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Original article

The Role of Sodium Valproate Prophylaxis in Preventing Recurrent Complex Febrile Seizures in Children: A Retrospective Study at Tripoli University Hospital, Libya

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Abstract
Complex febrile seizures represent a critical clinical scenario in pediatric neurology due to their association with prolonged ictal events, focal features, and heightened parental anxiety. While intermittent or continuous antiseizure prophylaxis is occasionally deployed, the clinical efficacy of prophylactic Depakin (sodium valproate) in preventing recurrent complex febrile seizures remains intensely debated. To evaluate and compare the recurrence rate of febrile seizures in children receiving prophylactic sodium valproate (Depakin) versus those managed without continuous prophylaxis. This retrospective observational comparative study was conducted at the Pediatric Neurology Outpatient Department of Tripoli University Hospital in Libya from February 2023 to March 2026. A total of 115 children aged 9-50 months (68 females [59.1%] and 47 males [40.9%]) with recurrent complex febrile seizures were analysed. Patients were categorised into Group A (n=70) receiving Depakin prophylaxis (15-20 mg/kg/day after normal baseline liver function tests, complete blood count, serum amylase, and coagulation profile) and Group B (n=45) receiving no prophylaxis. Follow-up spanned two years. Group A demonstrated a recurrence rate of 20.0% (14 out of 70 children; 56 with no recurrence), whereas Group B showed a recurrence rate of 24.4% (11 out of 45 children; 34 with no recurrence). The difference in recurrence proportions between the two cohorts was not statistically significant (p = 0.57, chi-square test; relative risk = 0.82). Prophylactic sodium valproate did not yield a statistically significant reduction in complex febrile seizure recurrence compared to unexposed controls. These findings corroborate international consensus advising against universal continuous prophylaxis, emphasising individualised risk-benefit assessments and rigorous safety monitoring.
Keywords. Complex Febrile Seizures; Recurrent Febrile Seizures; Depakin (Sodium Valproate); Prophylaxis.

Introduction

Febrile seizures constitute the most prevalent neurological morbidity in early childhood, affecting approximately 2% to 5% of children aged 6 months to 5 years [1-7]. Although simple febrile seizures carry a benign prognosis with negligible long-term neurological sequelae, complex febrile seizures—characterised by prolonged duration (>15 minutes), focal onset, or multiple recurrent events within a single 24-hour window—pose formidable diagnostic and therapeutic challenges [7, 8]. Children presenting with recurrent complex episodes frequently experience repeated emergency department visits and trigger profound anxiety among caregivers [2,9]. The management of complex febrile seizures remains a subject of considerable divergence across international pediatric neurology practice. While major professional guidelines, including those issued by the American Academy of Paediatrics (AAP) and the National Institute for Health and Care Excellence (NICE), generally discourage routine continuous long-term antiseizure prophylaxis due to potential adverse drug reactions, clinicians in various regions frequently consider prophylactic agents such as sodium valproate (Depakin) for patients exhibiting high recurrence frequency or severe electroclinical phenotypes [1,10-12].

Sodium valproate is a potent broad-spectrum antiseizure medication; however, its administration in young infants and toddlers mandates strict clinical vigilance owing to well-documented risks of hepatotoxicity, pancreatitis, haematological abnormalities, and metabolic alterations [13,14-20]. Moreover, historical and contemporary clinical trials evaluating prophylactic regimens offer conflicting conclusions regarding whether continuous medication genuinely alters the natural history of febrile seizure recurrence when compared to supportive care, intermittent antipyresis, and parental reassurance [3, 15-26]. Against this clinical backdrop, the present retrospective study was undertaken at Tripoli University Hospital, Libya, to evaluate the comparative outcomes of pediatric patients receiving Depakin prophylaxis versus those managed without continuous pharmacotherapy. The primary aim was to compare the recurrence rate of complex febrile seizures between children receiving continuous Depakin (sodium valproate) prophylaxis and those managed without prophylactic therapy. The secondary objectives were:

Patients and Methods

Study Design

This was a retrospective observational comparative study.

Study Setting and Period

The study was conducted at the Pediatric Neurology Outpatient Department of Tripoli University Hospital, Tripoli, Libya, spanning from February 2023 to March 2026.

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Study Population
A total of 115 children aged 9 to 50 months presenting with recurrent complex febrile seizures were enrolled. The cohort comprised 68 females (59.1%) and 47 males (40.9%).

Group Classification
Participants were stratified into two groups according to their therapeutic management. Group A comprised 70 children who received continuous prophylactic treatment with Depakin (sodium valproate) following recurrent complex febrile seizures. Group B, serving as the control group, included 45 children who did not receive continuous prophylactic antiseizure medication.

Inclusion and Exclusion Criteria
The study included children aged between 9 and 50 months who had a documented clinical history of recurrent complex febrile seizures and regularly attended the Pediatric Neurology Outpatient Clinic at Tripoli University Hospital during the study period. Eligible participants were required to have comprehensive medical records documenting baseline clinical evaluations, treatment protocols, and seizure outcomes.
Children were excluded if they had evidence of acute central nervous system infections, including bacterial meningitis or viral encephalitis, or a pre-existing diagnosis of structural brain lesions, metabolic encephalopathy, or non-febrile epilepsy. Children presenting with isolated simple febrile seizures were also excluded. Additionally, patients with incomplete medical records or unverified follow-up data were excluded from the study.

Treatment Protocol
Patients in Group A were prescribed Depakin (sodium valproate) syrup or tablets at a standard therapeutic dosage of 15-20 mg/kg/day [13]. Before treatment initiation, comprehensive baseline laboratory investigations—including liver function tests (LFTs), complete blood count (CBC), serum amylase, and coagulation profile—were systematically performed and verified as normal to exclude hepatic, pancreatic, or haematological contraindications [14, 20]. Clinical follow-up was maintained for two consecutive years following prophylaxis initiation [15].

Outcome Measures
The primary outcome measure was the occurrence of recurrent complex febrile seizures during the two-year observation window. The proportion of patients experiencing recurrence in Group A was directly compared against Group B.

Statistical Analysis
Categorical variables were summarised as frequencies and percentages. Comparative analysis of seizure recurrence between cohorts was executed utilising the chi-square test (and Fisher's exact test where applicable) [21]. Relative risk (RR) and 95% confidence intervals (CI) were calculated. Statistical significance was defined as a p-value < 0.05.

Ethical Considerations
Ethical approval was granted by the institutional review board and research ethics committee of Tripoli University Hospital, ensuring strict adherence to patient confidentiality and the ethical principles of the Declaration of Helsinki [17].

Results
One hundred and fifteen pediatric patients met all inclusion criteria and were included in the final analysis. The cohort comprised 70 children in Group A (Depakin prophylaxis) and 45 children in Group B (no prophylaxis). Overall gender distribution included 68 females (59.1%) and 47 males (40.9%) [16].

Table 1. Study population and baseline demographic characteristics.

Characteristic	n (%)
Total participants	115 (100%)
Female	68 (59.1%)
Male	47 (40.9%)
Group A: Depakin (sodium valproate) prophylaxis	70 (60.9%)
Group B: No prophylaxis (Control)	45 (39.1%)

Table 2. Seizure outcomes during the two-year follow-up period.

Outcome	Group A: Depakin Prophylaxis (n = 70)	Group B: No Prophylaxis (n = 45)
No further febrile seizures (No recurrence)	56 (80.0%)	34 (75.6%)
Recurrence of febrile seizures	14 (20.0%)	11 (24.4%)

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As detailed in (Table 2), seizure recurrence was observed in 14 out of 70 children (20.0%) in Group A compared to 11 out of 45 children (24.4%) in Group B. The absolute risk reduction was 4.4 percentage points, with a relative risk of 0.82 (95% CI: 0.41-1.65). Chi-square analysis yielded a p-value of 0.57, indicating no statistically significant difference in recurrence between the two cohorts [21].

Table 3. Statistical comparison of seizure recurrence between study groups.

Statistical Parameter	Value
Recurrence Rate in Group A (n = 70)	14 (20.0%)
Recurrence Rate in Group B (n = 45)	11 (24.4%)
Absolute Risk Difference	4.4 percentage points
Relative Risk (RR) [95% CI]	0.82 (0.41 - 1.65)
Chi-Square Test (p-value)	0.57 (Not Significant)

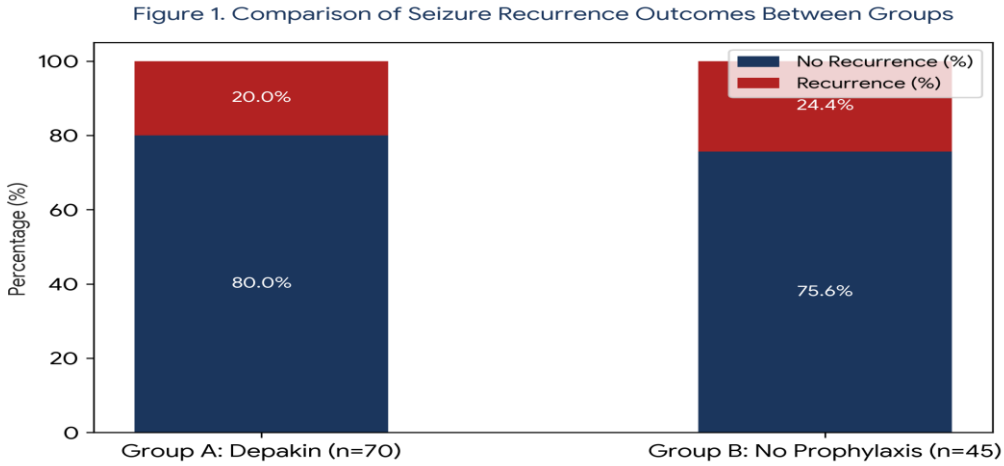


Figure 1. Graphical comparison of seizure recurrence and non-recurrence proportions between children receiving Depakin prophylaxis (Group A) and those receiving no prophylaxis (Group B).

Discussion

In this retrospective observational study conducted at Tripoli University Hospital, the administration of prophylactic sodium valproate (Depakin) to children with recurrent complex febrile seizures resulted in a recurrence rate of 20.0%, compared to 24.4% among children managed without continuous prophylaxis. Although patients receiving valproate demonstrated a modest numerical decrease in seizure recurrence (absolute risk reduction of 4.4%), this difference did not attain statistical significance (p = 0.57, RR = 0.82). These empirical observations contribute valuable regional data to the ongoing global discourse regarding the efficacy and clinical utility of continuous antiseizure prophylaxis in complex febrile seizures [1, 2, 16].

Our findings closely parallel landmark clinical investigations and systematic reviews evaluating the prophylactic efficacy of antiepileptic medications in febrile seizures [2, 3, 15]. For instance, Pavlidou et al. (2007) investigated the clinical utility of sodium valproate in children presenting with complex febrile seizures and reported that while short-term electrical and clinical parameters appeared stable, continuous prophylaxis failed to produce a dramatic, statistically unassailable reduction in long-term recurrence when weighed against the natural history of the condition [3]. Similarly, comprehensive Cochrane systematic reviews by Offringa and Newton (2013) concluded that intermittent or continuous pharmacologic prophylaxis (including valproate and phenobarbital) exposes young children to substantial pharmacological toxicity without offering definitive protection against subsequent seizure recurrence or subsequent epilepsy development [2]. Conversely, earlier historical studies—such as those by Farwell et al. (1990)—highlighted that continuous barbiturate or valproate therapy could suppress short-term breakthrough seizures in highly selected high-risk cohorts [15]; however, these benefits were consistently counterbalanced by adverse neurocognitive profiles and metabolic burdens. In our cohort, the absence of a statistically significant divergence between Group A and Group B reinforces the prevailing guidelines established by the American Academy of Paediatrics (AAP) and the National Institute for Health and Care Excellence (NICE), which advocate against routine universal prophylaxis in favour of aggressive acute fever management and rescue protocols [1, 12].

A critical dimension of our study protocol involved the rigorous pre-treatment evaluation of all children in Group A. Before initiating Depakin at 15-20 mg/kg/day, baseline liver function tests (LFTs), complete blood count (CBC), serum amylase, and coagulation profiles were verified as normal. This meticulous screening protocol aligns with established pediatric endocrinology and neurology safety guidelines emphasising that sodium valproate carries well-recognised risks of idiosyncratic hepatotoxicity, acute pancreatitis, thrombocytopenia, and coagulation defects, particularly in toddlers under two years of age [13, 14, 20]. The absence of reported severe adverse metabolic events in our treated cohort underscores the vital importance of baseline laboratory screening and vigilant clinical surveillance during chronic valproate therapy [20, 27].

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Limitations

Several methodological limitations inherent to our study design must be transparently addressed. First, the retrospective, non-randomised observational design introduces potential selection bias and confounding by indication [17, 22]. Specifically, pediatric patients presenting with more severe seizure phenotypes, prolonged focal episodes, or highly anxious parents were preferentially allocated to receive Depakin prophylaxis by treating physicians, which may have artificially elevated the baseline risk profile of Group A and masked a latent therapeutic benefit. Second, the moderate sample size (n = 115) derived from a single tertiary academic centre (Tripoli University Hospital) may constrain the statistical power required to detect subtle subgroup differences or execute multivariable adjustments for potential confounders such as family history of epilepsy, exact fever peaks, or precise intercurrent viral etiologies. Third, retrospective data extraction inherently relies on documented medical records, limiting our ability to independently verify exact parental adherence to daily medication schedules or capture mild, undocumented breakthrough episodes managed at home. Despite these limitations, this study provides vital tertiary-care data representing pediatric neurological practice within Libya.

Conclusion

In this retrospective comparative study of pediatric patients with recurrent complex febrile seizures, prophylactic sodium valproate (Depakin) did not yield a statistically significant reduction in seizure recurrence compared to unexposed controls (20.0% vs. 24.4%, p = 0.57). Given the retrospective design, potential selection biases, and established pharmacological risks associated with chronic valproate therapy in early childhood, routine continuous prophylaxis cannot be universally endorsed. Management must remain strictly individualised, prioritising rigorous baseline screening (LFTs, CBC, amylase, coagulation profile), parental education, and acute rescue protocols. Comprehensive multi-centre prospective randomised controlled trials are warranted to further define optimal therapeutic algorithms.

Recommendations

Routine continuous pharmacologic prophylaxis should not be universally prescribed for all children presenting with complex febrile seizures; treatment decisions must be highly individualised based on recurrence frequency, electroclinical characteristics, and caregiver preference. Whenever sodium valproate (Depakin) or other antiseizure agents are initiated, mandatory baseline laboratory evaluations—comprising liver function tests (LFTs), complete blood count (CBC) with platelet count, serum amylase, and coagulation profiles—must be performed and documented as normal, accompanied by scheduled periodic monitoring. Future investigations should focus on large-scale, multi-centre, prospective randomised controlled trials incorporating standardised follow-up intervals, rigorous adherence tracking, and multivariable control for confounding variables to definitively establish the risk-benefit ratio of prophylactic regimens.

Conflict of Interest

The author declares no conflict of interest.

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