Acta Scientific Pharmaceutical Sciences (ISSN: 2581-5423)

Volume 9 Issue 7 July 2025

Research Article

Safety Evaluation of Perampanel in the Pediatric Population: FAERS Database Analysis and Signal Mining

Hui Jing[1], Jing Tang[1], Yan Zhang[2], Xiting Tang[1], Chengliang Wang[1]* and Li Chen[3-5]

[1]Department of Pharmacy, People's Hospital of Ganzi Tibetan Autonomous Prefecture, Kangding 626000, China

[2]People's Hospital of Ganzi Tibetan Autonomous Prefecture, Kangding 626000, China

[3]Department of Pharmacy, West China Second University Hospital, Sichuan University, Chengdu, Sichuan, China

[4]Chinese Evidence-Based Medicine Center, West China Hospital, Sichuan University, Chengdu, Sichuan, China

[5]Department of Pharmacology, Faculty of Medicine and Nursing, University of the Basque Country, Leioa, Spain

***Corresponding Author:** Chengliang Wang, Department of Pharmacy, People's Hospital of Ganzi Tibetan Autonomous Prefecture, Kangding 626000, China.

Received: June 23, 2025

Published: June 30, 2025

Abstract

Objective: This study aimed to systematically evaluate the safety profile of perampanel in pediatric patients by analyzing adverse drug events (ADEs) reported in the FDA Adverse Event Reporting System (FAERS) database, identifying potential safety signals, and characterizing adverse drug reactions (ADRs) not documented previously.

Methods: A retrospective pharmacovigilance analysis was conducted using ADE reports from the FAERS database between 2012 and 2024, covering 52 consecutive quarters. The study population was stratified into four age groups: infants (0-2 years), preschool children (2-6 years), children (6-13 years), and adolescents (13-18 years). The Reporting Odds Ratio (ROR) and MHRA methods were applied to identify significant safety signals.

Results: A total of 394 ADE reports associated with perampanel use in minors were analyzed. The most frequently reported adverse reactions included aggression, somnolence, and seizures, with notable variations observed across different age groups. The most common adverse events were neurological and psychiatric disorders, such as aggression, epilepsy exacerbation, and somnolence. Several previously unrecognized adverse drug reactions (ADRs), including acute kidney injury, respiratory failure, psychotic disorders, and urinary retention, were identified.

Conclusion: The analysis identified significant safety signals for perampanel in pediatric populations, particularly involving neurological and psychiatric systems. Clinicians should implement individualized monitoring strategies tailored to different pediatric age groups to effectively detect and manage potential ADRs. Future prospective and comparative studies are recommended to further

Keywords: Perampanel; Pediatric Population; FAERS; Adverse Drug Reactions; Signal Detection; Pharmacovigilance

Introduction

Epilepsy is a common neurological disorder globally, with a notably higher incidence among minors [1]. This disorder presents serious health challenges to patients and places a considerable financial burden on their families [2]. The World Health Organization (WHO) reports that epilepsy is among the most prevalent chronic neurological disorders in minors, marked by diverse clinical presentations and substantial treatment challenges [3]. It significantly affects the growth, development, and social adaptation of affected individuals. Recent advancements in medical research have facilitated the development and clinical adoption of novel antiepileptic drugs (AEDs), markedly enhancing treatment outcomes and patients' quality of life [4]. However, the unique physiological characteristics of minors raise concerns about the safety, efficacy, and long-term risks of these medications in comparison to adults [5].

Perampanel (PER), a novel non-competitive AMPA receptor antagonist, was approved by the U.S. Food and Drug Administration (FDA) in 2012 for epilepsy treatment and has since been widely adopted worldwide [6]. Its distinct pharmacological mechanism offers a novel therapeutic approach for refractory epilepsy, with well-documented efficacy and safety in adults [7]. However, substantial physiological differences between minors and adults, including hepatic and renal function development, drug-metabolizing enzyme activity, and pharmacodynamic responses, may impact drug safety and efficacy [8]. Therefore, further research is warranted to assess the efficacy and safety of perampanel in minors [9]. Although perampanel's indication has been extended to include children aged four years and older, safety data for this population remain scarce [10].

Research on the safety of perampanel in minors remains limited [11]. Most studies have concentrated on adult patients or specific pediatric age groups, with limited comprehensive analysis of adverse drug reactions (ADRs) across the entire minor population [12]. Therefore, establishing the safety profile of perampanel in minors through real-world data is of considerable clinical significance. This study conducted a retrospective analysis of 52 quarters of complete data (2012-2024) from the FDA Adverse Event Reporting System (FAERS) to systematically identify and assess safety signals associated with perampanel in minors [13]. The primary objective was to identify potential safety risks, characterize adverse events, and offer evidence-based recommendations for clinicians, pharmacists, and regulatory authorities to optimize treatment strategies and minimize drug-related risks. Furthermore, the findings of this study may provide valuable insights into the safety of other antiepileptic drugs in minors, ultimately contributing to improved pharmacological treatment safety and efficacy in this population [14].

Materials and Methods

Data source

This study utilized data from the U.S. Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS), a comprehensive pharmacovigilance database. The FAERS database is updated quarterly and contains post-marketing adverse event reports, including data on report frequency, patient demographics (age and gender), and adverse event severity. The database comprises seven primary tables: the demographic and administrative data table (DEMO), drug information table (DRUG), adverse reaction table (REAC), patient outcome table (OUTC), report source table (RPSR), therapy start and end date table (THER), drug indication/diagnosis table (INDI), and deleted cases table (DELETED).

Data processing

During data processing, the study population was stratified into four age groups following PubMed classification standards: infants (0-2 years), preschool children (2-6 years), children (6-13 years), and adolescents (13-18 years) [15]. The study period encompassed 52 quarters, spanning from Q1 2012 to Q4 2024. Records containing the generic name "Perampanel" or the brand name "Fycompa" were extracted and processed in accordance with FDA deduplication guidelines [16]. If duplicate CASEIDs were identified, the record with the most recent report date (FDA_DT) was retained. If CASEID and FDA_DT were identical, the record with the highest PRIMARYID was retained. Entries recorded in the DELETED table were removed from the dataset. Data extraction and processing were performed using MySQL 8.0.

Data standardization

The FAERS database is structured according to the International Council for Harmonisation (ICH) Medical Dictionary for Regulatory Activities (MedDRA) [17,18]. This study utilized MedDRA version 27.1 to classify adverse drug events (ADEs) according to System

Organ Class (SOC) and Preferred Terms (PT). Standardization ensures uniformity in ADE classification, aligning with international regulatory guidelines and enhancing the precision of subsequent analyses.

Data analysis

Initially, the number of ADE reports associated with the target drug was extracted, and a disproportionality analysis (fourfold table) was applied to identify potential adverse event signals (Table 1) [19]. Subsequently, the Reporting Odds Ratio (ROR) and the combined standard method (MHRA) were utilized to compute ROR, the Proportional Reporting Ratio (PRR), and the chi-square (X^2) statistic [20-22]. To minimize false-positive signals, only values surpassing predefined thresholds were classified as valid signals (Table 2). Higher numerical values denote stronger signals, indicating a potential association between the target drug and specific adverse events; however, causality cannot be inferred [23].

Table 1: Fourfold table of measures of disproportionality.

Drug Category	Adverse event of interest	All other adverse events	Total
Drug of interest	a	b	a+b
All other drugs in FAERS	c	d	c+d
Total	a+c	b+d	N= a+b+c+d

Table 2: Formulas and thresholds of the ROR method and the MHRA method.

Method	Formula	Threshold value
ROR	ROR=ad/bc SE lnROR = $95\%CI= e^{\ln(ROR) \pm 1.96\sqrt{(\frac{1}{a}+\frac{1}{b}+\frac{1}{c}+\frac{1}{d})}}$	a signal is detected, if a≥3,and the lower limit of the 95%(ROR) 1
MHRA	PRR= $X^2=\frac{[(ad-bc)^2]*N}{(a+b)(c+d)(b+d)(a+c)}$	a signal is detected, if a≥3, and PRR≥2, and X2≥4

Results

Basic information on ADE reports

This study analyzed 394 adverse drug event (ADE) reports related to perampanel use in minors for signal detection. Regarding gender distribution, male patients constituted 50.25% of cases, female patients 44.42%, and 5.33% had unspecified gender. In terms of age distribution, ADE reports were most frequently observed in the adolescent group (52.03%), followed by the child group (31.47%), while reports were relatively infrequent in the preschool children and infant groups. The majority of reports (91.88%) were submitted by healthcare professionals, indicating their central role in pharmacovigilance. Geographically, Japan (84 cases) and the United States (73 cases) accounted for the highest number of reports.

In the analysis of severe outcomes, hospitalization was most frequently reported in adolescents (89 cases), followed by children (55 cases). Major medical events (OT) were predominantly observed in adolescents (71 cases) and children (55 cases). Life-threatening events (LT) were primarily reported in adolescents (23 cases), with fewer occurrences in children (4 cases). Additionally, fatal cases (DE) were more prevalent in adolescents (12 cases) than in children (4 cases). The detailed distribution is illustrated in Figure 1.

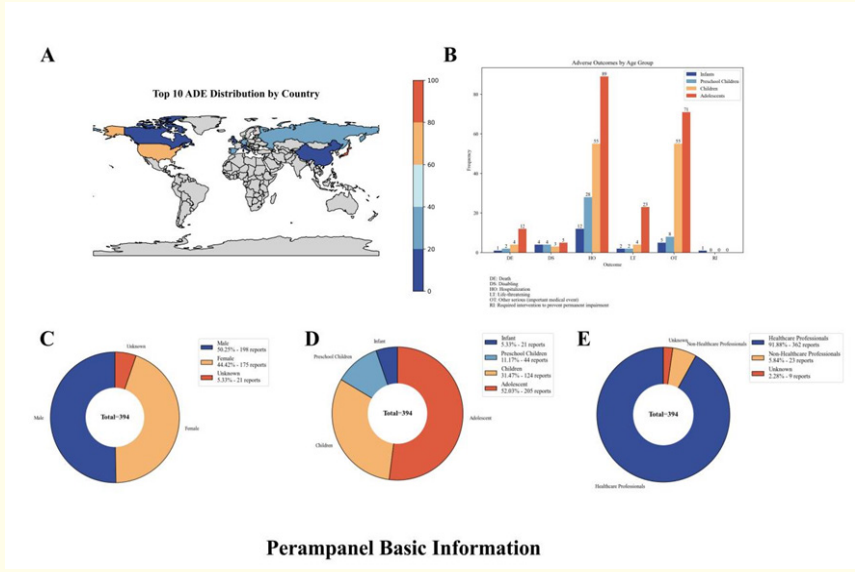

Figure 1: Basic Characteristics of Perampanel Use in Minors.

Distribution of system organ class (SOC) of ADEs across different age groups

An analysis of ADEs by System Organ Class (SOC) across different age groups demonstrated notable variations among groups. Among infants, ADEs were most frequently associated with renal and urinary disorders (62.50%, primarily acute kidney injury), followed by gastrointestinal disorders (18.75%, including vomiting and diarrhea) and congenital and genetic disorders (18.75%, primarily developmental delay).In preschool children, injury, poisoning, and procedural complications were the most common ADEs (41.30%, primarily accidental drug ingestion), followed by gastrointestinal disorders (36.96%, including vomiting and abdominal pain). Infectious and parasitic diseases (15.22%, primarily pneumonia) were also observed.Among children, ADEs were predominantly classified as nervous system disorders (42.86%, including status epilepticus and somnolence) and psychiatric disorders (38.57%, including aggression, agitation, and abnormal behavior). Additionally, injury, poisoning, and procedural complications (7.86%) were documented.Among adolescents, psychiatric disorders (45.53%, including aggression, agitation, and abnormal behavior) were the most frequently reported ADEs, followed by nervous system disorders (29.57%, including altered consciousness and seizures). Injury, poisoning, and procedural complications (8.56%), as well as infectious and parasitic diseases (4.28%), were also observed. The detailed SOC classification distribution is illustrated in Figure 2.

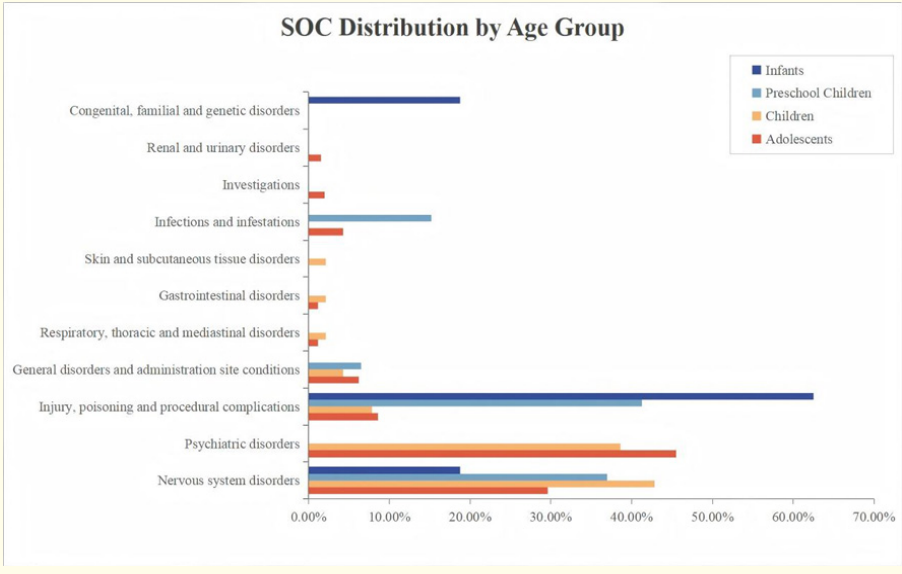

Figure 2: SOC Distribution by Age Group.

ADE signal detection results

A systematic analysis of 394 ADE reports associated with perampanel identified 49 Preferred Terms (PTs), as summarized in Table 3. The most frequently reported adverse events were aggression (68 cases), somnolence (36 cases), and seizures (33 cases). Calculation of the Reporting Odds Ratio (ROR) indicated that the three adverse events with the highest ROR values were elevated anticonvulsant drug levels (ROR 280.3, 95% CI: 105.89-741.98), status epilepticus (ROR 99.95, 95% CI: 35.64-280.34), and aggression (ROR 46.88, 95% CI: 33.73-65.15).Notably, of the 49 identified PTs, 20 (40.82%) were newly detected ADRs that were not previously listed in the drug's prescribing information. These newly identified ADRs are indicated with an asterisk (*) in Table 3.

Perampanel ADE Case Counts and Reporting Odds Ratios in Children by Age Group

Rank		Infants		Preschool Children		Children		Adolescents	
	PT	Cases	ROR Value (95%Cl)	Cases	ROR Value (95%Cl)	Cases	ROR Value (95%Cl)	Cases	ROR Value (95%Cl)
1	Ventricular septal defect*	3	11.77(3.46,40.01)						
2	Dysphagia					3	6.33(2.01,19.95)	3	4.82(1.54,15.11)
3	Asthenia					3	3.9(1.24,12.29)	6	3.85(1.71,8.68)
4	Drug interaction							7	4.25(2.00,9.03)
5	Fatigue			3	6.37(1.97,20.61)				
6	Gait disturbance					3	5.7(1.81,17.95)	3	3.92(1.25,12.29)
7	Infection*							3	3.55(1.13,11.13)
8	Pneumonia*			7	9.92(4.41,22.28)			5	3.27(1.34,7.94)
9	Pneumonia aspiration*							3	16.71(5.31,52.61)
10	Accidental exposure to product by child			8	5.12(2.38,11.03)				
11	Accidental overdose			7	9.5(4.23,21.35)				
12	Drug administered to patient of inappropriate age					5	5.41(2.21,13.26)		
13	Fall							11	14.1(7.66,25.96)
14	Foetal exposure during pregnancy	10	4.68(1.99,11.03)						
15	Intentional overdose							11	2.18(1.19,4.00)
16	Product administered to patient of inappropriate age					6	13.65(5.99,31.13)		
17	Product use issue			4	3.2(1.14,8.96)				
18	Anticonvulsant drug level increased*							5	280.3(105.89,741.98)

19	Altered state of consciousness*							10	25.84(13.61,49.06)
20	Ataxia			5	28.43(11.14,72.57)	5	28.2(11.42,69.61)		
21	Coma*			3	21.85(6.72,71.01)				
22	Disturbance in attention*							3	4.6(1.47,14.41)
23	Dizziness					5	4.24(1.73,10.39)	9	2.73(1.4,5.33)
24	Dysarthria*							3	6.31(2.01,19.78)
25	Epilepsy					5	8.3(3.38,20.36)	5	7.59(3.12,18.49)
26	Loss of consciousness			3	14.43(4.45,46.80)				
27	Petit mal epilepsy					3	15.07(4.76,47.69)		
28	Psychomotor hyperactivity*							3	9.05(2.88,28.40)
29	Seizure					14	5.78(3.31,10.10)	19	6.73(4.20,10.81)
30	Seizure cluster					4	99.95(35.64,280.34)		
31	Somnolence	3	11.55(3.40,39.25)	6	8.94(3.77,21.18)	18	13.99(8.47,23.10)	9	3.11(1.59,6.06)
32	Status epilepticus					6	22.09(9.67,50.48)	10	29.44(15.49,55.94)
33	Tremor							5	3.39(1.39,8.23)
34	Abnormal behaviour*					4	2.82(1.04,7.64)		
35	Aggression					21	14.7(9.18,23.55)	47	46.88(33.73,65.15)
36	Agitation*					4	4.14(1.53,11.23)	13	9.98(5.68,17.53)
37	Anger					3	3.58(1.14,11.28)	6	10.44(4.62,23.59)
38	Depressed mood							3	3.95(1.26,12.37)
39	Hallucination*					4	5.91(2.18,16.03)		
40	Homicidal ideation					3	50.18(15.63,161.07)		
41	Irritability					6	7.12(3.13,16.21)	7	9.34(4.38,19.89)
42	Psychotic disorder*					3	14.79(4.68,46.81)	10	21.51(11.34,40.81)
43	Restlessness*							4	11.07(4.10,29.9)
44	Suicidal ideation					6	7.68(3.37,17.47)	13	6.72(3.82,11.79)
45	Suicide attempt							14	4.26(2.47,7.33)
46	Urinary retention*							4	11.65(4.31,31.47)
47	Acute respiratory failure*							3	18.66(5.92,58.81)
48	Respiratory failure*					3	5.14(1.63,16.19)		
49	Drug reaction with eosinophilia and systemic symptoms*					3	5.91(1.87,18.62)		

Table 3: ADE PT Distribution In Minors Using Perampanel.

Discussion

Analysis of ADE reporting characteristics in minors using perampanel

This study systematically analyzed 394 adverse drug event (ADE) reports associated with perampanel use in minors utilizing the FAERS database [12]. In terms of gender distribution, male (50.25%) and female (44.42%) patients were reported in similar proportions, with no significant differences observed. This finding suggests that gender may not be a key determinant of perampanel-associated adverse events; however, further studies are required for validation. With respect to age distribution, the adolescent group (13-18 years) had the highest number of reports (52.03%), followed by the child group (6-13 years, 31.47%), whereas reports from preschool children and infants were comparatively rare. This trend may be attributed to the current clinical indications of perampanel, which primarily recommend its use in children aged four years and older [10]. Moreover, the higher prevalence of epilepsy in adolescents, frequent medication use, complex treatment regimens, and age-dependent metabolic and adherence factors may contribute to the increased ADE reports in this group. Geographically, the highest number of ADE reports originated from Japan (84 cases) and the United States (73 cases). This may be attributed to perampanel's initial approval and widespread use in these countries [6]. Furthermore, both nations have well-established pharmacovigilance systems, and higher awareness among healthcare professionals and the public likely contributes to increased reporting of drug safety events. Analysis of reporting sources revealed that most reports (91.88%) were submitted by healthcare professionals, emphasizing their pivotal role in pharmacovigilance. Future research should promote greater involvement of patients and their families in ADE reporting to improve data completeness.

Regarding severe adverse events, the adolescent group had significantly higher rates of hospitalization, major medical events (OT), life-threatening events (LT), and fatal cases (DE) compared to other age groups [9]. This may be due to the incomplete maturation of the nervous system, differences in drug metabolism, and the complexity of treatment regimens in this age group. Therefore, enhanced drug safety monitoring is essential in clinical practice for adolescent patients. Comprehensive assessment of medication risks, rational treatment planning, and cautious dose adjustments should be prioritized. A particularly alarming concern is the occurrence of fatal cases. This study identified 16 fatal cases, of which 12 occurred in the adolescent group and 4 in the child group. This finding indicates a potential risk of fatal outcomes related to perampanel use in minors. These fatal events may result from multiple factors, including drug overdose, central nervous system depression, severe complications, or drug interactions. However, the FAERS database has inherent limitations, including the lack of comprehensive patient clinical background, medical history, and detailed medication records, making it difficult to establish a direct causal relationship between perampanel and fatal events. Future studies should perform an in-depth analysis of clinical data on fatal cases to identify potential risk factors and develop strategies to mitigate severe adverse reactions in minors using perampanel.

Analysis of common adverse drug events (ADEs)

This study utilized the FAERS database to analyze common adverse drug events (ADEs) associated with perampanel use in minors and identified significant age-related differences based on System Organ Class (SOC) and Preferred Terms (PTs) [17]. Among infants, ADEs were predominantly associated with renal and urinary disorders (62.50%), primarily manifesting as acute kidney injury. Additionally, this age group exhibited gastrointestinal disorders (18.75%, including vomiting and diarrhea) and congenital or genetic disorders (18.75%, such as developmental delay). Due to the incomplete renal development during infancy, which reduces drug metabolism and excretion capacity, the risk of drug accumulation and kidney injury is elevated. Therefore, renal function monitoring and individualized dose adjustments are essential for this population. Among preschool children, ADEs were primarily classified as injury, poisoning, and procedural complications (41.30%, mainly accidental drug ingestion), followed by gastrointestinal disorders (36.96%, including vomiting and abdominal pain). Additionally, infectious and parasitic diseases (15.22%, primarily pneumonia) were reported, highlighting potential risks related to drug tolerance and household medication management in preschool children. In clinical practice, strengthening medication safety education for parents and caregivers is crucial to preventing accidental ingestion or overdose and monitoring for secondary infections. In children and adolescents, ADEs were most commonly associated with nervous system disorders (42.86% and 29.57%, respectively) and psychiatric disorders (38.57% and 45.53%, respectively) [24]. These ADEs primarily manifested as status epilepticus, somnolence, aggression, and agitation, potentially resulting from neurotransmitter

alterations due to perampanel's non-competitive antagonism of AMPA glutamate receptors. As these age groups are in crucial stages of neurodevelopment and psychological maturation, they may demonstrate increased sensitivity to the drug's effects. Therefore, regular evaluations and vigilant monitoring of neurological and psychiatric changes are recommended to facilitate early identification and management of ADEs. Furthermore, therapeutic drug monitoring (TDM) is recommended to optimize the safety and efficacy of perampanel therapy.

Clinical significance of newly identified adverse drug reactions (ADRs)

This study conducted an in-depth analysis of the FAERS database and identified several previously unreported adverse drug reactions (ADRs) associated with perampanel use in minors [19]. These newly identified ADRs have significant clinical implications and warrant careful consideration by clinicians and pharmacists. Further research is needed to confirm these findings. Among infants, ventricular septal defect was identified as a newly detected ADR, highlighting the need for close monitoring of cardiac structure and function when prescribing perampanel to this age group. Infants with a predisposition to congenital heart abnormalities should undergo regular echocardiographic assessments for early detection and timely intervention. Among preschool children, newly identified ADRs included coma and pneumonia. Coma may result from the central nervous system depressant effects of perampanel, necessitating rigorous monitoring of patients' consciousness levels. Pneumonia could arise from immune suppression or accidental aspiration during treatment, underscoring the importance of infection risk assessment and management in this population. Among children, newly identified ADRs included abnormal behavior, psychotic disorders, and respiratory failure, all of which are severe. Abnormal behavior and psychotic disorders may be associated with perampanel-induced neurotransmission disruption, necessitating close psychiatric monitoring and early intervention. Due to the severity of respiratory failure, further research is needed to elucidate its underlying mechanisms and risk factors and to develop effective clinical prevention strategies. Among adolescents, the highest number of newly identified ADRs was observed, including acute respiratory failure, altered consciousness, elevated anticonvulsant drug levels, psychomotor hyperactivity, and urinary retention [23]. These ADRs may suggest substantial central nervous system and respiratory depression, requiring vigilant clinical monitoring and timely intervention.

Clinical risk management and safety monitoring recommendations

This study identified distinct safety risks related to perampanel use in minors, emphasizing the necessity of individualized risk management and targeted safety monitoring strategies in clinical practice. Among infants, close monitoring of renal function markers (e.g., serum creatinine, blood urea nitrogen) and cardiac structure (via echocardiography) is recommended to enable early detection and prevention of acute kidney injury and potential cardiac abnormalities. Infants with a high risk of congenital heart defects should undergo more frequent monitoring. Among preschool children, accidental drug ingestion and dosing errors represent major concerns. Caregiver education on medication safety should be strengthened, alongside vigilant monitoring of consciousness, respiratory function, and infection risk to prevent aspiration or secondary infections. Among children and adolescents, routine neurological and psychiatric evaluations should be conducted to monitor seizures, somnolence, aggression, and altered consciousness. Therapeutic drug monitoring (TDM) is also recommended to prevent drug accumulation and mitigate associated severe adverse reactions. Given the newly identified severe ADRs—such as acute respiratory failure, altered consciousness, elevated anticonvulsant drug levels, and urinary retention—particular attention should be directed toward monitoring respiratory, neurological, and urinary functions. Healthcare professionals and pharmacists should actively report newly identified ADRs, while regulatory authorities must promptly update drug safety information and refine clinical guidelines to optimize the safe use of perampanel in minors.

Study Limitations and Future Research Directions

This study employed the FAERS database for a retrospective analysis, which is subject to inherent limitations, including underreporting, duplicate entries, incomplete clinical information, and difficulties in establishing causal relationships. Consequently, these findings should be regarded as preliminary evidence of potential drug safety risks rather than definitive conclusions. To enhance the accuracy of perampanel safety assessments in minors, future

studies should consider conducting prospective or large-scale cohort studies to systematically validate adverse event incidence and associated risk factors. Additionally, comparative safety studies evaluating perampanel and other novel antiepileptic drugs in minors are necessary to delineate differences in adverse event profiles and generate robust evidence for clinical decision-making. Furthermore, future research should prioritize elucidating the pharmacological mechanisms underlying perampanel-associated adverse reactions, particularly considering the unique physiological characteristics of minors. Comprehensive investigations into the pharmacokinetics and pharmacodynamics of perampanel in minors will contribute to optimizing treatment strategies and improving the effectiveness of drug safety monitoring.

Conclusion

This study represents the first systematic evaluation of the adverse reaction profile of perampanel in minors using the FAERS database, incorporating a comprehensive signal detection analysis. The findings indicate that the most frequently reported adverse reactions in minors predominantly affect the nervous system and psychiatric domains, with aggression, seizures, and behavioral abnormalities being the most prevalent. These results underscore the importance of clinicians closely monitoring neurological and psychiatric changes in affected patients. Furthermore, this study identified several newly recognized adverse reactions that were not previously documented in the drug's prescribing information, including acute kidney injury, respiratory failure, psychotic disorders, and urinary retention. These findings suggest that the current prescribing information lacks comprehensive safety data for minors and warrants revision to reflect these newly identified risks. In clinical practice, personalized safety monitoring and risk management strategies should be implemented according to the physiological characteristics and pharmacokinetic profiles of different pediatric age groups. Early detection and management of potential adverse reactions are critical for ensuring both treatment safety and efficacy. Future research should prioritize prospective studies and large-scale cohort analyses to validate the adverse reaction signals identified in this study. Further investigation into the pharmacological mechanisms underlying these adverse reactions, alongside comparative safety analyses between perampanel and other antiepileptic drugs, is essential for optimizing clinical decision-making and ensuring the long-term safety and efficacy of perampanel in minors.

Ethics Statement

This study was conducted using the U.S. Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS), a publicly accessible voluntary reporting database. All data were de-identified and contain no personally identifiable information. According to current regulations and the policies of our institution, this type of study does not require approval from an Institutional Review Board nor the acquisition of written informed consent.

Consent to Participate

Because this research relies on publicly available, secondary data that cannot be traced back to specific individuals, no additional informed consent from participants was required.

Conflict of Interest

All authors declare that they have no conflicts of interest related to this study.

Funding

No funding was received for this study.

Authors' Contributions

- Hui Jing: Proposed the study concept, was responsible for the initial study design, literature retrieval, and drafting the manuscript.
- Chengliang Wang*: Oversaw the overall study design and organization, supervised the progress, guided data analysis, and revised the final manuscript.
- Yan Zhang: Participated in data collection and organization.
- Jing Tang: Conducted part of the statistical analysis, and assisted with reviewing and editing the manuscript.
- Xiting Tang: Assisted with data processing, figure creation, and result verification.
- Li Chen*: Provided research resources and technical support, offered key suggestions on the study design, and approved the final manuscript.

All authors have read and approved the final submitted version.

Bibliography

1. Beghi E., *et al*. "Global epidemiology of epilepsy: a systematic review and meta-analysis". *Lancet Neurology* 18.4 (2019): 357-375.

2. Zack MM., *et al*. "National and State Estimates of the Numbers of Adults and Children with Active Epilepsy — United States 2015". *Morbidity and Mortality Weekly Report* 66.31 (2017): 821-825.

3. World Health Organization. Epilepsy: a public health imperative. Geneva: WHO (2019).

4. Knight EMP., *et al*. "Safety and efficacy of ganaxolone in patients with CDKL5 deficiency disorder: results from the double-blind phase of a randomised, placebo-controlled, phase 3 trial". *Lancet Neurology* 21.5 (2022): 417-427.

5. Anderson GD and Holford NHG. "Pharmacokinetics in children: developmental aspects". *British Journal of Anaesthesia* 120.5 (2018): 949-962.

6. French JA., *et al*. "Adjunctive perampanel for refractory partial-onset seizures: Randomized phase III study 304". *Neurology* 79.6 (2012): 589-596.

7. Chen Y., *et al*. "Efficacy and safety of perampanel in epilepsy: A systematic review and meta-analysis of randomised controlled trials". *Seizure* 101 (2022): 135-143.

8. Ramiro E., *et al*. "Factors and mechanisms for pharmacokinetic differences between pediatric population and adults". *Pharmaceutics* 3.1 (2011): 53-72.

9. Wang X., *et al*. "Real-world effectiveness and safety of perampanel for children and adolescents with epilepsy: A meta-analysis with at least 1-year follow-up". *Seizure* 119 (2024): 1-9.

10. Renfroe JB., *et al*. "Adjunctive perampanel oral suspension in pediatric patients from ≥2 to <12 years of age with epilepsy: Pharmacokinetics, safety, tolerability, and efficacy". *Journal of Child Neurology* 34.5 (2019): 268-275.

11. Fogarasi A., *et al*. "An evidence-based review on the use of perampanel for the treatment of focal-onset seizures in pediatric patients". *Neuropsychiatric Disease and Treatment* 15 (2019): 2789-2796.

12. Zhang J., *et al*. "Mining and analysis of adverse drug reactions associated with perampanel based on FAERS database". *Epilepsy Behavior* 144 (2023): 109256.

13. Gil-Nagel A., *et al*. "Long-term efficacy and safety of adjunctive perampanel in pediatric patients aged 4–19 years with epilepsy: A real-world study." *Scientific Report* 13 (2023): 13311.

14. Pellock JM., *et al*. "Extrapolating evidence of antiepileptic drug efficacy in adults to children ≥2 years of age with focal seizures: The case for disease similarity". *Epilepsia* 58.10 (2017): 1686-1696.

15. MEDICINE NLO. Age Groups EB/OL. (1998-2023-04-02).

16. Hu Y., *et al*. "Colitis following the use of immune checkpoint inhibitors: A real-world analysis of spontaneous reports submitted to the FDA adverse event reporting system". *International Immunopharmacology* 84 (2020): 106601.

17. SAKAEDA T., *et al*. "Data mining of the public version of the FDA Adverse Event Reporting System". *International Journal of Medical Sciences* 10.7 (2013): 796-803.

18. OMAR N E., *et al*. "Post marketing safety of anaplastic lymphoma kinase (ALK) inhibitors: an analysis of the FDA Adverse Event Reporting System (FAERS)". *ESMO Open* 6.6 (2021): 100315.

19. Luo L., *et al*. "Mining of adverse event signals of tocilizumab based on the FAERS database". *China Pharmacy* 32.15 (2021): 1874-1879.

20. CHEN J J., *et al*. "Data mining for adverse drug reaction signals of daptomycin based on real-world data: a disproportionality analysis of the US Food and Drug Administration adverse event reporting system". *International Journal of Clinical Pharmacy* 44.6 (2022): 1351-1360.

21. SAKAEDA T., *et al*. "Adverse event profiles of platinum agents: data mining of the public version of the FDA adverse event reporting system, AERS, and reproducibility of clinical observations". *International Journal of Medical Sciences* 8.6 (2011): 487-91.

22. Jin ZY., *et al*. "Signal detection of dementia-related events associated with benzodiazepines based on FAERS database". *Drug Evaluation Research* 40.10 (2021): 1356-1360.

23. Zhou Y., *et al*. "Difference in gastrointestinal risk associated with use of GLP-1 receptor agonists: a real-world pharmacovigilance study". *Diabetes, Metabolic Syndrome and Obesity* 15 (2022): 155-163.

24. Birnbaum AK., *et al*. "Antiepileptic drug exposure in children and adults: longitudinal analysis of the FDA Adverse Event Reporting System". *Epilepsia Open* 6.2 (2021): 467-475.