

Expert Perspectives on Levetiracetam use in Epilepsy Management Across India

Research Article

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Abstract

Background: Although there are several studies available regarding the efficacy and safety of levetiracetam for epilepsy management, there is a dearth of studies among clinicians in actual practice. This study aims to gather expert perspectives on the clinical use of levetiracetam for managing epilepsy in Indian settings.

Methodology: This cross-sectional study was conducted with a 23-item questionnaire among clinicians specializing in epilepsy management. It explored clinical practice patterns, treatment preferences, and levetiracetam-specific usage. The survey also assessed adverse effects, measures on patient adherence, and use of levetiracetam in special populations. Data analysis employed descriptive statistics, with results reported as frequencies and percentages.

Results: The survey included 293 participants, with the majority (90%) preferring levetiracetam as the first-line treatment for newly diagnosed adult epilepsy. For pediatric partial seizures, 68% preferred it as their first choice. In clinical practice, 49% reported that 41–60% of their epilepsy patients are currently on levetiracetam. While 52% had no experience using it in rare epilepsy syndromes, 49% reported the same regarding its use during pregnancy. Additionally, 48% of experts observed that 6–10% of their patients with resistant epilepsy were already on optimal doses. According to 41% of clinicians, levetiracetam was most often preferred for generalized motor seizures. Behavioral changes were reported by 53% of respondents in fewer than 10% of patients, and 67% considered 1000 mg/day the optimal dose, balancing efficacy and side effects.

Conclusion: The survey underscores the strong preference of levetiracetam among clinicians as an antiepileptic drug for both adult and pediatric epilepsy. Its broad clinical applicability and favorable safety profile contribute significantly to its widespread adoption.

Keywords: Epilepsy; Seizures; Antiepileptic Drugs; Levetiracetam

Introduction

Epilepsy is a chronic neurological disorder marked by recurrent seizures, affecting approximately 50 million people globally and ranking among the most prevalent neurological conditions. Nearly 80% of individuals with epilepsy live in low- and middle-income countries, where the condition poses a significant burden on both individuals and healthcare systems.[1,2] With an incidence of 50 per 100,000 person-years and a prevalence of 700 per 100,000, epilepsy contributes to over 0.5% of the global disease burden, accounting

for 2.4 million new cases and 20.6 million DALYs lost annually. [2,3] In India, prevalence estimates range from 3.0 to 11.9 per 1,000 population, with an incidence of 0.2 to 0.6 per 1,000 per year, making it the third most common disabling neurological disorder after stroke and headache.[4,5] The presence of a substantial treatment gap, especially among children, highlights epilepsy as a major public health concern in the country.[1]

Individuals with epilepsy face up to a threefold increased risk of premature death compared to the general population; however, with

accurate diagnosis and appropriate treatment, up to 70% can achieve seizure freedom.[1] Antiepileptic drugs (AEDs) remain the primary treatment for epilepsy, with approximately 70% of patients achieving effective seizure control through medication alone.[4] Levetiracetam (LEV), a second-generation AED from the pyrrolidone class, is recognized for its broad spectrum of activity. As a novel antiseizure medication, LEV acts mainly on synaptic vesicle protein 2A (SV2A), which helps regulate the balance of neurotransmitters in the brain. This action modulates neuronal excitability and inhibition, thereby reducing the excessive activity that can trigger seizures. Approved by the FDA in the early 2000s, LEV has since been widely used to manage both focal and generalized seizures, including myoclonic seizures in children and adults. Numerous studies have evaluated its efficacy and safety across various seizure types. LEV has demonstrated effectiveness as both monotherapy and adjunctive therapy, including in the prevention of early post-traumatic seizures. [6,7]

There is a lack of studies on clinicians' perspectives on LEV in epilepsy management. This study assessed the clinical practices and physician preferences in epilepsy management, with a focus on the use of LEV. It also aims to assess treatment patterns, drug effectiveness, patient adherence, and barriers to care.

Methods

We carried out a cross-sectional study among clinicians specialized in treating epilepsy patients in the major Indian cities from June 2024 to December 2024. The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee, which is recognized by the Indian Regulatory Authority, the Drug Controller General of India.

Questionnaire

The questionnaire booklet titled LIVIA (Levetiracetam Efficacy and Tolerability Profile) was sent to the physicians who were interested in participating in this study. The study questionnaire included 23 questions that explored various domains, including demographics and clinical practice patterns such as common epilepsy types, age group prevalence, and gender-specific seizure trends. It also examined treatment preferences for newly diagnosed epilepsy and add-on therapy, LEV-specific usage patterns, including preferred seizure types and dosing strategies, and adverse effects with their management. Additional areas covered included patient adherence, use in special populations like pregnant and pediatric patients, and strategies for patient education and healthcare accessibility. Survey questions were developed using the methods designed to collect perspectives from the practitioners. Reliability as determined by a split-half test (coefficient alpha) was adequate but should be improved in future versions of the questionnaire. A study of criterion validity was undertaken to test the questionnaire and to develop methods of testing the validity of measures of Physicians' Perspectives. However, the extraneous variable in this includes the clinician's experience, usage of the newer drugs etc. The two criteria used were the doctors' perspectives from the clinical practice and the assessment of an external assessor and statistician.

Participants

A convenience sampling method was adopted, where an invitation was sent to leading neurologists who were experts in managing epilepsy in the month of March 2024 for participation in this Indian survey. About 293 doctors from major cities of all Indian states, representing the geographical distribution, shared their willingness to participate and provide necessary data. Those physicians were included and asked to complete the questionnaire without discussing it with their peers. A written informed consent was obtained from each neurologist prior to initiation of the study. Clinicians who were experts in other specialities and who had not provided informed consent were excluded from the study.

Statistical analysis

The data were analyzed using descriptive statistics. Categorical variables were presented as percentages to depict their distribution. The frequency of occurrence and the corresponding percentage were used to represent the distribution of each variable. To visualize the distribution of the categorical variables, bar charts were created using Microsoft Excel 2013 (version 16.0.13901.20400).

Results

The survey included 293 experts, with the majority of clinicians (58.7%) indicating that generalized motor seizures are the most commonly encountered form of epilepsy in their clinical practice. Around 58% reported that epilepsy is most frequently seen in individuals aged 19-45 years. Nearly half of the clinicians (47.1%) observed that partial seizures, with or without impaired sensorium, are more common in females than in males. According to 48% of experts, individual counselling is the preferred method for educating patients about epilepsy-related myths, facts, and awareness. More than half of the clinicians (51.54%) believed that 6-15% of patients with epilepsy are still unable to access appropriate healthcare facilities for management.

Approximately 50% of respondents indicated that between 26-50% of their patients with epilepsy adhere to prescribed medication and follow-up visits. Almost half of the experts (49.15%) observed that 21-30% of patients with partial-onset seizures do not respond to older antiepileptic medications in their clinical practice. Around 58% strongly endorsed the view that interventions such as pill reminders, tele-calling, and push messages can significantly improve patient compliance with medication. Over half of the clinicians (53.92%) indicated that they manage epileptic seizures in children under 10 years of age and prefer initiating treatment with first-generation AEDs.

According to 68% of experts, LEV is the most preferred AED for managing partial seizures in pediatric patients (Table 1). The majority of the clinicians (90.1%) expressed a preference for LEV as the first-line treatment for adult patients with newly diagnosed epilepsy (Figure 1). Nearly half of the clinicians (49.49%) stated that 41-60% of their epilepsy patients are currently being treated with LEV in their clinical practice (Figure 2).

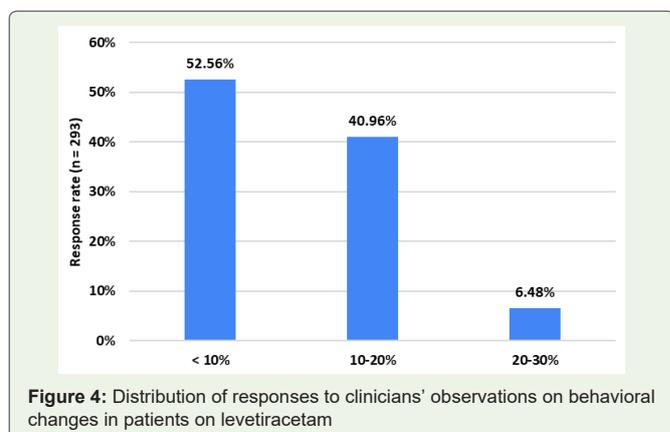
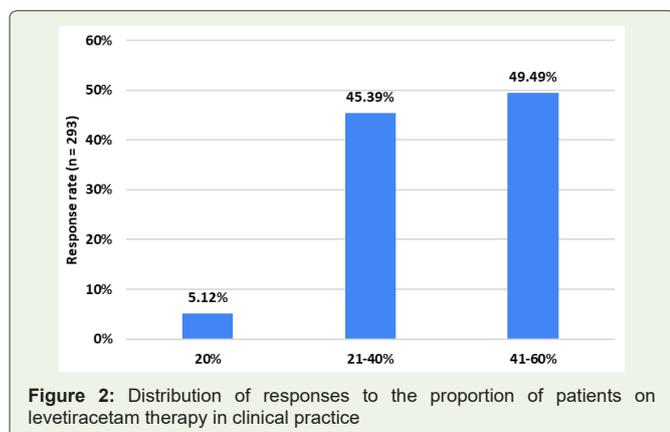
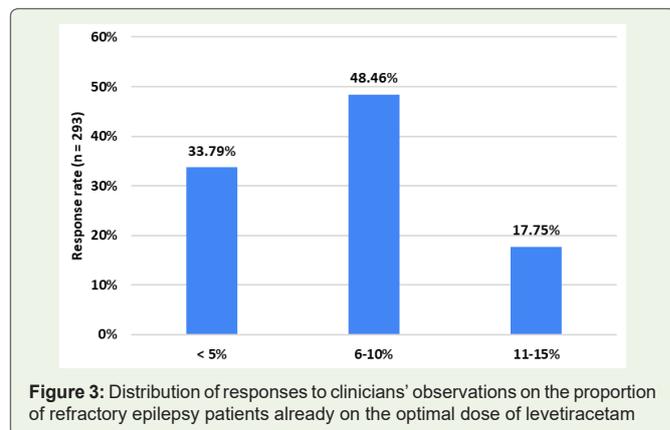
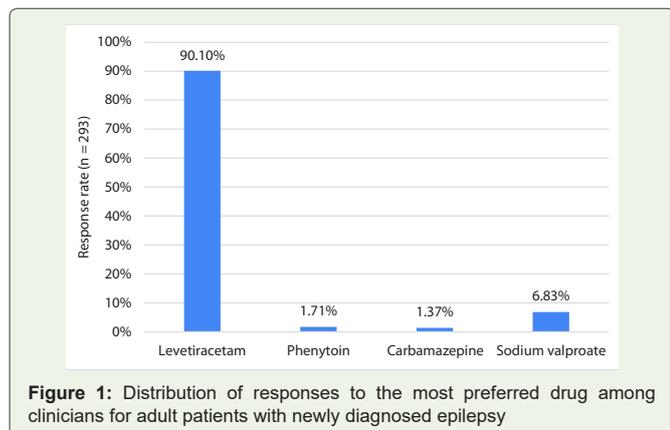


Table 1: Distribution of responses to clinicians' most preferred antiepileptic drug for partial seizures in the pediatric age group

Antiepileptic drug	Response rate (n = 293)
Levetiracetam	199 (67.92%)
Lamotrigine	3 (1.02%)
Brivaracetam	19 (6.48%)
Sodium valproate	52 (17.75%)
Oxcarbazepine	20 (6.83%)

Table 2: Distribution of responses to clinicians' views on the usefulness of levetiracetam in rare epileptic syndromes and its safety during pregnancy

Response Category	Response rate (n = 293)	
	Levetiracetam in Rare Epileptic Syndromes	Levetiracetam Safety in Pregnancy
Yes	36 (12.29%)	64 (21.84%)
No	106 (36.18%)	86 (29.35%)
No experience	151 (51.54%)	143 (48.81%)

Nearly 52% of experts reported having no experience with LEV in managing rarer forms of epileptic syndromes, while almost half (48.81%) similarly indicated no experience regarding its safety during pregnancy (Table 2). Around 46% stated that 26–50% of their epilepsy patients are adherent to both medication and follow-up visits in routine clinical practice. Approximately 48% observed that 6–10% of their patients with resistant or refractory epilepsy are already receiving an optimal dose of LEV (Figure 3).

Table 3: Distribution of responses to clinicians' preference for levetiracetam based on seizure type

Type of epileptic seizure	Response rate (n = 293)
Generalized motor seizures	120 (40.96%)
Partial seizures (with or without impaired sensorium)	85 (29.01%)
Myoclonic seizures	9 (3.07%)
All of the above	79 (26.96%)

About 41% of clinicians most often preferred LEV for treating generalized motor seizures (Table 3). More than half (52.56%) indicated that fewer than 10% of their patients on LEV exhibit behavioral changes (Figure 4). Two-thirds of the clinicians (66.55%) identified 1000 mg/day as the optimal dose of LEV, considering both seizure control and the risk of side effects (Table 4).

Table 4: Distribution of responses to clinicians' preferred optimal dose of levetiracetam balancing seizure control and side effects

Preferred daily dose of levetiracetam	Response rate (n = 293)
500 mg/day	57 (19.45%)
1000 mg/day	195 (66.55%)
1500 mg/day	37 (12.63%)
2000 mg/day	4 (1.37%)

Over half of the clinicians (54.27%) indicated that they typically

manage 5-10 epilepsy patients per month who require an add-on AED. Nearly half (49.15%) favored lacosamide as the second-generation AED of choice for patients whose seizures were not adequately controlled with first-line medications. Around 39% reported drowsiness as the most frequently encountered side effect of brivaracetam in the treatment of epileptic seizures. Approximately 42% of clinicians attributed the behavioral changes associated with LEV to an unknown mechanism.

Discussion

The survey results underscore a strong clinical preference for LEV as a first-line AED across diverse patient populations. A considerable proportion of clinicians favored its use in newly diagnosed adult epilepsy, reflecting its widespread acceptance in adult treatment protocols. Additionally, its preference for managing partial seizures in pediatric patients highlights its broad applicability across age groups.

In accordance with the current survey findings, multiple studies have supported the efficacy and tolerability of LEV across various age groups and epilepsy types. Alsaadi et al. reported the efficacy and tolerability of LEV therapy in patients with newly diagnosed epilepsy.[8] Similarly, Karlov et al. demonstrated that LEV is an effective monotherapy for newly diagnosed focal epilepsy (FE) and idiopathic generalized epilepsy (IGE), with significant reductions in epileptiform activity and high monotherapy retention rates (87.6% in IGE and 73.8% in FE).[9] An Indian open-label study reported that 62.96% of newly diagnosed partial seizure patients achieved seizure control at 6 months with LEV monotherapy at a dose of 20 mg/kg/day.[10]

A randomized controlled trial in India, involving 100 neonates with clinical seizures, found that LEV offered superior seizure control (86% vs. 62%) compared to phenobarbital, with no reported adverse drug reactions.[11] Additionally, a systematic review and meta-analysis of randomized controlled trials reported that, as monotherapy, LEV was more advantageous than carbamazepine (CBZ) for pediatric focal epilepsy (PFE), with a lower frequency of seizures and fewer dermatological adverse events.[12] Another meta-analysis confirmed that add-on LEV significantly reduces seizure frequency and is well tolerated in children with focal-onset seizures compared to placebo.[13]

The study data revealed that nearly half of clinicians prescribed LEV to 41–60% of their epilepsy patients, highlighting its practical advantages, strong tolerability, and consistent therapeutic effectiveness in everyday practice. However, almost 49% of respondents lacked experience regarding its safety during pregnancy, a key consideration given that AED exposure can affect fetal development at any stage.[14] A hospital-based retrospective study from a tertiary care center in Northeast India concluded that LEV monotherapy is a safer option for women of childbearing age with active epilepsy.[15] Similarly, a retrospective study conducted in Northern India involving 99 pregnant women with epilepsy receiving monotherapy found that none of the infants exposed to LEV exhibited congenital malformations.[16] Supporting these findings, results from the UK

and Ireland Epilepsy and Pregnancy Registers, which included a substantial cohort of first-trimester LEV exposures, confirmed that LEV monotherapy during pregnancy is associated with a low risk of major congenital malformations.[17]

More than half of clinicians (51.54%) reported no experience using LEV in rare epileptic syndromes. However, clinical and expert-based evidence supports its efficacy in such conditions. A North American expert consensus on Dravet syndrome supports LEV as a later-line option. While not recommended as first-line therapy, it was deemed moderately effective, alongside clonazepam and zonisamide, for patients unresponsive to standard treatments, highlighting its potential as an adjunct in drug-resistant cases.[18] Similarly, in an open-label, multicenter observational trial involving 55 pediatric patients with Lennox-Gastaut syndrome (LGS), add-on LEV led to a greater than 50% reduction in seizure frequency in 58.2% of patients, with 27.3% becoming seizure-free.[19] These findings indicate that LEV may provide therapeutic benefit even in syndromes with which many clinicians have limited experience.

According to the current survey findings, LEV is commonly utilized at optimal doses in the management of refractory epilepsy, reflecting its relevance in more difficult-to-treat cases. Its side effect profile is generally favorable, with behavioral changes reported in only a minority of patients. A daily dose of 1000 mg is often considered optimal, offering a balance between therapeutic efficacy and tolerability. Supporting these observations, Chen et al. reported that add-on LEV in 65 children with refractory epilepsy led to a rapid and significant reduction in seizures with minimal side effects, suggesting its suitability in pediatric cases.[20] Similarly, Viteva et al. evaluated LEV as adjunct therapy in 135 patients with drug-resistant epilepsy and found a sustained reduction in seizure frequency, mild improvement in seizure severity, and a favorable safety profile.[21]

A phase III randomized controlled trial by Manreza et al. confirmed that LEV, at doses of 1,000–3,000 mg/day for adults or 60 mg/kg/day for children, is effective and safe for treating refractory focal epilepsy.[22] Grant et al. observed a significant reduction in median seizure frequency across all dosing levels, with patients experiencing fewer weekly seizures compared to placebo.[23] Similarly, Cereghino et al. reported a significantly higher response rate, defined as a $\geq 50\%$ reduction in seizure frequency, in patients receiving 1,000 mg/day of LEV (33.0%) versus placebo (10.8%, $P < 0.001$).[24]

In the present survey, the majority of clinicians preferred LEV for treating generalized motor seizures, showcasing its versatility. A multicenter, randomized, double-blind, placebo-controlled trial by Berkovic et al. noted that adjunctive LEV significantly reduced generalized tonic-clonic seizures in idiopathic generalized epilepsy, with 72.2% achieving $\geq 50\%$ seizure reduction versus 45.2% in the placebo group ($p < 0.001$; OR 3.28; 95% CI: 1.68-6.38).[25] Similarly, a study by Krauss et al. found that LEV led to significant seizure reduction in patients with generalized seizures, including tonic-clonic, myoclonic, and absence seizures, who had failed multiple anticonvulsants, with 42% achieving complete seizure freedom.[26] These findings reinforce LEV's role as an effective option across a spectrum of generalized seizure types.

This survey offers valuable insights into clinicians' perspectives in actual practice on LEV use in epilepsy management, revealing significant observations supporting its role as a first-line therapy and aligning with current treatment guidelines. A key strength lies in the use of a validated questionnaire that captured expert opinions within an evidence-based framework, thereby supporting informed clinical decision-making. However, reliance on expert opinion introduces potential bias, as individual experiences and preferences may have influenced responses. Additionally, as a survey-based study, it is subject to response and recall bias, with findings potentially reflecting the characteristics of the sampled clinicians rather than the broader medical community. Future directions include conducting prospective studies or randomized controlled trials to validate these results, ideally by integrating objective measures of efficacy, tolerability, and patient outcomes.

Conclusion

The survey highlights LEV's strong standing as a preferred AED among clinicians for both adult and pediatric epilepsy. Its broad application and favorable side effect profile contribute to its widespread use. However, the reported lack of experience in treating rarer epileptic syndromes and during pregnancy points to areas where further research and clinician education are warranted to optimize patient care.

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