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Original Research Article

Insights into neurologists' practices and preferences in pharmacological management of paediatric epilepsy: a real-world survey-based study from India

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ABSTRACT

Background: Epilepsy is a chronic brain disorder marked by recurrent seizures. Many children experience a mild form that resolves naturally, while others have persistent cases requiring lifelong medication. In India, prevalence of paediatric epilepsy is about 0.8%. The objective of this survey was to explore neurologist's practices in the pharmacological management of paediatric epilepsy.
Methods: The cross-sectional, questionnaire-based, real-world survey was conducted amongst 245 neurologists across India from August 2024 to September 2024. The respondents were administered a validated 20-question survey. Analysis of the data was conducted in Microsoft Excel (365, Version 22502). Graphical representations were created to highlight significant trends and treatment preferences.
Results: In the survey, 43.7% of the neurologists reported that they examine around 5 to 10 cases per month, and majority (44.0%) of them also noted 2-to-6-year age group was most affected with the disease. Levetiracetam has emerged as the most preferred antiepileptic drug, with 42.1% of respondents using it for focal epilepsy, 42.4% for generalized epilepsy and 46.5% for myoclonic seizures. Syrup formulations were preferred by 93.9% of neurologists, with levetiracetam syrup at a dose of 10mg/kg twice a day being the most commonly preferred in the management of paediatric epilepsy.
Conclusions: The survey indicates rising trend in paediatric epilepsy cases in India. Levetiracetam was the frequently chosen drug for the treatment of focal, generalized and myoclonic seizures in children with epilepsy. In addition to its rapid onset of action and low frequency of drug-drug interactions, it was also favoured for its versatility in terms of dosage formulation, especially in the syrup form.

Keywords: Antiepileptic drugs, Levetiracetam, Neurologists, Paediatric epilepsy, Seizures

INTRODUCTION

Epilepsy is a chronic non-communicable brain disorder characterized by recurrent seizures, which involve involuntary movements and may include loss of consciousness or control of bodily functions. Seizures occur due to excessive electrical discharges in brain cells. A single seizure cannot be considered as epilepsy; it is diagnosed after having two or more unprovoked seizures.[1,2] Many children experience a mild form of epilepsy that tends to resolve on its own after a few years, with no long-term issues. Types like rolandic and absence epilepsy are often considered mild and do not require medication. However, some children have more severe, persistent epilepsy, which may be managed with medication, such conditions often require lifelong treatment.[3] In India, the overall prevalence of paediatric epilepsy is about 0.8%. However, rates are different in

various regions as the North-East has the highest rate at 2.3%, while Central India has the lowest at 0.4%. Community-based studies have shown a slightly higher rate of 0.8% compared to school-based studies which shows rates between 0.32% to 0.40%. The gender specific prevalence of the disease in India is almost similar with 0.6% of boys and 0.4% of girls affected.[4]

Diagnosis of epilepsy in children is generally based on the identification of continuous or recurrent seizures. However, electroencephalogram (EEG) evaluation is crucial as it helps to classify syndromes, predict seizure recurrence, and differentiate between non-epileptic and epileptic events. As magnetic resonance imaging (MRI) is more sensitive, it is preferred over computed tomography (CT) for neuroimaging in epilepsy, especially for surgical planning, while CT is useful in acute situations. As recommended by the guidelines for diagnosis and management of childhood epilepsy, neuroimaging is not necessary for benign epilepsies.[5,6]

Most children with new-onset epilepsy, especially those with idiopathic generalized types, can become seizure-free with the right antiepileptic drugs (AEDs). About 20% of children with idiopathic focal epilepsy experience only a few seizures before their condition naturally improves. However, around 20% of children with epilepsy continue having seizures despite treatment with AEDs. The options for treating epilepsy in children include first-generation AEDs, as well as second- and third-generation or newer AEDs. While these second- and third-generation drugs are mainly approved for adults, they are being used more often in children, especially those over 12 years of age, due to increasing evidence that they can be effective.[7]

The aim of this survey was to gather insights into the current practices and preferences among neurologists regarding the pharmacological management of paediatric epilepsy. Additionally, the survey explores the most common epilepsy types encountered in clinical practice and probes into the factors influencing the selection of AEDs for different seizure types, including first-line treatments for generalized tonic-clonic (GTC) seizures, absence seizures, and myoclonic seizures. This helps to highlight the choices paediatric neurologists make based on efficacy, tolerance, and specific patient factors. The survey also explores the challenges in treating drug-resistant epilepsy and the preferred management strategies when initial therapy fails. The survey provides valuable data that can guide future strategies for optimizing pharmacological management in paediatric epilepsy care.

METHODS

This was a cross-sectional, questionnaire-based, real-world survey conducted with a validated 20 questions among 245 neurologists across India between August 2024 to September 2024. The survey utilized a nationwide approach by reaching out to neurologists from various regions and practices in India, instead of focusing on a single hospital or institution. The participating neurologists were in the age range of 40–60 years, having more than 5 years of clinical experience, and were practicing in diverse settings including private clinics, nursing homes, and hospitals. Neurologists were chosen based on their educational qualifications and clinical experience in the field of epilepsy management. Neurologists with less than 5 years of clinical experience, those outside the specified age range, or without relevant qualifications in neurology practice were excluded. The primary objective of the survey was to gather insights into the current practices and preferences among neurologists regarding the pharmacological management of paediatric epilepsy. Additionally, the exploratory objective was to examine the role of levetiracetam (LEV) in paediatric epilepsy treatment, exploring its dosing preferences, advantages, and any associated challenges. The questionnaire was developed, focusing on aspects such as the frequency of paediatric epilepsy cases, preferred AEDs, diagnosis, etiology, treatment duration, and other treatment-related factors. The questionnaire was administered to 245 neurologists practicing in both academic and clinical settings. The responses were collected anonymously to ensure unbiased and accurate reporting. Microsoft Excel was used to gather and examine the responses (Microsoft Excel 365, version 22502, March 11). Data were analysed according to the frequency of individual response possibilities because participants were allowed to choose more than one response for some items, hence the number of responses are more than 245 and differ in every graph. Excel-generated graphs and charts were then used to display the data. Key elements impacting therapeutic decisions, formulation preferences, and trends in clinical practice were all interpreted and described using these graphic summaries.

RESULTS

A total of 245 neurologists, regularly managing paediatric epilepsy cases in both academic and clinical settings, completed the questionnaire. The majority (43.7%) reported handling 5 to 10 cases per month, followed by 37.1% treating 0 to 5 cases, and 19.2% managing >10 cases monthly. The 2 to 6-year age group was identified as the most affected (44.0%) by epilepsy, followed by other age groups. Notably, 31.0% of neurologists reported that the 6 to 12-year age group was most affected. Additionally, 12.5% of respondents in each group observed that either children under 2 years of age or those aged 12 years and older were most affected (Figure 1). Regarding epilepsy types, 62.9% of neurologists indicated that both generalized and focal epilepsy were the most common in paediatric patients. In contrast, 20.0% and 17.1% of respondents identified generalized epilepsy and focal epilepsy, respectively, as the most prevalent types in this population (Figure 2).

In terms of diagnostic methods, the majority of neurologists (72.7%) reported using a combination of clinical signs, EEG, and imaging techniques for diagnosis.

However, 15.5% of neurologists relied solely on EEG, 7.8% based their diagnosis solely on clinical signs and symptoms, and 4.1% preferred using both EEG and clinical signs for diagnosis. Concerning the etiology of paediatric epilepsy, 27.7% of neurologists indicated that genetic predisposition is the most common factor. Other common etiological factors included infectious diseases (27.4%), idiopathic causes (21.8%), brain tumors (13.0%), and cranial trauma (9.9%) (Figure 3). Approximately 25.5% of neurologists identified sleep deprivation as the most common seizure-triggering factor. A sizable proportion of respondents also cited other seizure triggers, including hyperthermia (23.7%), stress (16.0%), heat stroke (14.7%), hypoglycemia (13.7%), and the consumption of stimulating drinks such as tea and coffee (6.3%).

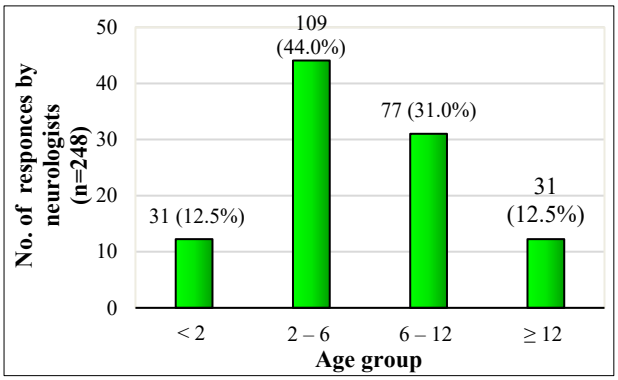

Figure 1: Paediatric epilepsy distribution by age group.

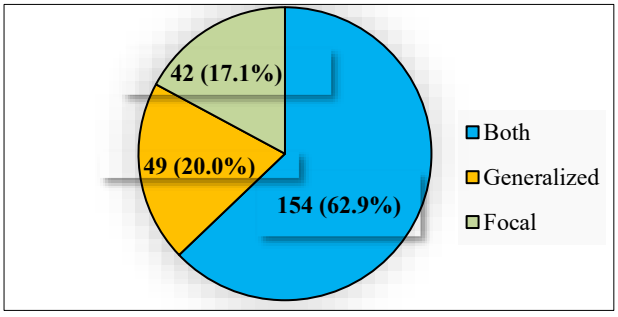

Figure 2: Types of epilepsy in paediatric population.

Regarding the treatment of paediatric patients with focal epilepsy, 42.1% of neurologists preferred LEV as first-line therapy. Other commonly prescribed medications included sodium valproate (24.2%), carbamazepine (12.3%), phenytoin (9.6%), and lamotrigine (6.4%). A smaller proportion (5.1%) of neurologists opted for phenobarbital for this condition. For the treatment of generalized epilepsy, the majority of neurologists (42.4%) preferred LEV. However, sodium valproate was favored by 30.1% of respondents, while carbamazepine (8.1%), phenytoin (8.6%), phenobarbital (6.5%), and lamotrigine (4.4%) were selected by smaller proportions of neurologists. For absence seizures, 36.9% preferred sodium valproate, and 36.2% favoured LEV, while phenytoin (9.3%), carbamazepine (8.3%), and lamotrigine (6.4%) were also selected, with phenobarbital chosen by only 2.9%. In managing myoclonic seizures, 46.5% preferred LEV, followed by sodium valproate (30.7%) and phenytoin (8.2 %) (Figure 4).

In cases of refractory focal epilepsy, 55.9% of neurologists recommended add-on therapy with LEV. Additional treatment options included increasing the dose of current medication (24.2%), trying a ketogenic diet (12.1%), and switching to zonisamide (7.8%) (Figure 5). Around 51.5% of neurologists preferred LEV as the first-line treatment for newly diagnosed GTC seizures in children, followed by sodium valproate (23.0%). Smaller proportions chose phenytoin (9.0%), carbamazepine (6.4%), lamotrigine (4.7%), and phenobarbital (5.5%). Levetiracetam was also the most common add-on therapy (46.8%), followed by sodium valproate (18.7%) and lamotrigine (14.8%) (Figure 6). Regarding AEDs requiring careful monitoring due to potential side effects, 20.8% and 20.2% of neurologists cited sodium valproate and LEV, respectively. Other drugs mentioned included phenytoin (18.1%), carbamazepine (16.5%), phenobarbital (14.1%), and lamotrigine (10.1%). The type of epilepsy (29.25%) was the primary factor influencing drug selection, followed by efficacy (27.5%), tolerance (22.8%), and cost (20.4%). For the duration of antiepileptic treatment in paediatric epilepsy, 46.9% of neurologists recommended 2 years, while others suggested 5 years (32.2%), 12 months (9.0%), or 6 months (5.7%). A small portion (6.1%) believed lifelong treatment might be necessary.

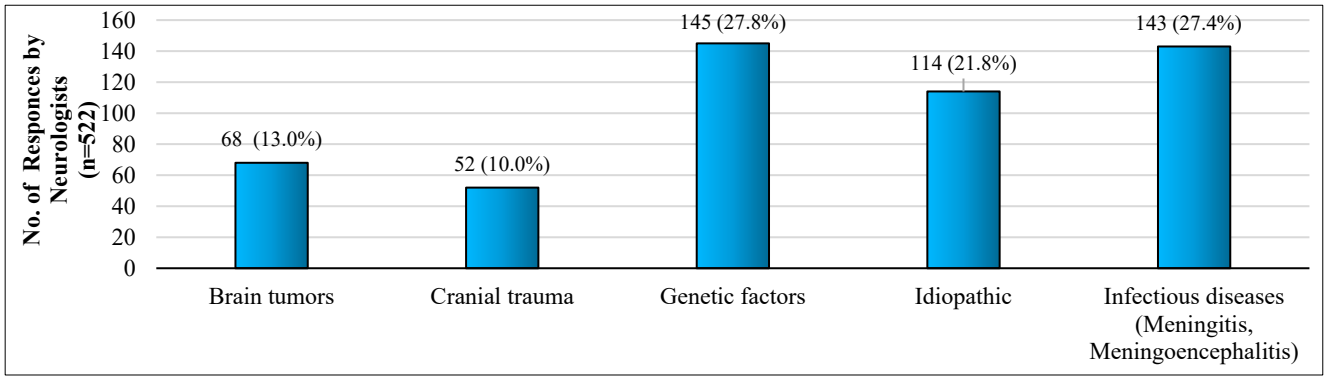

Figure 3: Common etiology in paediatric epilepsy.

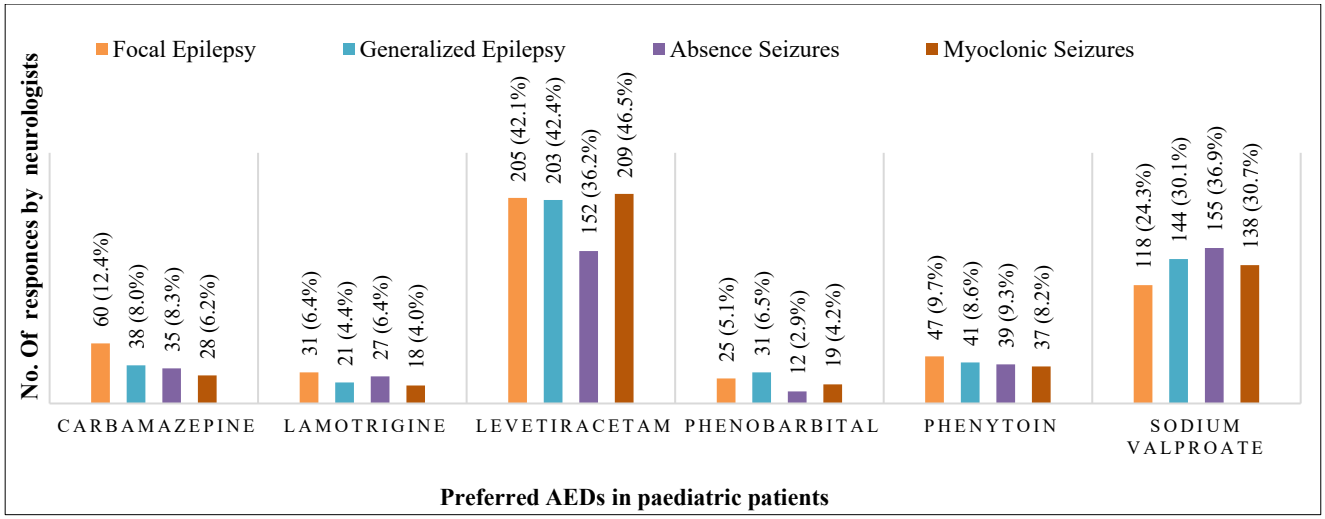

Figure 4: Preferred AEDs in types of paediatric epilepsy.

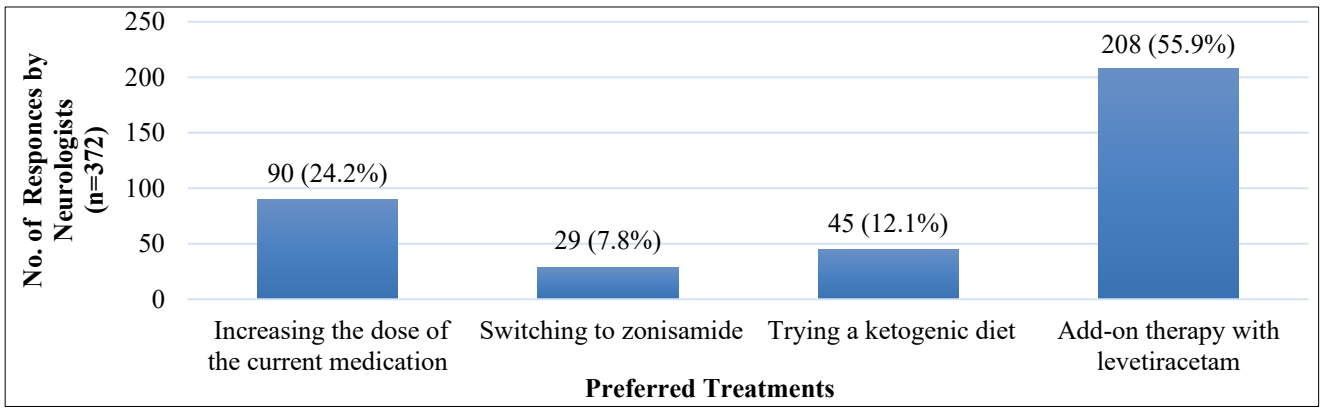

Figure 5: Preferred treatments for children with refractory focal seizures.

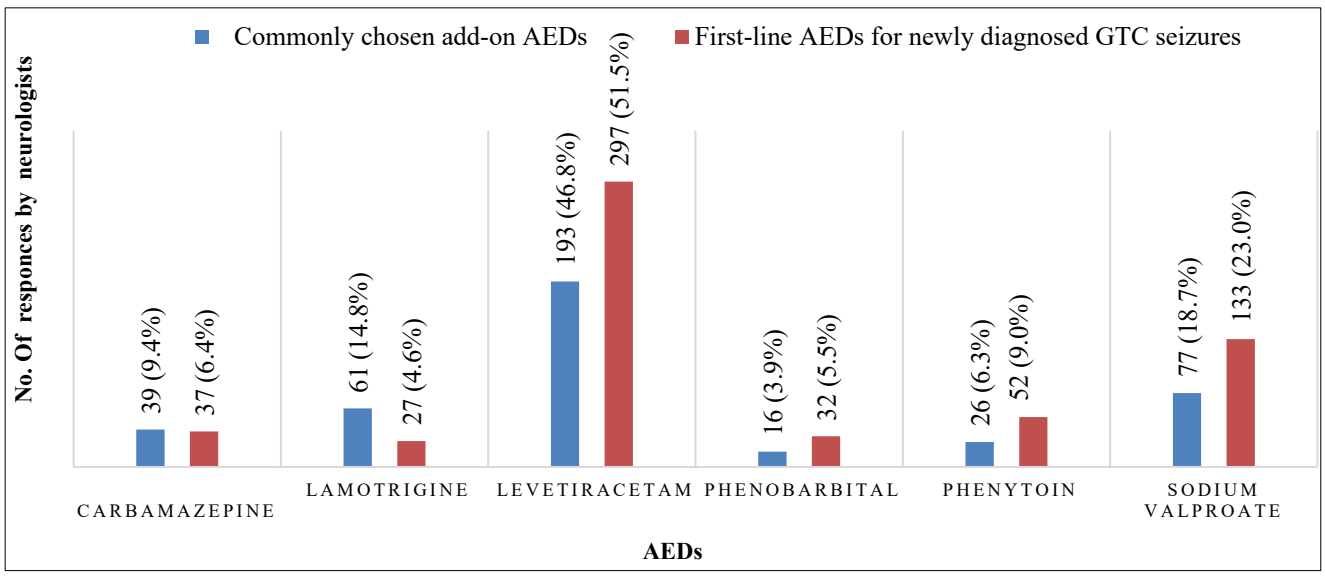

Figure 6: First line and commonly add-on AEDs in paediatric epilepsy.

Levetiracetam and sodium valproate were the most preferred AEDs for patients with a history of behavioral issues, each chosen by 30.7% of respondents. Lamotrigine (14.1%), carbamazepine (13.1%), phenytoin (6.8%), and phenobarbital (4.6%) were less frequently selected. Syrup formulations were preferred by 93.9% of neurologists,

with LEV syrup at a dose of 10mg/kg twice a day being the most common (64.5%). Lower (7 mg/kg) and higher (20 mg/kg) doses were selected by 23.7% and 11.4%, respectively. Regarding advantageous properties of levetiracetam, 29.5% of neurologists cited minimal drug interactions, 26.2% emphasized rapid onset of action, 25.4% noted minimal risk of cognitive side effects, and 18.9% valued flexible dosing options.

DISCUSSION

The survey was conducted to gather real-world insights into the current practices and preferences among neurologists in India regarding the management of epilepsy in children in routine clinical settings. This survey-based study indicated that significant number of neurologists handle approximately 5 to 10 cases per month of epilepsy in children. There was variation in rate of prevalence amongst age groups, majority of neurologists reported prevalence more in 2 to 6 year age group followed by 6-to-12-year age group. The data from a study conducted by Aaberg et al also suggest that approximately 1 out of 150 children is diagnosed with epilepsy during the first 10 years of life.[8] Pratibha et al also noted that, more than 60% of epilepsy cases starts in childhood; hence, the subject is of great importance to paediatricians.[9]

The high prevalence of epilepsy in children highlights the burden of paediatric epilepsy in the country, necessitating effective management strategies. The survey revealed that both generalized and focal epilepsy were most prevalent among the children. The result of this survey is well in agreement with the results of an observational study conducted by Baranala et al which demonstrated that generalized seizures were the most prevalent followed by absence seizures and focal seizures.[10] The survey also demonstrated the preferred methods of diagnosis wherein around 72.7% of neurologists used combination of clinical signs, EEG, and imaging techniques. However, a small number of neurologists relied solely on EEG, or clinical signs, or imaging techniques.

Epilepsy is clinically diagnosed in children who experience two or more unprovoked seizures or if the predicted risk of recurrence after a first seizure is 60% or greater. The decision to initiate an AED primarily depends on the risk of seizure recurrence. Factors linked to increased recurrence after first seizure include abnormal neurological examination findings, abnormal brain MRI or EEG results, and a history of nocturnal seizures. Treatment choices in these conditions are more complex and imply different, relatively specific first-line choices and second-line options.[11]

In current survey LEV has emerged as the most preferred AED, with 42.1% of respondents using it for focal epilepsy and 42.4% for generalized epilepsy. Additionally, neurologists have also frequently reported LEV for the management of absence (36.2%) and myoclonic seizures (46.5%). LEV was originally approved as an adjunctive treatment for refractory partial seizures in adults. In 2005, it has gained approval for use in children aged 4 years and above, particularly in the treatment of myoclonic seizures, juvenile myoclonic epilepsy, and generalized tonic-clonic seizures. In addition, Indian Academy of Paediatrics suggest that it should be used only as an add-on drug to refractory partial and some generalized epilepsies like, refractory absence or progressive myoclonic epilepsies.[12]

Sedation related adverse events (AEs) are the most commonly reported AEs associated with LEV. Moreover, some trials have reported behavioral AEs as most common type of AEs with LEV.[12] Adverse events associated with sodium valproate are primarily gastrointestinal (nausea, vomiting, and dyspepsia), along with weight gain, tremor, and transient hair loss. Minor neurologic AEs, such as sedation, ataxia, and cognitive impairment, compared with other AEDs, a finding that may be of particular relevance in many children with epilepsy.[13] Therefore, even if sodium valproate and LEV are effective, they need to be closely monitored because of the possibility of adverse effects, which is especially concerning for children. According to the survey results, neurologists emphasized the need of monitoring for AEs in children on treatment with sodium valproate and LEV.

An important aspect of paediatric epilepsy management is to identify and manage the seizures triggering factors. The survey highlighted lack of sleep (25.5%) and hyperthermia (23.7%) as the most common triggering factors observed by neurologists in their day-to-day clinical practice. Existing literature also supports the current findings which identifies lack of sleep and stress as common causes, which disrupt normal brain activity, increasing the likelihood of seizures. Additionally, hyperthermia often associated with fevers or heat stroke, and hypoglycemia, can also play significant roles.[14]

The dose of LEV in paediatric population remains a crucial aspect of management, as both underdosing and overdosing can lead to suboptimal outcomes or AEs. According to the survey, the most common dose of LEV preferred by neurologists was 10 mg/kg twice a day, with a smaller group of neurologists preferring a dose of 20 mg/kg twice a day. This is in line with the dosing recommendations from the Indian Academy of Paediatrics, which suggest a range of 20-60 mg/kg/day, starting at 20 mg/kg/day and titrating upwards. This discrepancy in prescribing dose of LEV may reflect the individual experience of neurologists, with some preferring a more conservative approach to minimize the risk of AEs, influenced by the specific conditions of the disease and the other therapies given in combination to LEV. Additionally, as LEV is mainly given in combination with other AEDs.[6]

The factors which contribute to the discontinuation of AED therapy include side effects, medication costs, and psychological dependence. The decision to discontinue therapy, much like the initiation of treatment, should be

guided by an analysis of risks and benefits. It is essential to evaluate the benefits in relation to the potential risk of epilepsy recurrence. These assessments primarily focus on the likelihood of recurrence rather than determining the appropriate timing for stopping AEDs. Most studies suggest discontinuing AEDs after 2 to 3 years, an established practice, though assessing the effect of seizure-free duration on relapse rates is challenging without randomizing patients, which may be ethically difficult.[15] The current survey highlights views of neurologists on the ideal duration of antiepileptic treatment for paediatric epilepsy. There was significant variation in the responses, with many neurologists recommending a 2-year treatment duration, while others suggested even lifelong treatment among others. The duration of antiepileptic treatment is dependent upon the type of epilepsy and the patient's unique characteristics. Current guidelines suggest that AEDs can be withdrawn after two years of being seizure-free for most epilepsy cases, however for the conditions such as adolescent-onset or symptomatic epilepsy longer treatment may be required. Certain conditions, such as febrile seizures or neurocysticercosis, may require treatment durations of one to two years or six months, respectively. In idiopathic generalized epilepsies, discontinuation of medication often leads to relapse, which may require some patients to maintain a lifelong low-dose treatment.[6]

This study has certain limitations. It is a cross-sectional, questionnaire-based survey relying on self-reported data, which may introduce recall and response biases. Voluntary participation could lead to selection bias, limiting generalizability to all epilepsy practitioners. Regional differences in clinical practice may also affect the applicability of findings. Moreover, the survey focused on neurologists' perceptions without patient outcome data, limiting objective assessment of AEDs effectiveness and safety in paediatric epilepsy.

CONCLUSION

This survey offers insightful information regarding pharmacological management of epilepsy in children with the focus on current practices and preferences among Indian neurologists. The etiology and seizure-triggering factors of childhood epilepsy have been found to be frequently influenced by genetic factors and sleep deprivation. Typically based on the complexity of the condition neurologists determines the duration of treatment with AEDs, however there was huge variation observed the opinions of the neurologists regarding the treatment duration. This variation emphasizes how crucial it is to conduct additional study in order to develop precise therapy recommendations. Levetiracetam was the frequently chosen drug for the treatment of focal, generalized and myoclonic seizures in children with epilepsy. In addition to its rapid onset of action and low frequency of drug-drug interactions, it was also favoured for its versatility in terms of dosage formulation, especially in the syrup form. However, compared to other AEDs, the majority of neurologists pointed out that LEV, in addition to sodium valproate, warrants the most cautious monitoring because of the possible AEs. When choosing a course of treatment, neurologists consider the type of epilepsy, efficacy, and tolerance of the drug. Overall, the results of this survey highlight the necessity of more research and awareness to refine treatment protocols and warrants the best possible results for children with epilepsy.

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Conflict of interest: Dr. Kunal Khobragade and Nitinkumar S. Doshi are the employees of Mankind Pharma Ltd
Ethical approval: Ethical approval was not sought for this survey as it was conducted among qualified healthcare professionals, involved no patient data or intervention.

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