North Clin Istanb 2025;12(6):707–711
doi: 10.14744/nci.2025.43789

ORIGINAL ARTICLE PEDIATRICS

Effects of levetiracetam monotherapy on thyroid function in pediatric epilepsy patients

Gulcan Seymen,[1] **Busra Isin Kutlubay**[2]

[1]Department of Pediatric Endocrinology, Umraniye Training and Research Hospital, Istanbul, Türkiye
[2]Department of Pediatric Neurology, Umraniye Training and Research Hospital, Istanbul, Türkiye

ABSTRACT

OBJECTIVE: Childhood epilepsy requires long-term antiepileptic drug (AED) therapy, and its potential endocrine effects are a critical consideration. While the impact of AEDs on thyroid function is well documented in adults, data on pediatric populations remain scarce. Levetiracetam (LEV), a broad-spectrum AED widely prescribed for children, has an unclear influence on thyroid function. This study aims to evaluate the effects of LEV on thyroid function in children with epilepsy.

METHODS: A retrospective observational study was conducted at the Pediatric Neurology Clinic of Umraniye Hospital between 2020 and 2022. One hundred pediatric patients, aged 2.3 to 18 years, diagnosed with epilepsy and using LEV monotherapy for at least 12 months were included. Thyroid-stimulating hormone (TSH) and free thyroxine (fT4) levels were measured at baseline and at 3, 6, and 12 months. Statistical analyses were performed using paired t-tests, with a p-value <0.05 considered statistically significant.

RESULTS: The mean TSH levels increased from 1.46±0.3 mIU/L at baseline to 1.60±0.3 mIU/L at 12 months (p=0.0017). Despite the statistically significant rise, TSH levels remained within normal reference ranges, and no clinically significant hypothyroidism was observed. Changes in fT4 levels were not statistically significant, except for a borderline increase at 12 months (p=0.05). Four patients exhibited transient TSH elevations but did not require thyroid hormone replacement therapy.

CONCLUSION: LEV monotherapy does not appear to significantly impact thyroid function in pediatric epilepsy patients. While a slight but statistically significant increase in TSH levels was observed, these changes were clinically insignificant. These findings suggest that LEV is a safe option regarding thyroid function in children with epilepsy. Further long-term prospective studies are warranted to confirm these results.

Keywords: Antiepileptic drugs; levetiracetam; pediatric epilepsy; thyroid function.

Cite this article as: *Seymen G, Kutlubay BI. Effects of levetiracetam monotherapy on thyroid function in pediatric epilepsy patients. North Clin Istanb 2025;12(6):707–711.*

Epilepsy is one of the most common chronic neurological disorders in children, characterized by recurrent unprovoked seizures. It affects approximately 0.5–1% of the pediatric population worldwide, significantly impacting the quality of life and development of affected individuals [1]. Antiepileptic drugs (AEDs) are the cornerstone of epilepsy management, aiming to achieve seizure control and prevent neurological complications. While older generation AEDs like valproate and carbamazepine are effective, they are often associated with adverse effects, including potential impacts on endocrine function, particularly thyroid hormones [2, 3].

Thyroid hormones play a critical role in growth, brain development, and metabolic regulation in children. Disruptions in thyroid function can lead to growth retardation, cognitive impairments, and other developmental issues [4]. Previous studies have reported that AEDs such

Received: February 14, 2025 *Accepted:* October 10, 2025 *Online:* December 29, 2025

Correspondence: Gulcan SEYMEN, MD. Umraniye Egitim ve Arastirma Hastanesi, Cocuk Endokrinolojisi Klinigi, Istanbul, Turkiye.
Tel: +90 505 377 25 25 e-mail: gulcansk@gmail.com

Istanbul Provincial Directorate of Health - Available online at www.northclinist.com

as valproate and carbamazepine can reduce free thyroxine (fT4) levels and induce subclinical hypothyroidism in pediatric patients [5, 6]. These effects are thought to be due to hepatic enzyme induction or interference with thyroid hormone synthesis and metabolism.

Levetiracetam (LEV) is a newer, broad-spectrum AED widely used in the treatment of pediatric epilepsy due to its favorable pharmacokinetic properties, efficacy, and tolerability [7]. Unlike many other AEDs, LEV does not undergo significant hepatic metabolism and has minimal drug–drug interactions, making it a convenient option for long-term therapy [8]. However, the impact of LEV on thyroid function in children remains unclear, with limited and inconclusive data available.

Understanding the potential endocrine effects of LEV is essential for optimizing treatment strategies and ensuring the safety of pediatric patients on long-term AED therapy. This study aims to investigate the effects of LEV monotherapy on thyroid function in children with epilepsy over a 12-month period.

Highlight key points

- The effects of levetiracetam (LEV) monotherapy on thyroid function were evaluated in children with epilepsy.
- A statistically significant increase in TSH levels was observed during follow-up; however, values remained within normal reference ranges.
- Free thyroxine (fT4) levels showed no clinically meaningful changes over the 12-month treatment period.
- No patients developed clinical hypothyroidism or required thyroid hormone replacement therapy.
- LEV appears to be a safe antiepileptic option with minimal impact on thyroid function in pediatric patients.

Table 1. Epilepsy classification

Epilepsy type	Number of patients (n)
Childhood rolandic epilepsy	46
Childhood occipital lobe epilepsy	28
Frontal lobe epilepsy	8
Juvenile myoclonic epilepsy	18

MATERIALS AND METHODS

Study Design and Setting

A retrospective observational study was conducted at the Pediatric Neurology Clinic of Umraniye Training and Research Hospital between January 2020 and December 2022. Ethical Approval: This study was approved by the Clinical Research Ethics Committee of Umraniye Training and Research Hospital on September 7, 2023 (ethics committee no:22432288), and all procedures adhered to the principles of the Declaration of Helsinki.

Patient Selection

Inclusion Criteria

- Pediatric patients under 18 years of age diagnosed with epilepsy according to the International League Against Epilepsy (ILAE) classification [9].
- Patients who had been on LEV monotherapy for at least 12 months.
- Availability of thyroid function tests (TSH and fT4) at baseline, 3 months, 6 months, and 12 months.

Exclusion Criteria

- Patients with pre-existing thyroid disease or endocrine disorders.
- Use of medications known to affect thyroid function other than LEV.
- Incomplete medical records or missing thyroid function tests.

Treatment Protocol

LEV therapy was initiated at a dose of 10 mg/kg/day and titrated up to 30–40 mg/kg/day over one month, based on clinical response and tolerability. All patients received LEV as monotherapy throughout the study period.

Data Collection

Demographic data, epilepsy classification, seizure frequency, and LEV dosage were recorded from medical records. Thyroid function tests, including thyroid-stimulating hormone (TSH) and free thyroxine (fT4) levels, were obtained at baseline (prior to initiation of LEV) and at 3, 6, and 12 months of therapy. Blood samples were collected in the morning after an overnight fast and analyzed using chemiluminescent immunoassay methods.

Statistical Analysis

Statistical analyses were performed using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA). Data

TABLE 2. Thyroid function tests over time and p-values

Time point	TSH (mIU/L) (mean±SD)	fT4 (ng/dL) (mean±SD)	p-value for TSH	p-value for fT4
Baseline	1.46±0.3	1.05±0.2	–	–
3 months	1.50±0.4	1.07±0.2	0.26	0.48
6 months	1.55±0.4	1.09±0.3	0.013	0.26
12 months	1.60±0.3	1.12±0.3	0.0017	0.05

SD: Standard deviation; TSH: Thyroid stimulating hormone; fT4: Free thyroxine; p-values were calculated using paired t-tests comparing each time point to the baseline values. Statistical significance: $p<0.05$ was considered statistically significant.

are expressed as mean±standard deviation (SD). Paired t-tests were used to compare thyroid function at each time point with baseline values. A p-value less than 0.05 was considered statistically significant.

RESULTS

Patient Characteristics

A total of 100 patients met the inclusion criteria, comprising 56 females and 44 males, with a mean age of 10.6±3.4 years (range: 2.3–18 years). The types of epilepsy diagnosed in the patients are presented in Table 1. The mean TSH and fT4 levels at each time point are detailed in Table 2.

At 6 months, TSH levels showed a statistically significant increase from baseline ($p=0.013$), and this increase remained significant at 12 months ($p=0.0017$). Despite these statistical differences, TSH levels remained within normal reference ranges (0.5–4.5 mIU/L). Changes in fT4 levels were not statistically significant at 3 and 6 months. At 12 months, there was a borderline significant increase in fT4 levels compared to baseline ($p=0.05$), but values remained within normal limits (0.8–1.8 ng/dL).

Clinical Outcomes

Four patients exhibited transient elevations in TSH levels above the upper normal limit at either 6 or 12 months. These patients were asymptomatic and were referred to pediatric endocrinology for further assessment. None required thyroid hormone replacement therapy, and TSH levels normalized upon subsequent follow-up.

No patients displayed clinical symptoms indicative of hypothyroidism, such as fatigue, weight gain, or growth retardation, throughout the study period.

DISCUSSION

The present study evaluated the impact of levetiracetam (LEV) monotherapy on thyroid function in pediatric patients with epilepsy over a one-year period. Our findings indicate that while there are slight but statistically significant increases in thyroid-stimulating hormone (TSH) levels during LEV therapy, these changes are clinically insignificant and do not result in thyroid dysfunction. Our findings align with limited existing research on LEV's impact on thyroid function. Cebeci et al. [9] conducted a study comparing LEV and valproate monotherapy in children and found no significant changes in thyroid function tests in the LEV group over six months. Similarly, Adhimoolam et al. [8] reported that chronic LEV treatment did not significantly alter thyroid hormone levels in adult patients. These studies, along with our findings, support the notion that LEV has a minimal effect on thyroid function. In contrast, several studies have documented that older generation AEDs, such as carbamazepine and valproate, can significantly affect thyroid function. Verrotti et al. [2] and Elshorbagy et al. [3] demonstrated reductions in fT4 levels and increases in TSH levels in pediatric patients on these medications, leading to subclinical hypothyroidism. The mechanisms proposed include hepatic enzyme induction enhancing the metabolism of thyroid hormones and interference with hormone synthesis. LEV's favorable thyroid profile may be attributed to its unique pharmacokinetic and pharmacodynamic properties. LEV is not significantly metabolized by hepatic enzymes and does not induce or inhibit cytochrome P450 enzymes [1, 7]. This reduces the likelihood of interactions that could accelerate the metabolism of thyroid hormones or alter their synthesis. Additionally, LEV's primary mechanism of action involves binding to the synaptic vesicle protein 2A (SV2A), which is not directly associated with endocrine function [10]. This contrasts with other AEDs that may impact hormonal pathways.

Maintaining normal thyroid function is crucial in the pediatric population due to the essential role of thyroid hormones in growth, neurodevelopment, and metabolism [4]. Hypothyroidism in children can lead to serious complications, including cognitive delays, growth retardation, and developmental abnormalities. Therefore, the selection of AEDs that do not adversely affect thyroid function is of paramount importance.

Our study suggests that LEV is a safe and effective option for treating epilepsy in children without significant risk to thyroid health. This has practical implications for clinicians when choosing an AED, particularly for long-term management. The minimal impact on thyroid function reduces the need for frequent endocrine monitoring and potential interventions, thereby decreasing the burden on patients and healthcare systems.

Strengths of the Study

- Comprehensive Follow-Up: The study evaluated thyroid function at multiple time points over a one-year period, providing insight into both short-term and longer-term effects of LEV therapy.
- Monotherapy Focus: Including only patients on LEV monotherapy eliminates confounding effects from other AEDs, allowing for a clearer assessment of LEV's impact.
- Clinical Correlation: Monitoring for clinical signs of hypothyroidism reinforces the clinical relevance of the findings.

Limitations

This study has limitations, including its retrospective design and relatively small sample size, which may not detect rare adverse effects. The follow-up period of one year may not capture long-term changes in thyroid function. Additionally, other thyroid parameters, such as triiodothyronine (T3) levels and thyroid antibody status, were not evaluated, which could provide a more comprehensive understanding of thyroid function dynamics.

Conclusion

Levetiracetam appears to be a safe antiepileptic drug option concerning thyroid function in children with epilepsy. The slight increases in TSH levels observed were statistically significant but clinically insignificant, with no cases of hypothyroidism detected. These results support the continued use of LEV in the pediatric population without heightened concern for thyroid dysfunction. Further prospective studies with larger cohorts and extended follow-up periods are recommended to confirm these findings and evaluate long-term thyroid health, including a broader range of thyroid parameters. Investigating the underlying mechanisms of LEV's minimal impact on thyroid function may also contribute to the development of AEDs with favorable endocrine profiles.

Ethics Committee Approval: The Umraniye Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 07.09.2023, number: B.10.1.TKH.4.34.H.G.P.0.01/310).

Informed Consent: Informed consent was obtained from all patients and/or their legal guardians where applicable.

Conflict of Interest: The authors declare that they have no conflicts of interest related to this study.

Financial Disclosure: The authors declared that this study has received no financial support.

Use of AI for Writing Assistance: The authors confirm that artificial intelligence (AI)-assisted technologies (such as Large Language Models, chatbots, or image creators) were not used in the production of this manuscript.

Authorship Contributions: Concept – GS, BIK; Design – GS, BIK; Supervision – GS; Data collection and/or processing – GS, BIK; Analysis and/or interpretation – GS, Literature review – GS, BIK; Writing – GS, BIK; Critical review – GS.

Acknowledgments: The authors would like to acknowledge the Pediatric Neurology and Pediatric Endocrinology departments for their support in data collection and patient follow-up.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Patsalos PN. Pharmacokinetic profile of levetiracetam: toward ideal characteristics. Pharmacol Ther 2000;85:77-85. [Crossref]
2. Verrotti A, Scardapane A, Manco R, Chiarelli F. Antiepileptic drugs and thyroid function. J Pediatr Endocrinol Metab 2008;21:401-8. [Crossref]
3. Elshorbagy HH, Barseem NF, Suliman HA, Talaat E, AlSHOKARY AH, Abdelghani WE, et al. The Impact of Antiepileptic Drugs on Thyroid Function in Children with Epilepsy: New Versus Old. Iran J Child Neurol 2020;14:31-41.
4. Zimmermann MB. The importance of adequate iodine during pregnancy and infancy. World Rev Nutr Diet 2016;115:118-24. [Crossref]
5. Kim SH, Chung HR, Kim SH, Kim H, Lim BC, Chae JH, et al. Subclinical hypothyroidism during valproic acid therapy in children and adolescents with epilepsy. Neuropediatrics 2012;43:135-9. [Crossref]
6. Aggarwal A, Rastogi N, Mittal H, Chillar N, Patil R. Thyroid hormone levels in children receiving carbamazepine or valproate. Pediatr Neurol. 2011;45:159-62. [Crossref]
7. Svalheim S, Sveberg L, Mochol M, Taubøll E. Interactions between antiepileptic drugs and hormones. Seizure 2015;28:12-7. [Crossref]
8. Adhimoolam M, Arulmozhi R. Effect of antiepileptic drug therapy on thyroid hormones among adult epileptic patients: An analytical

cross-sectional study. J Res Pharm Pract 2016;5:171-4. [Crossref]

9. Cebeci D, Gurkas E, Aribas Oz N, Gungor AA, Kuruc AI, Buyukyilmaz G. The Effect of Antiseizure Medications on Thyroid Functions in Children With Epilepsy. Clin Pediatr (Phila) 2025;64:326-31. [Crossref]
10. Lynch BA, Lambeng N, Nocka K, Kensel-Hammes P, Bajjalieh SM, Matagne A, et al. The synaptic vesicle protein SV2A is the binding site for the antiepileptic drug levetiracetam. Proc Natl Acad Sci U S A 2004;101:9861-6. [Crossref]