neurobehavioral comorbidities in children with active epilepsy: a population-based study. *Pediatrics*. 2014;133(6):e1586-e1593. **[Crossref]**
2. Rahman M. Use of new generation antiepileptic drugs in children. *Bangladesh J Child Health*. 2013;vol37(3):136-137. **[Crossref]**
3. Bachmann T, Bertheussen KH, Svalheim S, et al. Haematological side effects of antiepileptic drug treatment in patients with epilepsy. *Acta Neurol Scand Suppl*. 2011;(191):23-27. **[Crossref]**
4. O'Connor CR, Schraeder PL, Kurland AH, O'Connor WH. Evaluation of the mechanisms of antiepileptic drug-related chronic leukopenia. *Epilepsia*. 1994;35(1):149-154. **[Crossref]**

5. Ramsay RE. Use of phenytoin and carbamazepine in treatment of epilepsy. *Neurol Clin*. 1986;4(3):585-600. [Crossref]
6. Murphy JE, Stewart RB, Springer PK. Carbamazepine-induced leukocytosis. Am J Hosp Pharm. 1980;37(4):550-552. [Crossref]
7. Vigevano F. Levetiracetam in pediatrics. *J Child Neurol*. 2005;20(2):87-93. [Crossref]
8. Harden C. Safety profile of levetiracetam. *Epilepsia*. 2001;42(Suppl 4):36-39. [Crossref]
9. Ben-Menachem E, Falter U. Efficacy and tolerability of levetiracetam 3000 mg/d in patients with refractory partial seizures: a multicenter, double-blind, responder-selected study evaluating monotherapy. European Levetiracetam Study Group. *Epilepsia*. 2000;41(10):1276-1283. [Crossref]
10. Betts T, Waegemans T, Crawford P. A multicentre, double-blind, randomized, parallel group study to evaluate the tolerability and efficacy of two oral doses of levetiracetam, 2000 mg daily and 4000 mg daily, without titration in patients with refractory epilepsy. *Seizure*. 2000;9(2):80-87. [Crossref]
11. Cereghino JJ, Biton V, Abou-Khalil B, Dreifuss F, Gauer LJ, Leppik I. Levetiracetam for partial seizures: results of a double-blind, randomized clinical trial. *Neurology*. 2000;55(2):236-242. [Crossref]
12. Aktas G, Duman TT, Atak BM, et al. Irritable bowel syndrome is associated with novel inflammatory markers derived from hemogram parameters. *Fam Med Prim Care Rev*. 2020;22(2):107-110. [Crossref]
13. Verrotti A, Scaparrotta A, Grosso S, Chiarelli F, Coppola G. Anticonvulsant drugs and hematological disease. *Neurol Sci*. 2014;35(7):983-993. [Crossref]
14. Ozkaya H, Aydemir G, Akcan AB, et al. Carbamazepine-induced red blood cell aplasia: a case report. *Turk J Haematol*. 2012;29(2):195-196. [Crossref]
15. Tekgül H, Gencpinar P, Çavuşoğlu D, Dündar NO. The efficacy, tolerability and safety of levetiracetam therapy in a pediatric population. *Seizure*. 2016;36:16-21. [Crossref]
16. Briggs DE, French JA. Levetiracetam safety profiles and tolerability in epilepsy patients. Expert Opin Drug Saf. 2004;3(5):415-424. [Crossref]
17. French J, Edrich P, Cramer JA. A systematic review of the safety profile of levetiracetam: a new antiepileptic drug. *Epilepsy Res*. 2001;47(1-2):77-90. [Crossref]
18. Alzahrani T, Kay D, Alqahtani SA, Makke Y, Lesky L, Koubeissi MZ. Levetiracetam-induced pancytopenia. *Epilepsy Behav Case Rep*. 2015;4:45-47. [Crossref]
19. Oghlakian R, Nock C, Koubeissi M. A case of levetiracetam-induced thrombocytopenia. *Epileptic Disord*. 2010;12(4):335-337. [Crossref]
20. Glauser TA, Ayala R, Elterman RD, et al.; N159 Study Group. Double-blind placebo-controlled trial of adjunctive levetiracetam in pediatric partial seizures. *Neurology*. 2006;66(11):1654-1660. [Crossref]
21. Taberner Bonastre MT, Peralta Muñoz S, Boza FM, Gumà I Padró J. Neutropenia secondary to exposure to levetiracetam. *Tumori*. 2015;101(5):e145-e146. [Crossref]
22. Unkun R, Kizilkilic EK, Delil S, Kemerdere R, Ozkara C. Levetiracetam-associated pancytopenia. *Acta Neurol Belg*. 2023;123(4):1625-1626. [Crossref]
23. Ammad Ud Din M, Ather Hussain S, Bodrog A. Delayed recognition of levetiracetam-induced pancytopenia. *Eur J Case Rep Intern Med*. 2021;8(3):002449. [Crossref]
24. Ucar HK, Sarigecili E, Bilen S, Sari S. Short-term and long-term effects of levetiracetam monotherapy on hematological parameters in children with idiopathic epilepsy. *Med Bull Sisli Etfal Hosp*. 2023;57(1):46-53. [Crossref]
25. Çağ İ, Altun Y, Altunışık E. Do antiepileptic drugs have any effect on neutrophil/lymphocyte and platelet/lymphocyte ratio? *Med Sci Discov*. 2019;6(4):76-81. [Crossref]
26. Meschede A, Runge U, Sabolek M. Thrombocytopenia during levetiracetam therapy. *Epilepsy Res*. 2008;80(1):91-92. [Crossref]
27. Dilber B, Yıldız N, Yaman H, et al. Evaluation of long-term effects of levetiracetam monotherapy on hematological and liver function parameters in children with idiopathic epilepsy. *Turk J Pediatr Dis*. 2022;16(2):144-149. [Crossref]
28. Orum MH, Kara MZ, Egilmez OB. Mean platelet volume and neutrophil to lymphocyte ratio as parameters to indicate the severity of suicide attempt. *J Immunoassay Immunochem*. 2018;39(6):647-659. [Crossref]
29. Arıkanoğlu A, Çevik MU, Uzar E, et al. The increase of the mean platelet volume in patients with intracerebral haemorrhage. *Turk J Neurol*. 2012;18(2):054-056. [Crossref]
30. Lippi G, Targher G, Montagnana M, Salvagno GL, Zoppini G, Guidi GC. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. *Arch Pathol Lab Med*. 2009;133(4):628-632. [Crossref] Erratum in: *Arch Pathol Lab Med.* 2009;133(8):1186. [Crossref]
31. Horne BD, Anderson JL, John JM, et al.; Intermountain Heart Collaborative Study Group. Which white blood cell subtypes predict increased cardiovascular risk? *J Am Coll Cardiol*. 2005;45(10):1638-1643. [Crossref]
32. Öksüm Solak E, Baran Ketencioglu B, Cinar SL, Kartal D, Borlu M. The role of new inflammatory markers in determining disease activation and severity in patients with hidradenitis suppurativa. *Int J Dermatol*. 2023;62(8):1076-1081. [Crossref]
33. Zahorec R. Neutrophil-to-lymphocyte ratio, past, present and future perspectives. *Bratisl Lek Listy*. 2021;122(7):474-488. [Crossref]

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Original Article

Assessment of Physical Activity Behaviors and Perspectives in Epilepsy Patients

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Abstract

Objective: Physical exercise has been shown to improve mood, memory, and overall quality of life in people with epilepsy. Still, studies indicate that individuals with epilepsy are less active than the general population. We aimed to determine the physical activity levels of individuals with epilepsy and to gain insight into their perspectives on it.

Methods: This study administered a survey to patients with epilepsy at a single tertiary care center between July 2024 and February 2025. The questionnaire developed by the research team had 21 questions and three sections. The survey assessed participants' frequency of physical activity, their opinions on sports and epilepsy, and sociodemographic information.

Results: A total of 202 participants (59.4% female) completed the survey. 49.0% of the patients did not exercise regularly, while 13.9% exercised more than three times a week. The most preferred sports were walking (16.8%) and running (11.4%). The patients stated the reasons for not exercisingr of having a seizure (35.1%), lack of time (33.2%), lack of motivation (21.3%), not seeing it as necessary (20.8%), and side effects of epilepsy medications (4.5%). 77.2% of patients had not asked their doctor any questions about physical exercise, and 66.8% had never been informed by their doctor about the importance of physical activity. 45.5% of the patients were supported by their environment regarding physical exercise, while 25.7% were discouraged from engaging in physical exercise.

Conclusion: Patients with epilepsy require improved information regarding the benefits of physical exercise, and neurologists should address this need.

Keywords: Epilepsy, physical activity, seizure

INTRODUCTION

Epilepsy is a common, chronic neurological disorder that affects over 50 million people worldwide.[1] The stigma and prejudice associated with epilepsy continue to affect sports participation, physical activity, and many other areas of an individual's life.[2] Despite the well-documented benefits of sports and physical activity for quality of life and disease prevention in the general population,[3,4] participation in sports by individuals with epilepsy had been regarded as risky until recent years.[5] This recommendation likely stemmed from concerns that sports activities could cause injuries, trigger seizures, and adversely affect the course of the disease.[5] Recently, there has been a trend towards encouraging, rather than restricting, participation in sports activities, as it has been shown to contribute to seizure control,[6,7] to lower the risk of diabetes, hypertension, obesity, and coronary heart disease, and to have positive psychosocial effects.[8-11] The International League Against Epilepsy (ILAE) Task Force on Sports and Epilepsy published a consensus statement in 2016.[12] This consensus statement provides recommendations to promote general well-being in sports activities and to facilitate the globalization of treatment certifications related to sports participation. The patient's eligibility for almost every sport was determined by the seizure-free period, seizure type, seizure timing, and other factors.[12] However, despite a recent trend encouraging participation in sports activities, research has shown that epilepsy patients do not engage in sufficient physical activity and sports.[11,13,14]

In our study, participants were asked about their knowledge, attitudes, and behaviors regarding exercise to identify factors that increase or decrease the likelihood of engaging in exercise.

METHODS

Study Design

The study was conducted at Karaman Training and Research Hospital Neurology Clinic, and participants were included between July 2024 and February 2025. Karamanoğlu Mehmetbey University Ethics Committee approved the study protocol in accordance with the

ethical standards outlined in the Declaration of Helsinki (approval no: 08-2024/02, date: 24.07.2024). All participants were informed of the possible risks and benefits, and written informed consent was obtained.

Partipicants

Eligible participants were patients aged 18 years or older who had a clinical and electrophysiological diagnosis of epilepsy at Karaman Training and Research Hospital. Those with comorbid psychiatric disorders and those who had diseases that could lead to serious physical disabilities (such as cerebral palsy) were excluded from the study. According to the specified criteria, 202 patients participated in the study. Participation was entirely voluntary; no incentives were offered. Furthermore, no sanctions were imposed on patients in the event of non-participation.

Questionnaire Study

The survey form was developed by the research team based on literature reviews and personal experiences. The survey assessed participants' physical activities, general views of and knowledge about sports and epilepsy, and sociodemographic information. This survey study consists of 21 questions divided into three sections. The first section contains demographic information and comprises six questions. The second section focuses on participants' disease status and contains four questions. In the third part, the physical exercise habits and perspectives of patients with epilepsy are examined using 11 questions. The results were compared with the medical records of neurologists to enhance the accuracy of the answers.

Statistical Analysis

Recorded data were analyzed using the SPSS, version 27.0 (SPSS Inc., Armonk, NY). A reliability analysis was performed on the survey questionnaire (Cronbach's alpha: 0.720). Also, a validity analysis was performed with a Kaiser-Meyer-Olkin value of 0.739 and Bartlett's test $p<0.001$.

The normality of numerical data distribution was examined using the Shapiro-Wilk test. Normally distributed continuous variables were presented as the mean and standard deviation, non-normally distributed continuous variables were presented as the median and interquartile range (25^{th}-75^{th} percentiles), and qualitative data were expressed as frequencies and percentages. Numeric variables were analyzed using the t-test or the Mann-Whitney U test depending on whether the data followed a parametric distribution. The categorical variables were compared using Pearson's chi-square test and the linear-by-linear association test, based on expected counts and numbers of cases. Binary logistic regression analyses were performed to identify variables associated with exercise status. Spearman correlation analysis was applied to assess correlations involving exercise frequency. A 95% confidence level and a 5% margin of error were used. Therefore, the p-value was considered significant when $p<0.05$.

MAIN POINTS

- The levels of physical activity among people with epilepsy remain lower than those in the general population.
- Fear of experiencing a seizure is a primary reason patients with epilepsy do not engage sufficiently in physical activity.
- Patients should informed about the benefits of physical exercise, and healthcare professionals should emphasize its importance.

RESULTS

Overall, 210 patients were approached to complete the survey. Of these, eight declined to participate, leaving 202 patients included in the study. Approximately 90% of patients were under the age of 55. 59.4% (n=120) of the patients were female and 40.6% (n=82) were male; 77.2% graduated from high school or had a lower level of education, and 22.8% (n=17) graduated from university or had a higher level of education. 31.2% of the patients were working full-time, 6.9% were working part-time, and 61.9% were not working. Based on body mass index (BMI), 45% of the patients were of normal weight, 33.7% were overweight, and 19.3% were obese or morbidly obese; the mean BMI of the patients was 25.3. The sociodemographic characteristics of the patients are shown in Table 1.

According to the ILAE 2017 seizure classification, 72 patients had generalized onset seizures, 124 patients had focal onset seizures, and 34 patients had unknown onset seizures. 53.5% of patients had epilepsy for more than 10 years, 52.5% had seizures once or twice per year or less, and 36% (n=73) had not had a seizure in the past year. More than 80% have no systemic disease; the most common systemic conditions are hypertension, diabetes mellitus, and asthma. Seven patients presented with a single seizure episode, whereas 19 patients experienced seizures exclusively during nocturnal sleep. 56.4% (n=114) of patients received monotherapy; 43.6% (n=88) received polytherapy.

Table 1. Sociodemographic characteristics of patients (n=202)

Age category (n/%)	
18-24	43 (21.3)
25-34	49 (24.3)
35-44	52 (25.7)
45-54	37 (18.3)
55-64	19 (9.4)
65 or older	2 (1.0)
Gender (n/%)	
Female	120 (59.4)
Male	82 (40.6)
Basal mass index (n/%)	
Underweight	4 (2.0)
Normal	91 (45.0)
Overweight	68 (33.7)
Obese	36 (17.8)
Extremely obese	3 (1.5)
Education (n/%)	
High school or less	156 (77.2)
University or more	46 (22.8)
Employment (n/%)	
Full time (35 h/week or more)	63 (31.2)
Part time (less than 35 h/week)	14 (6.9)
Unemployed	125 (61.9)

49.0% of the patients did not exercise at all, while 13.9% exercised more than three times per week. The most preferred sports were walking (16.8%) and running (11.4%). Patients reported the following reasons for insufficient exercise: fear of having a seizure (35.1%); lack of time (33.2%); lack of motivation (21.3%); not seeing it as necessary or not feeling the need (20.8%); side effects of epilepsy medications (4.5%); and 7.4% did not specify a reason (Figure 1). 77.2% of the patients had not asked the doctor any questions about physical activity, and 66.8% had never been informed about physical activity by their doctors. 45.5% of the patients were supported by their environment about physical exercise, while 25.7% were discouraged.

Patients who did not engage in physical exercise had a median BMI of 25.9 (7.6), whereas those who engaged in physical exercise had a median BMI of 24.5 (6.1). BMI in the exercise group was significantly lower ($p<0.01$).

In binary logistic regression analysis, compared with the 18-24 age group, the 35-44 age group was associated with a decreased likelihood of exercising [odds ratio (OR)=0.071, $p<0.001$], whereas being male was associated with an increased likelihood of exercising (OR=2.863, $p=0.024$). Working part-time (OR=0.036, $p<0.001$) and full-time (OR=0.296, $p<0.01$) were found to be associated with a decreased likelihood of exercising compared with not working. Receiving polytherapy (OR=0.210, $p<0.001$) was also associated with a decreased likelihood of exercising.

No statistically significant association was observed between the level of physical activity and seizure frequency ($p=0.371$). Among patients who exercised, no correlations were found among age, gender, BMI, education status, and employment status (Table 2). Similarly, no correlation was found among focal and generalized seizures, disease duration, monotherapy and polytherapy status, time of last seizure, history of single seizures, history of nocturnal seizures, and exercise frequency.

Patients were divided into four categories according to the anti-seizure drugs they were using: those using drugs with at least one high BMI and strong evidence of weight gain (Valproate, Carbamazepine, Pregabalin, Gabapentin, Vigabatrin); those using drugs with at least one low BMI and strong evidence of weight loss (Topiramate, Zonisamide); those using these drugs in combination; and those using other anti-seizure drugs not thought to affect weight control significantly. Patients taking medications that had no effect on BMI (n=70), those taking medications that increased BMI (n=92), and those taking medications that decreased BMI (n=32) were compared with respect to BMI and exercise frequency. Patients taking both BMI-increasing and BMI-decreasing drugs (n=8) were excluded from the comparison.

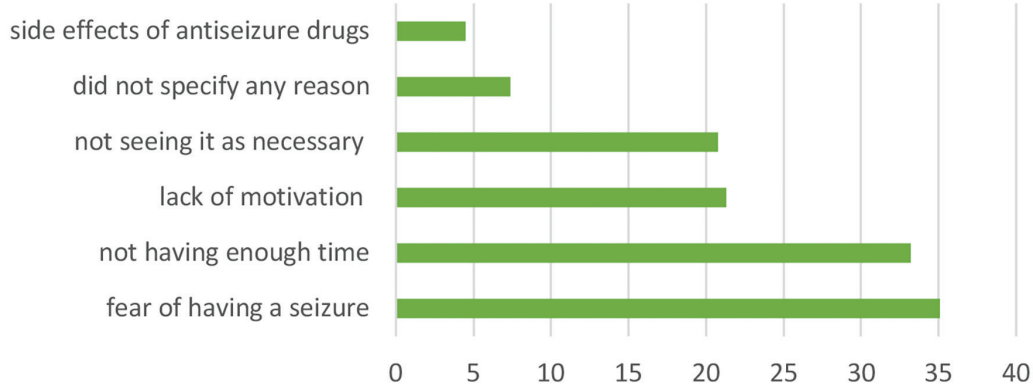

Figure 1. Reasons why patients with epilepsy do not exercise regularly

Table 2. Logistic regression analysis of exercise status

	B	SE	P	OR	95% CI for OR	
Age					**Lower**	**Upper**
18-24			<0.01			
25-34	-0.666	0.577	0.248	0.514	0.166	1.592
35-44	-2.650	0.700	**<0.001**	**0.071**	0.018	0.279
45-54	-1.322	0.708	0.062	0.267	0.067	1.068
55-64	-1.501	1.829	0.412	0.223	0.006	8.039
>65 age	-0.666	0.577	0.248	0.514	0.166	1.592
Gender	1.052	0.465	0.024	2.863	1.152	7.116
Working status						
Non-working			<0.001			
Full time	-3.315	0.879	**<0.001**	**0.036**	0.006	0.204
Part-time	-1.218	0.468	**<0.01**	**0.296**	0.118	0.741
Constant	1.965	3.110	0.527	7.135		

Nagelkerke R^2: 0.435, SE: Standard error, OR: Odds ratio, CI: Confidence interval

No significant differences were found between anti-seizure drugs and BMI or exercise frequency (p=0.228 and p=0.666, respectively).

DISCUSSION

We investigated the physical activity levels and perspectives of patients with epilepsy. It was determined that 49.0% of the patients did not exercise regularly. A study conducted in Norway found that a sedentary lifestyle is more common in patients with epilepsy than in healthy individuals.[15] In Brazil, another study reported that 49% of patients with epilepsy do not engage in regular physical activity.[16] Research in Germany showed that 42% of healthy individuals participate in regular sports, compared with only 25% of patients with epilepsy.[17] Additionally, in our country, the rate in the general population was 22% among women and 39% among men, according to the 2022 data from the World Health Organization.[18] In a study conducted among university students in our country, the prevalence of physical inactivity was 29.9%.[19] This rate indicates that patients with epilepsy are less likely to exercise than the general population.

We found that the most common barriers to exercise in patients with epilepsy were fear of having a seizure (35.1%), insufficient time (33.2%), lack of motivation (21.3%), and not seeing it as necessary (20.8%). Our findings are consistent with the literature. In a similar study, lack of motivation (41%) was the most prominent factor, followed by personal safety concerns (27%), fear of seizures (19%), and limited access to exercise facilities (18%).[20] In another study, "fatigue after activity" and "not having time for activity" were the most common barriers.[21] In a recent study, lack of time (24.7%) and fear of having a seizure (19.7%) were the most frequently reported reasons.[14] Although it is believed that the fatigue and weight-loss side effects of anti-seizure drugs could pose an obstacle, this rate was only 4.9% in our study. Among patients with epilepsy who engage in regular physical activity, walking (16.8%) and running (11.4%) are the most preferred forms of exercise. Another study found that epilepsy patients most frequently engaged in hiking (18%) and walking (14%).[21] In a single-center survey, walking was the preferred form of physical activity, chosen by 97.8% of participants.[14]

In our study, 14.3% of epilepsy patients experienced a seizure during physical activity, and 13.8% had a seizure afterward. A similar study found that about 18% of people with epilepsy reported having a seizure before, during, or after physical activity. In this study, 56% of those who believed that seizures prevented them from exercising reported having a seizure during physical activity, while only 9% of those who thought seizures did not prevent them from exercising reported experiencing a seizure.[20] In another study, 47% of epilepsy patients reported having seizures during or immediately after exercise at least once, with 11% experiencing them very frequently (>10%); however, only 2% actually experienced seizures during or immediately after exercise.[15] This highlights the subjective nature of patient reports in survey studies. This could have been the case in our study as well.

The study revealed no significant correlation between the frequency of seizures and participation in physical activity. Several studies suggest that physical activity can help control seizures.[6,7,22] A study examining the consequences of physical activity in people with epilepsy suggested that physical activity may reduce the incidence of epileptic seizures by decreasing the production of proinflammatory biomarkers.[22] Another study examining the impact of an exercise program on overall health and seizure frequency in epilepsy patients found that exercise decreases seizure occurrences.[6] However, meta-analysis studies have not demonstrated a clear link between seizure frequency and physical activity.[11,23] One meta-analysis included three studies examining the relationship between physical activity and seizure frequency, and only one found that physical activity was associated with fewer seizures.[11] Another meta-analysis study suggested that exercise seemed to decrease seizure frequency; however, it emphasized that the changes were not statistically significant and cannot be recommended for seizure control in patients with drug-resistant epilepsy.[23]

According to the BMI, 19.3% of the patients were classified as obese, compared with 17% in the general population of our country.[24] From this perspective, obesity rates in patients with epilepsy did not differ from those in the general population. A recent study revealed that the obesity rate in patients with epilepsy (20.4%) is higher than that in healthy adults (9.6%).[25] Another study involving 822,071 patients with epilepsy identified an obesity rate of 28.3%.[26] Furthermore, as anticipated, our study revealed that individuals who did not engage in regular physical exercise had significantly higher BMI than individuals who engaged in regular physical exercise.

Our study did not detect correlations among anti-seizure drugs, BMI, and physical activity. Although anti-seizure drugs have been implicated in causing obesity in patients with epilepsy, specific studies on this topic are lacking, and the underlying mechanisms remain unclear.[25] Recent studies largely support the notion that topiramate and zonisamide cause weight loss, with mechanisms that may involve hypothalamic insulin and leptin signaling.[27,28] Several studies indicate that valproic acid causes weight gain by increasing leptin levels and inducing hyperinsulinemia, while carbamazepine promotes weight gain by enhancing adipogenesis through inhibition of Wnt/β-catenin expression.[29,30] Additionally, gabapentin, pregabalin, vigabatrin, and perampanel have been shown to contribute to weight gain.[30,31] In our study, the results may not have been statistically significant because group distributions were not homogeneous and group sizes were unequal. There are no studies specifically examining the relationship between anti-seizure drugs and physical activity. One study compared the physical activity rates of patients receiving monotherapy and those receiving polytherapy and showed that polytherapy affected exercise habits independently of seizure frequency.[21] Our study found no significant difference in exercise habits between patients receiving polytherapy and those receiving monotherapy.

Our study found that 25.7% of patients' relatives attempted to discourage patients from engaging in physical exercise. A study conducted in Brazil reported a rate of 14%, while a survey in South Korea reported a rate of 52.8%.[16,21] The differences in rates may stem from cultural variations in the stigma associated with epilepsy. This discouragement appears to stem from the belief, among family members and the public, that physical exercise can trigger seizures.

We determined that 77.2% of the patients did not ask their doctors any questions about physical exercise, and 66.8% were not informed by their doctors about physical activity. Another study on physical activity and exercise reported that approximately 45% of patients patients had never discussed sports-related recommendations with their doctors.[17] A study of 60 patients reported that 6 were prevented from exercising by their families and doctors.[16] In 2015, the ILAE Task Force on Sport and Epilepsy released a comprehensive report that provided guidance on the sports and types of exercise considered safe based on seizure frequency and type. After the ILAE published this report, Arida et al.[32] surveyed neurologists to assess their knowledge of the importance of physical activity for people with epilepsy and their awareness of the ILAE report. Over 90% of neurologists participating in the survey endorsed physical activity for individuals with epilepsy and agreed that exercise can reduce comorbidities. However, only 40% were aware of the ILAE recommendations, whereas 35% reported having no knowledge of physical activity for people with epilepsy. Arida et al.[32] emphasized that doctors are aware of the benefits of exercise, but discussing exercise with patients is a different matter; doctors should also proactively provide information about exercise rather than merely responding when patients ask.[33]

Study Limitations

First, as with most survey data, our data were based on self-reporting; however medical records were reviewed to account for possible false recall or rejection. Second, the representativeness of the results may be limited, particularly with respect to socioeconomic characteristics, because our patients were recruited from a single small city.

CONCLUSION

Patients with epilepsy should be encouraged to exercise, as with the general population. Regular exercise positively impacts both the mental and physical health of individuals. Furthermore, studies have demonstrated that physical activity can help control seizures and reduce comorbidities associated with epilepsy, such as depression. Conversely, some patients may avoid exercise because of fear of experiencing a seizure during physical activity, and their families often attempt to dissuade them. Neurologists must fully comprehend the ILAE consensus published in 2015 and inform patients about it. Additionally, all physicians should promote regular physical activity and educate caregivers about the benefits of exercise and the necessary precautions, such as wearing protective clothing.

Ethics

Ethics Committee Approval: Karamanoğlu Mehmetbey University Ethics Committee approved the study protocol in accordance with the ethical standards outlined in the Declaration of Helsinki (approval no: 08-2024/02, date: 24.07.2024).

Informed Consent: All participants were informed of the possible risks and benefits, and written informed consent was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Z.Y., Concept: Z.Y., Design: Z.Y., M.A.G., Data Collection or Processing: M.A.G., Analysis or Interpretation: M.A.G., Literature Search: Z.Y., Writing: Z.Y.

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REFERENCES

1. Fiest KM, Sauro KM, Wiebe S, et al. Prevalence and incidence of epilepsy. *Neurology*. 2017;88(3):296-303. [Crossref]
2. Mayor R, Gunn S, Reuber M, Simpson J. Experiences of stigma in people with epilepsy: a meta-synthesis of qualitative evidence. *Seizure*. 2022;94:142-160. [Crossref]
3. Dhuli K, Naureen Z, Medori MC, et al. Physical activity for health. *J Prev Med Hyg*. 2022;63(2 Suppl 3):E150-E159. [Crossref]
4. Mahindru A, Patil P, Agrawal V. Role of physical activity on mental health and well-being: a review. *Cureus*. 2023;15(1):e33475. [Crossref]
5. Pimentel J, Tojal R, Morgado J. Epilepsy and physical exercise. *Seizure*. 2015;25:87-94. [Crossref]
6. Häfele CA, Rombaldi AJ, Feter N, et al. Effects of an exercise program on health of people with epilepsy: a randomized clinical trial. *Epilepsy Behav*. 2021;117:107904. [Crossref]
7. Green R, Abe C, Denney DA, et al. Physical activity status and quality of life in patients with epilepsy - survey from level four epilepsy monitoring units. *Epilepsy Res*. 2021;173:106639. [Crossref]
8. Vooturi S, Potharaju A, Kandula A, et al. Prevalence of overweight and obesity and trends of physical activity in people with epilepsy - an observational study. *J Med Sci Res*. 2019;7(3):66-69. [Crossref]
9. Bhatt G, Mukkamala N. Impact of exercise intervention on cardiovascular fitness in patients with epilepsy: a quasi-experimental study. *J Clin Diagn Res*. 2024;18(10):15-18. [Crossref]
10. Hu Z, Tang L, Xu X, Zhan Y. Association between physical activity and psychosocial status in adults with epilepsy: results from the 2022 National Health Interview Survey. *Epilepsy Behav*. 2024;156:109836. [Crossref]
11. Johnson EC, Helen Cross J, Reilly C. Physical activity in people with epilepsy: a systematic review. *Epilepsia*. 2020;61(6):1062-1081. [Crossref]
12. Capovilla G, Kaufman KR, Perucca E, Moshé SL, Arida RM. Epilepsy, seizures, physical exercise, and sports: a report from the ILAE task force on sports and epilepsy. *Epilepsia*. 2016;57(1):6-12. [Crossref]
13. Tedrus GMAS, Sterca GS, Pereira RB. Physical activity, stigma, and quality of life in patients with epilepsy. *Epilepsy Behav*. 2017;77:96-98. [Crossref]
14. Alexander HB, Arnel M, O'Connell N, et al. A single-center survey on physical activity barriers, behaviors and preferences in adults with epilepsy. *Epilepsy Behav*. 2023;149:109491. [Crossref]
15. Nakken KO. Clinical research physical exercise in outpatients with epilepsy. *Epilepsia*. 1999;40(5):643-651. [Crossref]
16. Arida RM, Scorza FA, de Albuquerque M, Cysneiros RM, de Oliveira RJ, Cavalheiro EA. Evaluation of physical exercise habits in Brazilian patients with epilepsy. *Epilepsy Behav*. 2003;4(5):507-510. [Crossref]
17. Steinhoff BJ, Neusiiss K, Thegeder H, Reimers CD. Leisure time activity and physical fitness in patients with epilepsy. *Epilepsia*. 1996;37(12):1221-1227. [Crossref]
18. World Health Organization. Physical activity Türkiye 2022 country profile. 2022 [cited 2025 Apr 24]. [Crossref]
19. Kundakcı YE, Karaman S, Ateş MS. Physical activity, leisure-time management, perceived barriers to physical activity and mental well-being among Turkish university students. *Discover Mental Health*. 2024;4(1):54. [Crossref]

20. Ablah E, Haug A, Konda K, et al. Exercise and epilepsy: a survey of midwest epilepsy patients. *Epilepsy Behav*. 2009;14(1):162-166. [Crossref]
21. Han K, Choi-Kwon S, Lee SK. Leisure time physical activity in patients with epilepsy in Seoul, South Korea. *Epilepsy Behav*. 2011;20(2):321-325. [Crossref]
22. Cavalcante BRR, Improta-Caria AC, Melo VH de, De Sousa RAL. Exercise-linked consequences on epilepsy. *Epilepsy Behav*. 2021;121:108079. [Crossref]
23. Duñabeitia I, Bidaurrazaga-Letona I, Diz JC, Colon-Leira S, García-Fresneda A, Ayán C. Effects of physical exercise in people with epilepsy: a systematic review and meta-analysis. *Epilepsy Behav*. 2022;137:108959. [Crossref]
24. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü, Sağlıklı Beslenme ve Hareketli Hayat Dairesi Başkanlığı. Obezite. [cited 2025 Apr 24]. [Crossref]
25. Li YX, Chen RX, Lv XR, Zi Q, Zhang FM, Li Y. Investigation of the relationship between body mass index and epilepsy. *Epilepsy Behav.* 2025;165:110295. [Crossref]
26. Pfeifer MT, Kostev K, Doege C. Sex-related associations between body mass index and the incidence of epilepsy. *Epilepsy Behav*. 2022;136:108926. [Crossref]
27. Wajid I, Vega A, Thornhill K, et al. Topiramate (topamax): evolving role in weight reduction management: a narrative review. *Life*. 2023;13(9):1845. [Crossref]
28. Domecq JP, Prutsky G, Leppin A, et al. Drugs commonly associated with weight change: a systematic review and meta-analysis. *J Clin Endocrinol Metab*. 2015;100(2):363-370. [Crossref]
29. Im DU, Kim SC, Chau GC, Um SH. Carbamazepine enhances adipogenesis by inhibiting Wnt/β-catenin expression. *Cells*. 2019;8(11):1460. [Crossref]
30. Nazish S. Obesity and metabolic syndrome in patients with epilepsy, their relation with epilepsy control. *Ann Afr Med*. 2023;22(2):136-144. [Crossref]
31. Hamed SA. Antiepileptic drugs influences on body weight in people with epilepsy. *Expert Rev Clin Pharmacol*. 2015;8(1):103-114. [Crossref]
32. Arida RM, Sales EP do N, Teixeira-Machado L, Prado GF do, Gutierre RC, Carrizosa J. Neurologists' knowledge of and attitudes toward physical exercise for people with epilepsy in Latin America. *Epilepsy Behav.* 2022;131:108705. [Crossref]
33. Volkers N. Stop stigma, start exercising: how clinicians can encourage people with epilepsy to engage in physical activity. *Epigraph*. 2023;25(1):14-20. [Crossref]

Overprotection and the Associated Factors Among People with Epilepsy: A Cross-sectional Study

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Abstract

Objective: To examine overprotection in people with epilepsy and the demographic and clinical factors affecting it.

Methods: The study was a descriptive, cross-sectional investigation involving 104 people with epilepsy attending the neurology outpatient clinic of Giresun Training and Research Hospital between September 2022 and February 2023. While a descriptive information form and an overprotection scale were used to collect research data, descriptive statistics (percentages, mean, and standard deviation) and linear regression analysis were used to analyze the data.

Results: It was determined that 66.3% of the participants were male; 53.8% were primary school graduates; 53.8% were married; 34.6% had generalized epilepsy; and 69.2% did not have seizure control. The overall mean score on the perceived overprotection scale was 29.09±12.63. The linear regression analysis using the significant regression model (F=5.111; p=0.000) revealed that 24.2% (R^2=0.242) of the change in overprotection was explained by demographic and clinical variables.

Conclusion: Primary and high school education, polytherapy, and generalized epilepsy were associated with higher perceived overprotection, whereas being married was associated with lower perceived overprotection. These findings underscore the importance of interventions focusing on patient and family education.

Keywords: Adult, epilepsy, perceived overprotection

INTRODUCTION

Epilepsy is a neurological disorder characterized by recurrent seizures and associated cognitive, psychological, and social consequences.[1] There are approximately 50 million people with epilepsy (PWE) worldwide, with about 2 million new cases recorded each year.[2,3] The prevalence of epilepsy is 6 per 1,000 in developed countries, compared with 18.5 per 1,000 reported in developing countries. The prevalence of epilepsy in Türkiye is 6.1-10.2 per 1,000 population.[4,5] Epilepsy has been recognized as a dangerous and feared condition since antiquity.[3,6] PWE more often contend with psychosocial problems related to seizures than with the seizures themselves. Therefore, treating epilepsy as a neurological disease alone is insufficient.[4]

Research on overprotection has primarily focused on children and adolescents with epilepsy.[7,8] According to Thomasgard and Metz,[9] overprotective parenting is characterized by excessive control and caution, difficulty with separation, and the inhibition of a child's independent behaviors. Overprotection is associated with controlling behaviors, such as excessive physical or social contact, infantilization, parental overcontrol, intrusiveness, and anxious parenting.[8] Overprotected children with epilepsy may face risks, including excessive dependence, heightened emotionality, delayed maturity relative to peers, and failure to acquire essential social skills.[10] Consequently, this pattern may lead to significant psychological problems such as reliance on others and low self-esteem.[6,11]

Across studies conducted in different countries, findings indicate that autonomy, epilepsy type, educational level, and familial overprotection affect employability. Many restrictions appear to stem not from objectively increased seizure-related risks but from excessively protective caregiving behaviors; caregivers are frequently reported as overprotective, a pattern associated with feelings of shame, reduced social participation, and social isolation. Conversely, some individuals—particularly those following surgery or awaiting surgical treatment—report increased independence and greater engagement in social activities.[1,3,12-17] In light of Kleinman et al.'s[18] emphasis on the cultural shaping of illness perceptions, these results suggest that perceived restrictions influence notions of dignity, vulnerability, and independence

among PWE, and that further comparative research is required to disseminate and deepen understanding of these cross-cultural dynamics.[19]

Research on perceptions of overprotection among PWE in Türkiye is limited. Existing studies predominantly address the medical aspects of epilepsy, while its social and psychological consequences remain underexamined. Although findings concerning stigma and mental health have been reported, the specific effects of perceived overprotection on social participation, independence, and psychological wellbeing have not been thoroughly investigated. While relevant international literature exists, further comparative research is needed to determine the applicability of those findings to the Turkish context. The aim of this study was to evaluate perceived overprotection and associated demographic and clinical variables among PWE in Türkiye.

METHODS

Study Design

This research was a descriptive, cross-sectional study conducted between September 2022 and February 2023. The data were collected face-to-face, and each form took approximately 15 minutes to complete.

Population and Sample

The research was conducted in Giresun, Türkiye. The study population consisted of 132 PWE who were registered at Giresun Training and Research Hospital, attended the neurology outpatient clinic for examination, and were treated in the neurology clinic. In the power analysis conducted using the G*Power 3.1.9.4 package, based on the study of Aydemir,[17] an effect size of d=0.372, a 95% confidence interval, a 0.05 margin of error and a minimum sample size of n=96 were calculated. Of the PWE individuals constituting the universe, 24 did not meet the inclusion criteria, and 4 did not agree to participate in the study. The sample comprised 104 patients meeting the study's inclusion criteria. The data were collected by the researcher using face-to-face interviews in an empty room in the outpatient clinic and in patient rooms in the inpatient clinic. Each interview lasted approximately 15 minutes. Criteria for inclusion in the study;

- having been diagnosed with epilepsy in the last year,
- aged 18 years or older,
- having no problems with vision, reading, writing and communication,
- no neurological disease or psychiatric disease other than epilepsy,
- agreeing to participate in the study.

MAIN POINTS

- People with epilepsys who went out alone and took responsibility often reported overprotection.
- Generalized type epilepsy and multiple antiepileptic drug use often led to overprotection.
- The participants who were married reported less overprotection.

Data Collection Methods and Tools

Descriptive Information Form

The researchers created a survey based on previous studies. The survey included 10 questions on participants' demographic and clinical information, including age; duration of epilepsy; education; marital status; professional activity; type of epilepsy; seizure control; number of medications used; unintentional harm to others during a seizure; and accidents.

Overprotection Scale

The scale was adapted into Turkish by Kaya and Yildiz[20] This scale was developed to assess a person's perceived parental overprotection in the context of epilepsy (e.g., "my family does not allow me to go out for a movie or a walk unless a family member or a friend is with me"). It consists of 10 items with a single factor. Responses are rated on a five-point Likert scale (5=strongly agree; 1=strongly disagree). The minimum score on the scale is 18; the maximum is 83. Higher scores indicate higher perceived overprotection. The reliability of the original scale is 0.85.[20] In this study, the reliability of the scale, measured using Cronbach's alpha, was 0.958.

Statistical Analysis

SPSS version 22.00 was used for data analysis. Percentages, means, and standard deviations were used for descriptive statistics. Homogeneity of variances was evaluated using Levene's test. Parametric methods were used to analyze the data. Multivariate linear regression was applied to determine the factors associated with overprotection. Variables with high representativeness and relatedness, identified by pairwise comparisons (univariate analysis), were included in the model. Categorical independent variables were encoded as dummy variables. Linear regression analysis was performed to determine the impact of descriptive information on overprotection. The significance level was set at $p<0.05$.

Ethical Considerations

This study was approved by Ordu University Clinical Research Ethics Committee (approval no: 202, date: 02.09.2022). Written informed consent was obtained from participants in face-to-face interviews; the consent form provided necessary explanations about the purpose of the research and the data collection. The study was conducted in accordance with the Declaration of Helsinki.

RESULTS

Of the participants, 66.3% were male; 53.8% were elementary school graduates; 53.8% were married; 34.6% had generalised epilepsy; 69.2% did not have seizure control; 59.6% received single-drug therapy; 65.4% did not have an accident during a seizure; and 89.4% did not harm anyone during a seizure. The participants' mean age was $\bar{x}$=39.88±16.61 years; mean epilepsy duration was $\bar{x}$=16.35±14.08; and mean overprotection score was $\bar{x}$=29.09±12.63 (Table 1).

Item 1 exhibited the highest negative response, whereas items 2 and 7 exhibited the highest positive responses (Table 2).

Overprotection perception scores in PWE differed significantly by educational status (F=4.194, p=0.018, η^2=0.077). The observed differences indicate that the overprotection perception scores for primary school graduates ($\bar{x}$=29.125±12.758) and for high school graduates ($\bar{x}$=32.688±12.460) are higher than those for university graduates ($\bar{x}$=21.813±9.745) (p<0.05). The overprotection perception scores of married PWE ($\bar{x}$=26.196) were lower than those of singles ($\bar{x}$=32.479) (t=-2.597, p=0.011, d=0.511, η^2=0.062). Furthermore, overprotection perception scores varied significantly by epilepsy type (F=3.557, p=0.017, η^2=0.096). Specifically, individuals with generalized epilepsy ($\bar{x}$=33.750±12.573) had higher perceived overprotection scores than those who lacked sufficient information about their epilepsy diagnosis ($\bar{x}$=23.862±11.376) (p<0.05). Additionally, overprotection perception scores of those without seizures ($\bar{x}$=25.063) were lower than those of participants with a seizure frequency of at least once per month ($\bar{x}$=30.889) (t=-2.210; p=0.029; d=0.470; η^2=0.046). Similarly, overprotection perception scores of individuals on monotherapy ($\bar{x}$=25.113) were lower than those of individuals on polytherapy ($\bar{x}$=34.976) (t=-4.210; p<0.001; d=0.841; η^2=0.148). No significant differences in overprotection perception scores were found by gender, occupational activity, or having an accident or harming someone during a seizure (p>0.05). Correlation analyses of overprotection perception scores with age and with epilepsy duration did not reveal statistically significant relationships (p>0.05). Consequently, the variables identified as being strongly represented in these pairwise comparisons (univariate analyses) were included in the regression analysis.[21,22]

Table 1. Demographic and clinical characteristics of the participants

	n=104	%
Gender		
Female	35	33.7
Male	69	66.3
Educational status		
Primary education	56	53.8
High school	32	30.8
University	16	15.4
Marital status		
Married	56	53.8
Single	48	46.2
Occupational activity		
Not working	84	80.8
Working	20	19.2
Epilepsy type		
Generalized epilepsy	36	34.6
Focal epilepsy	21	20.2
Epilepsy of unknown onset	18	17.3
Unclassified epilepsy	29	27.9
Seizure control		
My seizures are under control (I have not had a seizure in the past year)	32	30.8
My seizures are not under control; I have had at least one seizure in the last year	72	69.2
Number of medications used		
Single medication therapy	62	59.6
Multiple drug therapy	42	40.4
Having accident during your seizure		
Yes (once or twice)	36	34.6
No	68	65.4
Hurting someone during seizure		
Yes (just once)	11	10.6
No	93	89.4
	±SD	**Min-max**
Age	39.88±16.61	18-83
Duration of epilepsy (year)	16.35±14.08	1-31
Overprotection scale	29.09±12.63	10-50

$\bar{x}$: Mean, SD: Standard deviation, min: Minimum, max: Maximum

A regression analysis was conducted to determine the cause-and-effect relationships between primary school graduation, high school graduation, marital status, types of epilepsy (generalized, focal, and unknown-onset), uncontrolled seizures, number of medications used, and overprotection perception scores. Significant relationships were identified (F=5.111, p<0.001). The total variance in overprotection perception levels, amounting to 24.2% (R^2=0.242), was explained by being a primary school graduate, being a high school graduate, marital status, having generalized, focal, and unknown-onset epilepsy, uncontrolled seizures, and the number of medications used, demonstrating that these factors influence the perception of overprotection. Overall, the change in perceived overprotection levels was explained by a combination of these factors. Attaining a primary school education (β=0.335) and a high school education (β=0.285) were associated with increased perceived overprotection. Conversely, being married (β=-0.270) was linked to lower levels of perceived overprotection, whereas having generalized epilepsy (β=0.225) and being on multiple medications (β=0.286) were linked to higher levels. However, focal epilepsy (p=0.170), epilepsy of unknown onset (p=0.638), and uncontrolled seizures (p=0.569) did not significantly influence levels of perceived overprotection (Table 3).

DISCUSSION

This study aimed to determine whether participants' responses to the perceived overprotection scale varied according to demographic variables and to explain any observed variance. Most participants answered "totally agree" or "agree" to items related to going out alone. This may reflect the family's concerns about the possibility of PWE having a seizure outdoors, the lack of family support during seizures, and the possibility of PWE having an accident. Family members may also be worried about the possibility of inappropriate interventions during seizures. For instance, in South Vietnam, PWE avoid all bodies of water, including lakes, rivers, and ponds, all of which are extremely common in the region, because of fear of seizure-related harm.[6,23] Shore et al.[24] reported that PWE were overprotected by their families, particularly by not being left alone in social settings. Thus, the present results are consistent with the literature. In addition, participants provided predominantly positive responses to items concerning greater familial tolerance and reduced responsibility for PWE. While family members are overprotective, they are unlikely to be malicious. However, this behavior can undermine autonomy and independence in PWE, impair their social bonding skills, and have

Table 2. Responses in percentages to different items of the overprotection scale

	Item content	Completely agree	Agree	Not sure	Disagree	Completely disagree
1	I believe my family is overprotective of me because of my epilepsy	12.5	20.2	5.8	27.9	33.7
2	My family does not let me go out, for example, to the cinema or for a walk, unaccompanied by a friend or family member	42.3	25.0	9.6	10.6	12.5
3	I believe my family is more tolerant toward me because of my epilepsy	13.5	24.0	11.5	26.0	25.0
4	I think my family gives me less responsibility than I am able to manage because of my epilepsy	25.0	22,1	11.5	15.4	26.0
5	I think that if I did not have epilepsy, my family would have higher expectations of me	25.0	24.0	14.4	19.2	17.3
6	I think my family's high level of concern for me stems from my epilepsy	27.9	24.0	10.6	17.3	20.2
7	My family never allowed me go out alone	38.5	25.0	5.8	14.4	16.3
8	I think my family gives me fewer domestic responsibilities because of my epilepsy	24.0	26.0	6.7	20.2	23.1
9	I think my family shows me excessive attention	19.2	20.2	9.6	26.9	24.0
10	I think my family shows greater concern for my welfare because of my epilepsy	21.2	21.2	13.5	23.1	21.2

Table 3. Factors affecting overprotection

Independent variable	Non-standardised coefficients		Standardised coefficients	t	p	95% confidence interval	
	B	SE	ß			Lower	Upper
Fixed	18.551	3.436		5.398	0.000	11.728	25.373
Level of education (being an elementary school graduate)	8.459	3.818	0.335	2.216	**0.029**	0.879	16.039
Level of education (being a high school graduate)	7.754	3.653	0.285	2.123	**0.036**	0.502	15.005
Marital status (married)	-6.815	2.403	-0.270	-2.836	**0.006**	-11.585	-2.044
Type of epilepsy (generalised)	5.954	2.887	0.225	2.062	**0.042**	0.223	11.685
Type of epilepsy (focal)	4.464	3.230	0.142	1.382	0.170	-1.948	10.877
Type of epilepsy (epilepsy of unknown onset)	1.614	3.421	0.049	0.472	0.638	-5.178	8.407
Seizure control (my seizures are not under control)	1.541	2.695	0.057	0.572	0.569	-3.809	6.891
Number of drugs used (multi-drug therapy)	7.343	2.386	0.286	3.078	**0.003**	2.607	12.079

Dependent variable: overprotection, R=0.549, R2=0.242, F=5.111, p=0.000, Durbin-Watson value =1.727, p<0.005

negative economic consequences in their work life.[8,17] Yetkin et al.[25] reported that overprotective attitudes in patients with epilepsy significantly reduced quality of life and, together with depression, constituted independent predictors of poorer outcomes. In another study conducted by Yetkin et al.,[26] perceived overprotection and stigma were found to significantly contribute to suicidal ideation in patients with epilepsy. This highlights that overprotective behaviors, which are often driven by concerns for safety, may exacerbate psychosocial distress and increase vulnerability to severe mental health problems. Therefore, overprotectiveness, even if well-intentioned, may be harmful to PWE in the long term.[27]

Moreover, several descriptive characteristics were associated with perceived familial overprotection, either positively or negatively. In this study, PWEs with elementary or high school education perceived greater familial overprotection. Indeed, as individuals' levels of education increase, their health literacy, positive lifestyle behaviors related to the disease, and adherence to treatment also increase.[28,29] Therefore, as individuals with higher levels of education develop disease management skills, the need for family members to intervene may decrease; this may lead to a lower perception of overprotection. Therefore, perceived familial overprotection may be lower among people with higher education levels. Previous studies have reported that unemployment rates are higher among PWE with low educational attainment.[3,30] Wo et al.[1] argued that education level affects the ability of PWE to work. Therefore, the economic burden of accessing health professionals in case of problems may lead to excessive protection of PWE with lower educational levels.

In this study, married participants reported lower levels of overprotection, which may reflect reduced parental control and intervention associated with cohabitation with their spouses. Marriage expands the social support networks of PWE, enabling them to receive emotional and practical support beyond the family.[31] Increased social support can enhance autonomy and independence, thereby reducing the need for overprotective behaviors by family members.[32] Additionally, marriage has been associated with improved health management. Married PWE are more likely to achieve better seizure control and demonstrate higher treatment adherence, which may contribute to a decrease in overprotective attitudes among family members.[33] However, comprehensive longitudinal and descriptive studies are needed to clarify the causal relationships between marital status and perceived overprotection.

Furthermore, individuals with generalized epilepsy perceived greater familial overprotection. According to Wo et al.[1] generalized epilepsy predicted employability among PWE. Another study found that forgetfulness and fatigue-like complaints were common in PWE, attributable to involvement of the seizure focus and to the side effects of antiepileptic drugs.[34] Individuals with generalized

epilepsy may experience increased familial overprotection as a result of these issues. Furthermore, the adverse effects on social integration and quality of life may reinforce familial overprotection tendencies.[35] These findings are in line with Yetkin et al.,[25] who reported that heightened overprotection not only limits autonomy but also interacts with stigma to increase the risk of psychological burden, including suicidal ideation, thereby amplifying the negative consequences of severe clinical forms of epilepsy. Consequently, neurological and treatment-related challenges faced by individuals with generalized epilepsy may elicit excessive familial protection, thereby restricting patients' social and economic participation.

As expected, the overprotection perceived by participants receiving multi-drug therapy was higher than that perceived by participants receiving single-drug therapy. Antiseizure medications have adverse effects, including effects on cognitive function (e.g., thinking and memory), fatigue, and dizziness. These drugs also have adverse effects on social lives, including social isolation, dependent behaviour, lower marriage rates, unemployment, and decreased quality of life.[36] Beghi et al.[37] emphasized that quality of life is lower in individuals receiving polytherapy and that these individuals require greater family support. Loring et al.[38] showed in a systematic review that the use of multiple antiseizure drugs had significant negative effects on basic cognitive functions such as attention span, memory retention, and processing. Park and Kwon[39] stated that antiseizure drugs affected cognitive functions, although the effects varied depending on the dose taken, and that these effects were especially evident in individuals receiving polytherapy. Another review by Gilliam et al.[40] indicated that polytherapy reduced an individual's physical functioning and could limit their ability to perform activities of daily living independently. Such cognitive and psychological problems limiting the daily living skills of PWE may cause family members to perceive the individual as fragile or in need of protection. As family members witness these difficulties, they may lose confidence in the individual's ability to assume responsibility independently and instead make decisions and intervene. Thus, well-intentioned but overprotective behaviors may develop. This may lead to a weakened independence, reduced self-confidence, and social withdrawal in PWE. As a result, individuals who take multiple medications may experience greater overprotection due to both physiological and environmental factors.

Study Limitations

This study had several limitations. First, this study was conducted at a single center and included a limited number of patients. This may prevent the generalization of research results to other regions. Second, although the participants did not have diagnosed cognitive or psychiatric disorders, they were likely to have memory deficits, which may have affected the accuracy of their answers.

CONCLUSION

In this study, the participants reported that they were largely overprotected with respect to going out alone and assuming responsibility. Groups reporting higher levels of overprotection included elementary and high school graduates, individuals with generalised epilepsy, those with uncontrolled seizures, and those on multiple medications. Married participants reported lower levels of overprotection. There is growing evidence that excessive familial overprotection may adversely affect the psychosocial well-being of PWE, including reduced autonomy, impaired social functioning, and an increased risk of emotional distress. Therefore, it is crucial that future studies comprehensively examine the psychosocial burden resulting from overprotection. Such research will contribute to a better understanding of the long-term effects of overprotection on quality of life and mental health outcomes and provide a foundation for developing interventions that balance necessary support with the promotion of independence among PWE.

Ethics

Ethics Committee Approval: This study was approved by the Ordu University Clinical Research Ethics Committee (approval no: 202, date: 02.09.2022).

Informed Consent: Written informed consent was obtained from participants in face-to-face interviews; the consent form provided necessary explanations about the purpose of the research and the data collection.

Footnotes

Authorship Contributions

Surgical and Medical Practices: F.G.O., G.A., D.Ş., Concept: F.G.O., G.A., D.Ş., Design: F.G.O., D.Ş., Data Collection or Processing: F.G.O., D.Ş., Analysis or Interpretation: F.G.O., Literature Search: F.G.O., G.A., Writing: F.G.O., G.A.

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REFERENCES

1. Wo MC, Lim KS, Choo WY, Tan CT. Factors affecting the employability in people with epilepsy. *Epilepsy Res*. 2016;128:6-11. [Crossref]
2. World Health Organization. Epilepsy: a public health imperative. Internet. Geneva: World Health Organization; 2019. Cited: April 28, 2024. [Crossref]
3. Yaşar H, Alay S, Kendirli T, et al. Genç erkek epilepsi hastalarında yaşam ve uyku kalitesi. *Epilepsi Derg*. 2014;20(1):17-22. [Crossref]
4. Aktürk T, Tanık N, Saçmacı H, Chia ZJ, Lim KS. Validity and reliability of the Turkish version of public attitudes toward epilepsy scale. *Epilepsy Behav*. 2020;111:107245. [Crossref]
5. Aksun ZÖ, Yiğit A. Investigation of behaviors of the epilepsy patients' relatives during seizure and its association with their knowledge regarding epilepsy. *Arch Epilepsy.* 2021;27(2):96-101. [Crossref]
6. Yıldırım Z, Ertem DH, Ceyhan Dirican A, Baybaş S. Stigma accounts for depression in patients with epilepsy. *Epilepsy Behav*. 2018;78:1-6. [Crossref]
7. Rodenburg R, Meijer AM, Deković M, Aldenkamp AP. Family factors and psychopathology in children with epilepsy: a literature review. *Epilepsy Behav.* 2005;6(4):488-503. [Crossref]
8. Rodenburg R, Meijer AM, Scherphof C, et al. Parenting and restrictions in childhood epilepsy. *Epilepsy Behav*. 2013;27(3):497-503. [Crossref]
9. Thomasgard M, Metz WP. Parental overprotection revisited. *Child Psychiatry Hum Dev*. 1993;24(2):67-80. [Crossref]
10. Ellis N, Upton D, Thompson P. Epilepsy and the family: a review of current literature. *Seizure*. 2000;9(1):22-30. [Crossref]

11. Cao F, Su L. Internet addiction among Chinese adolescents: prevalence and psychological features. *Child Care Health Dev*. 2007;33(3):275-281. [Crossref]
12. Carpay HA, Vermeulen J, Stroink H, et al. Disability due to restrictions in childhood epilepsy. *Dev Med Child Neurol.* 1997;39(8):521-526. [Crossref]
13. Guo W, Wu J, Wang W, et al. The stigma of people with epilepsy is demonstrated at the internalized, interpersonal and institutional levels in a specific sociocultural context: findings from an ethnographic study in rural China. *Epilepsy Behav.* 2012;25(2):282-288. [Crossref]
14. Mugumbate J, Nyanguru A. Measuring the challenges of people with epilepsy in Harare, Zimbabwe. *Neurol Asia*. 2013;18(1):29-33. [Crossref]
15. Aydemir N, Ozkara C, Canbeyli R, Tekcan A. Changes in quality of life and self-perspective related to surgery in patients with temporal lobe epilepsy. *Epilepsy Behav.* 2004;5(5):735-742. [Crossref]
16. Aydemir N. Familiarity with, knowledge of, and attitudes toward epilepsy in Turkey. *Epilepsy Behav*. 2011;20(2):286-290. [Crossref]
17. Aydemir N. Overprotection and determinants of overprotection in adults with epilepsy. *Seizure.* 2020;79:14-19. [Crossref]
18. Kleinman A, Eisenberg L, Good B. Culture, illness, and care: clinical lessons from anthropologic and cross-cultural research. *Ann Intern Med*. 1978;88(2):251-258. [Crossref]
19. Leventhal H, Diefenbach M, Leventhal EA. Illness cognition: using common sense to understand treatment adherence and affect cognition interactions. Cognit Ther Res. 1992;16(2):143-163. [Crossref]
20. Kaya B, Yildiz G. Developing scales to measure felt-stigma, concerns, overprotection and disclosure for Turkish individuals with epilepsy. In: 18th National Psychology Students Congress. İzmir, Turkey: İzmir University of Economics; 2013. [Crossref]
21. George D, Mallery P. IBM SPSS statistics 29 step by step: a simple guide and reference. Routledge; 2024. [Crossref]
22. Tabachnick BG, Fidell LS, Ullman JB. Using multivariate statistics. Boston, MA: pearson; 2007. [Crossref]
23. Aydemir N, Trung DV, Snape D, Baker GA, Jacoby A; CREST Study Team. Multiple impacts of epilepsy and contributing factors: findings from an ethnographic study in Vietnam. *Epilepsy Behav*. 2009;16(3):512-520. [Crossref]
24. Shore CP, Buelow JM, Austin JK, Johnson CS. Continuing psychosocial care needs in children with new-onset epilepsy and their parents. *J Neurosci Nurs*. 2009;41(5):244-250. [Crossref]
25. Yetkin H, Görmez A, Yeni Elbay R, Kurtulmuş A, Tombul T, Orhan Varoğlu A. Separation anxiety disorder, perceived overprotection and quality of life in epilepsy patients. *Epilepsy Behav*. 2024;159:109972. [Crossref]
26. Yetkin H, Cetin OE, Sancar EN, Tascan IS. Stigma, overprotection, and suicidal ideation in epilepsy: a cross-sectional study on psychosocial predictors. *Epilepsy Behav*. 2025:100815. [Crossref]
27. Reis R. Epilepsy and self-identity among the Dutch. *Med Anthropol*. 2001;19(4):355-382. [Crossref]
28. Kutlu G. Kadın ve epilepsi. Muğla Sıtkı Koçman Üniversitesi Tıp Dergisi. 2018;5(2):27-9. [Crossref]
29. Yel P, Karadakovan A. Epilepsi hastalarında tedaviye uyum ve etkileyen faktörler. Ege Üniversitesi Hemşirelik Fakültesi Dergisi. 2021;37(3):223-238. [Crossref]
30. Mollaoğlu M, Durna Z, Bolayir E. Validity and reliability of the quality of life in epilepsy inventory (QOLIE-31) for Turkey. *Noro Psikiyatr Ars*. 2015;52(3):289-295. [Crossref]
31. Baker GA, Jacoby A, Buck D, Stalgis C, Monnet D. Quality of life of people with epilepsy: a European study. *Epilepsia.* 1997;38(3):353-362. [Crossref]
32. Jacoby A, Snape D, Baker GA. Epilepsy and social identity: the stigma of a chronic neurological disorder. *Lancet Neurol*. 2005;4(3):171-178. [Crossref]
33. Reilly C, Atkinson P, Das KB, et al. Factors associated with quality of life in active childhood epilepsy: a population-based study. *Eur J Paediatr Neurol.* 2015;19(3):308-313. [Crossref]
34. Shiota MN, Simpson ML, Kirsch HE, Levenson RW. Emotion recognition in objects in patients with neurological disease. *Neuropsychology*. 2019;33(8):1163-1173. [Crossref]
35. Jacoby A, Baker GA, Crossley J, Schachter S. Tools for assessing quality of life in epilepsy patients. *Expert Rev Neurother.* 2013;13(12):1355-1369. [Crossref]
36. Mutanana N, Tsvere M, Chiweshe MK. General side effects and challenges associated with anti-epilepsy medication: a review of related literature. *Afr J Prim Health Care Fam Med.* 2020;12(1):e1-e5. [Crossref]
37. Beghi E, Gatti G, Tonini C, et al.; BASE Study Group. Adjunctive therapy versus alternative monotherapy in patients with partial epilepsy failing on a single drug: a multicentre, randomised, pragmatic controlled trial. *Epilepsy Res.* 2003;57(1):1-13. [Crossref]
38. Loring DW, Marino S, Meador KJ. Neuropsychological and behavioral effects of antiepilepsy drugs. *Neuropsychol Rev*. 2007;17(4):413-425. [Crossref]
39. Park SP, Kwon SH. Cognitive effects of antiepileptic drugs. *J Clin Neurol*. 2008;4(3):99-106. [Crossref]
40. Gilliam F, Hecimovic H, Sheline Y. Psychiatric comorbidity, health, and function in epilepsy. *Epilepsy Behav*. 2003;4(Suppl 4):S26-S30. [Crossref]