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Evaluation of the clinical characteristics of antiepileptic drug poisoning in children: A retrospective cross-sectional study

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Abstract

Aim: The objective of this study was to delineate the clinical and laboratory manifestations of antiepileptic drug toxicity in pediatric patients, to ascertain the characteristics of intoxication according to age group, and to appraise the management of these patients.

Methods: This retrospective, cross-sectional, descriptive study included 39 pediatric patients aged 1 month to 18 years who presented with antiepileptic drug poisoning to a tertiary pediatric emergency department between January 1, 2014, and December 31, 2017. Demographic characteristics, clinical presentations, laboratory and electrocardiogram findings, antiepileptic drug types and levels, gastrointestinal decontamination practices, hospitalization units, length of stay, and outcomes were recorded. Patients were stratified by poisoning intent (accidental vs. intentional) and age group. Continuous variables were compared using the Mann–Whitney U test, while categorical variables were analyzed using the Pearson chi-square test, continuity correction chi-square test, or Fisher's exact test, as appropriate. A two-sided p-value of ≤0.05 was considered statistically significant.

Results: Twenty-two (56.4%) of the cases were accidental, while 17 (43.6%) were intentional and aimed at self-harm. Twenty-five (64.1%) of the patients had no underlying disease; however, seven (17.9%) had epilepsy, three (7.8%) had epilepsy and intellectual disability, two (5.1%) had bipolar disorder, one (2.6%) had substance addiction, and one (2.6%) had syncope. Among the patients, 18 (46.2%) were poisoned with carbamazepine, 13 (33.3%) with sodium valproate, two (5.1%) with phenobarbital, two (5.1%) with diazepam, one (2.6%) with clonazepam, one (2.6%) with levetiracetam, one (2.6%) with oxcarbazepine, and one (2.6%) with lacosamide. All self-harm cases (n = 17) involved individuals aged ≥ 12 years, and a positive correlation was observed between age and self-harm cases, particularly at age 12 and above (p = 0.001). Girls were more likely to engage in self-harm, whereas boys were more likely to be accidentally poisoned (p = 0.011). Additionally, a significant relationship was observed between self-harm cases and multiple drug ingestion (p = 0.022).

Conclusion: The present study observed a higher frequency of poisoning cases involving carbamazepine and sodium valproate, which are frequently used for epilepsy and non-epileptic indications, compared to other antiepileptic drugs. It is imperative for clinicians to exercise caution and refrain from prescribing these medications in excessive quantities or at elevated doses. It is also noteworthy that symptoms of poisoning may emerge even in cases where the antiepileptic dose is non-toxic or the drug level is low.

Keywords: Antiepileptic drugs, poisoning, childhood, accident, self-harm

Introduction

Epilepsy is one of the most common neurological diseases in childhood (1). Accordingly, antiepileptic drugs (AEDs) are frequently prescribed and stored in households for long periods. Although AEDs account for a smaller proportion of pediatric poisonings than some other medication classes, their narrow therapeutic index and central nervous system toxicity make overdoses clinically important. Accidental ingestions are typically seen in younger children, whereas intentional ingestions are more common in adolescents (2, 3). Children diagnosed with epilepsy are more likely to exhibit behavioral problems, and the challenges associated with caregiving may result in an increased incidence of accidents and undesirable situations (4, 5). Despite their ostensible innocuousness, AEDs have the potential to induce excessive adverse effects, including central nervous system suppression, respiratory arrest, arrhythmia, behavioral changes, agitation, and gastrointestinal symptoms, such as vomiting and abdominal pain (6).

In recent years, there has been an increase in acute poisoning with antiepileptic drugs in children. The clinical signs and symptoms of overdose can be difficult to recognize and diagnose. Current treatment is based on cardiac and respiratory support, fluid management, and correction of electrolyte imbalances. Some authors have used activated charcoal and extracorporeal circulation techniques for drug removal in the most severe cases (7).

This study aimed to determine the frequency of AED drug poisoning, identify which AEDs pose a higher risk of poisoning in children using these medications, and investigate the measures needed to prevent such incidents.

Materials and Methods

The study design was retrospective, cross-sectional, and descriptive. Ethical approval was obtained from the Clinical Research Ethics Committee of the University of Health Sciences, Ankara Pediatric Health and Diseases Hematology Oncology Training and Research Hospital, in accordance with the ethical standards of the 2024 Declaration of Helsinki (approval number and date: 2019-064, March 25, 2019).

This study included children aged 1 month to 18 years who were diagnosed with antiepileptic drug (AED) poisoning and presented to the Pediatric Emergency Department of the University of Health Sciences, Ankara Dr. Sami Ulus Maternity, Child Health, and Diseases Research Center between January 1, 2014, and December 31, 2017.

A comprehensive evaluation was conducted, encompassing the patients' medical histories, physical examination findings, laboratory and electrocardiogram (ECG) results, hospitalization status, intensive care needs, mortality status, follow-up duration, and the presence of any underlying morbidity. The poisoning symptoms were then compared by age group. In addition, cases of intentional versus unintentional poisoning were analyzed, as well as the frequency of the drug involved.

Cases with toxic blood levels of antiepileptic drugs or doses exceeding toxic thresholds based on age and weight, and those exhibiting dramatic and/or life-threatening symptoms, which were classified as acute or acute-on-chronic poisoning.

The inclusion criteria for the study were as follows:

- The participants' ages ranged from 1 month to 18 years.
- Presence of acute and/or acute-on-chronic antiepileptic drug poisoning.
- The presence of clinical symptoms was also a prerequisite for inclusion.
- Central nervous system: dose-related neurotoxicity, drowsiness, sedation, ataxia, nystagmus, dizziness, somnolence, speech disorder, psychomotor slowing, tics, diplopia, depressive mood changes, aggressive outbursts, cognitive dysfunction, vertigo, seizures, tremor, rigidity, hypokinesia, akinesia, hyperkinesia, and paresthesia.
- Gastrointestinal System: Increased saliva and secretions, recurrent nausea, and vomiting episodes.
- The respiratory system may exhibit the following signs: Apnea, hypoventilation, laryngospasm, respiratory depression, and arrest.
- Cardiovascular system: Bradycardia, hypotension, syncope, electrocardiographic (ECG) changes, and elevated cardiac enzymes.
- Skin: Exfoliative dermatitis, rash, Stevens-Johnson syndrome, and hair loss.
- Urinary system: Decreased urine output, enuresis, polyuria, and polydipsia.
- Hematological System: Leukopenia, agranulocytosis, and thrombocytopenia.
- Additional manifestations: Hyponatremia, fever, hyperammonemia, encephalopathy, and liver and pancreatic toxicity.
- A history of ingestion of toxic doses or documented elevated drug levels is also a contraindication.

The exclusion criteria were as follows:

- Common mild side effects observed within therapeutic ranges.

Statistical analysis

The obtained data were statistically analyzed using the Statistical Package for Social Sciences (SPSS) software (Version 25.0; IBM Inc., Armonk, NY, US). Descriptive statistics for categorical variables are expressed as frequencies and percentages. Continuous variables are reported as mean ± standard deviation (SD) and median (minimum–maximum) values. The normality of the

continuous data distribution was evaluated using visual methods, including histograms and probability plots, as well as analytical methods such as the Kolmogorov-Smirnov and Shapiro-Wilk tests. As the continuous variables did not exhibit a normal distribution, nonparametric analytical approaches were used for all group comparisons. The Mann–Whitney U test was employed to compare continuous variables between two independent groups. Associations between categorical variables were assessed using the Pearson chi-square test, continuity correction chi-square test, or Fisher's exact test, as appropriate based on expected cell counts. A two-sided p-value of ≤0.05 was considered statistically significant.

Results

A total of 39 pediatric patients were included. Most patients were female (28; 71.8%), and 11 (28.2%) were male. The mean age was 8.84 ± 5.98 years. According to age, 15 patients (38.6%) were <5 years, 12 (30.7%) were 5–13 years, and 12 (30.7%) were ≥14 years. Regarding comorbidity, 25 patients (64.1%) had no chronic/underlying disease, whereas epilepsy was present in 7 (17.9%), epilepsy with mental retardation in 3 (7.7%), bipolar disorder in 2 (5.1%), drug addiction in 1 (2.6%), and arrhythmia in 1 (2.6%). Poisoning was accidental in 22 patients (56.4%) and due to a suicide attempt in 17 patients (43.6%). Multiple-drug ingestion occurred in 14 patients (35.9%). The most common primary antiepileptic drugs involved were carbamazepine (18; 46.2%) and sodium valproate (13; 33.3%); less frequently, phenobarbital (2; 5.1%), diazepam (2; 5.1%), levetiracetam (1; 2.6%), clonazepam (1; 2.6%), lacosamide (1; 2.6%), and oxcarbazepine (1; 2.6%) were implicated. Gastrointestinal decontamination (activated charcoal and/or gastric lavage) was performed in 36 patients (92.3%). Clinically, 22 patients (56.4%) were asymptomatic despite toxic-dose ingestion. Central nervous system manifestations were observed in 13 patients (33.3%), while respiratory and gastrointestinal symptoms were each recorded in 2 patients (5.1%). ECG findings were normal in all cases (39; 100%). Laboratory evaluation was normal in 38 patients (97.4%), with elevated liver function enzymes detected in 1 patient (2.6%). In terms of disposition, 21 patients (53.8%) were managed in the pediatric emergency department, 12 (30.8%) were admitted to the pediatric intensive care unit, and 6 (15.4%) were hospitalized in the general pediatric ward. The overall length of stay was 45.21 ± 32.12 hours. Mean hospitalization time by unit was 76.67 ± 43.56 hours in the general pediatric ward, 61.92 ± 27.54 hours in the pediatric intensive care unit, and 26.67 ± 15.59 hours in the pediatric emergency department. All patients were discharged in good health (39; 100%) (Table 1). Compared with accidental ingestions, the suicide-attempt group had a higher proportion of female patients (94.1% vs. 54.5%; p = 0.011) and a significantly higher mean age (179.35 ± 22.07 vs. 49.41 ± 35.52 months; p = 0.001). Consistently, all patients in the suicide-attempt group were ≥12 years (100.0% vs. 4.5%; p = 0.001). Multiple-drug poisoning was also more frequent among suicide attempts (58.8% vs. 18.2%; p = 0.022). Disposition/unit of hospitalization did not differ significantly between groups (p = 0.905). The mean length of stay was numerically longer in the suicide-attempt group (50.78 ± 33.24 vs. 42.05 ± 31.12 hours), but this difference was not statistically significant (p = 0.259) (Table 2).

When the length of stay was compared across units, the mean duration was highest in the pediatric emergency department and lowest in the pediatric intensive care unit, with the general pediatric service showing intermediate values. In pairwise comparisons, the length of stay differed significantly between the general pediatric service and the pediatric intensive care unit (p = 0.003) and between the pediatric intensive care unit and the pediatric emergency department (p = 0.001). In contrast, there was no statistically significant difference between the general pediatric service and the pediatric emergency department (p = 0.814) (Fig. 1).

A graphical illustration of the study is shown in Figure 2. It was enhanced with the assistance of Google NotebookLM Pro (Google LLC, San Francisco, CA, USA).

Table 1. Baseline demographic, clinical, and laboratory characteristics (N=39).

	n (%)
Gender	
Female	28 (71.8)
Male	11 (28.2)
Age Groups	
Under 5 Years	15 (38.6)
5-13 Years	12 (30.7)
Ages 14 and over	12 (30.7)
Age, Years	
Mean ± SD	8.84 ± 5.98
Chronic or Underlying Disease	
None	25 (64.1)
Epilepsy	7 (17.9)

Epilepsy and Mental Retardation	3 (7.7)
Bipolar	2 (5.1)
Drug Addiction	1 (2.6)
Arrhythmia	1 (2.6)
Cause of Poisoning	
Accidental	22 (56.4)
Suicide	17 (43.6)
Multiple Drug Poisoning	
No	25 (64.1)
Yes	14 (35.9)
Antiepileptic agent involved (primary)	
Carbamazepine	18 (46.2)
Sodium Valproate	13 (33.3)
Phenobarbital	2 (5.1)
Diazepam	2 (5.1)
Levetiracetam	1 (2.6)
Clonazepam	1 (2.6)
Lacosamide	1 (2.6)
Oxcarbazepine	1 (2.6)
Gastrointestinal decontamination (activated charcoal and/or gastric lavage)	36 (92.3)
Symptom	
Asymptomatic (toxic dose ingestion)	22 (56.4)
Central Nervous System	13 (33.3)
Respiratory System	2 (5.1)
Gastrointestinal System	2 (5.1)
ECG	
Normal	39 (100)
Blood Tests	
Normal	38 (97.4)
Elevated Liver Function Enzyme	1 (2.6)
Hospitalization	
Pediatric Emergency Department	21 (53.8)
Pediatric Intensive Care Unit	12 (30.8)
General Pediatrics Service	6 (15.4)
Length of stay, Hours (mean ± SD)	45.21 ± 32.12
Time of Hospitalization, Hours (mean ± SD)	
General Pediatrics Service	76.67 ± 43.56
Pediatric Intensive Care Unit	61.92 ± 27.54
Pediatric Emergency Department	26.67 ± 15.59
Outcome	
Discharged with health	39 (100)

Table 1 summarizes the baseline demographic, clinical, and laboratory characteristics of the 39 pediatric patients with antiepileptic drug poisoning included in this study.

Table 2. Comparison of patients with AED poisoning due to accidental and suicidal attempt.

	Accidental (n=22) N (%)	Suicide attempt (n=17) N (%)	p
Gender, N (%)			
Female	12 (54.5)	16 (94.1)	0.011
Age,			
Months (mean ± SD)	49.41 ± 35.52	179.35 ± 22.07	0.001
Age Groups, N (%)			
Ages 12 and over	1 (4.5)	17 (100.0)	0.001
Multiple-drug poisoning, N (%)			
Yes	4 (18.2)	10 (58.8)	0.022
Disposition/Unit of hospitalization, N (%)			
Pediatric Emergency Department	12 (54.5)	9 (52.9)	0.905
General Pediatrics Service	3 (13.6)	3 (17.6)	
Pediatric Intensive Care Unit	7 (31.8)	5 (29.4)	
Length of Stay, Hours Mean ± SD	42.05 ± 31.12	50.78 ± 33.24	0.259

Table 2 compares the clinical and demographic characteristics of patients with antiepileptic drug poisoning according to poisoning intent, namely accidental ingestion and suicide attempt.

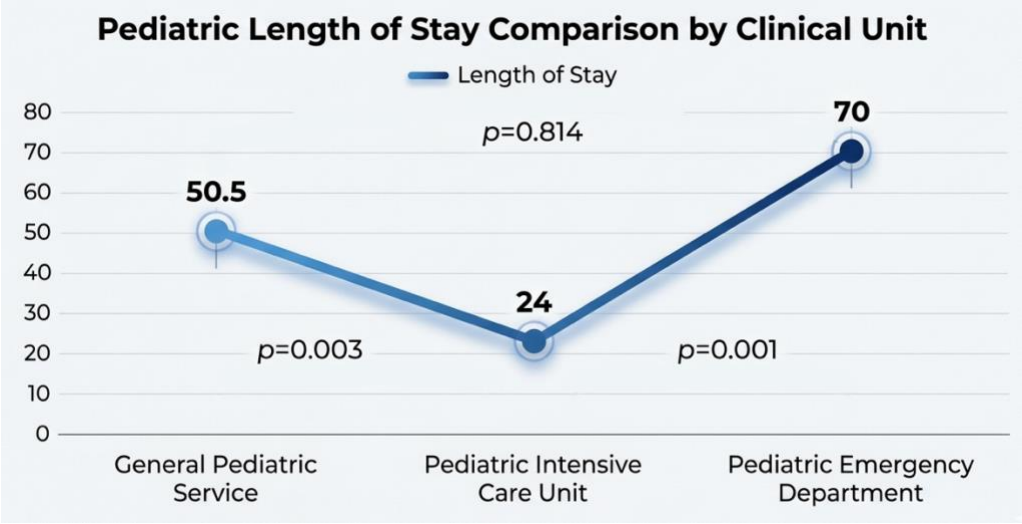

Figure 1. The line graph compares the mean length of stay across three units: General Pediatric Service, PICU, and Pediatric Emergency Department.

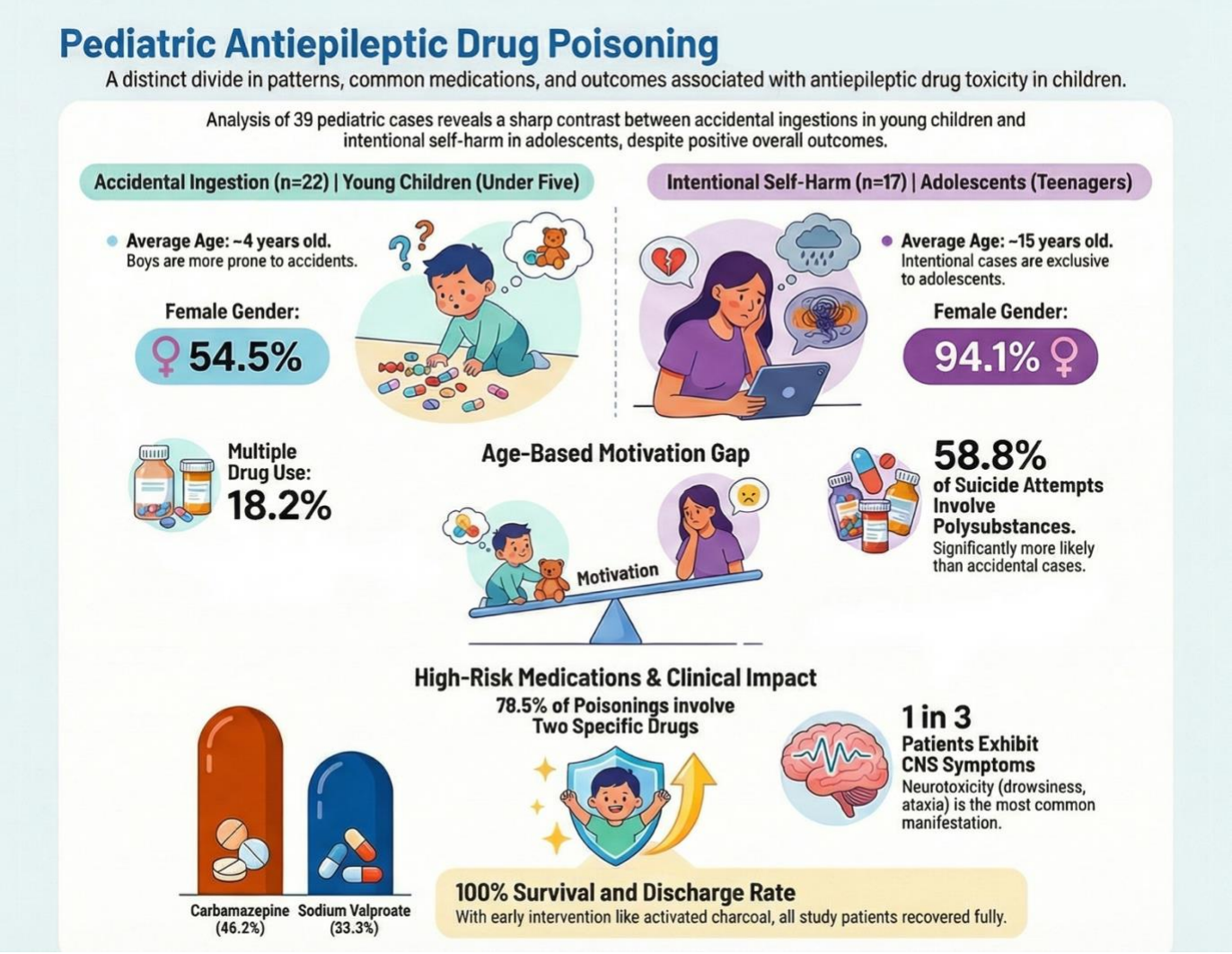

Figure 2. Graphical illustration of the study (Enhanced with the assistance of Google NotebookLM Pro).

Discussion

Pediatric antiepileptic drug (AED) poisonings can be more clearly interpreted when the literature is stratified by age group and intent. AEDs are prescribed across the pediatric age spectrum and are also used for non-epileptic indications (e.g., migraine), which increases household availability (8). Prior pediatric studies have reported the highest incidence in children <5 years and a male predominance, consistent with general patterns of unintentional pediatric drug poisoning (9). In our cohort, AED poisonings accounted for 1.5% of all poisoning presentations, a proportion level lower than that reported in adults (10). Importantly, all intentional ingestions occurred exclusively in adolescents ≥12 years, and suicide attempts increased with age. Intentional cases demonstrated a female predominance and were associated with multiple drug ingestion, whereas boys were more likely to have accidental exposures. This age- and context-dependent profile aligns with reports that adolescent self-harm poisonings often involve polysubstance exposure and are more frequently observed in girls (11), while developmental changes in risk-taking behavior across adolescence may contribute to the observed age gradients (12). Recent data also suggest a rising burden of AED-related poisonings, with one report indicating an approximately 30% increase in such cases over recent years (11).

When AED type was considered, we observed that the distribution was dominated by carbamazepine (46.2%) and sodium valproate (33.3%), which resembles adult patterns, in which carbamazepine and valproate constitute a substantial proportion of AED poisonings (10). The frequent use of these agents for indications beyond epilepsy may plausibly contribute to both accidental and intentional ingestion risk (13). Clinically, central nervous system (CNS) symptoms were present in one-third of our patients (33.3%), whereas respiratory and gastrointestinal manifestations were less common, and no cardiac symptoms were observed. Although fatal arrhythmias related to carbamazepine toxicity have been reported, our findings may reflect differences in case severity and early management. Prior pediatric series have similarly described CNS involvement, including coma, in approximately one-third of cases, which is comparable to our CNS symptom rate (13, 14). Moreover, the literature has documented cases of central nervous system findings, including coma, in 35% of patients, which aligns with the findings of our study (14, 15). Finally, management practices and outcomes should be interpreted with consideration of early interventions and triage decisions. In our cohort, 92.3% of cases received activated charcoal administration and gastric lavage within the first hour. A pediatric carbamazepine series from our country reported a lower early intervention rate (≈80%) and documented severe presentations including coma, respiratory failure, arrhythmia, and status epilepticus (14).

In terms of prevention and context, several system-level factors have been implicated in the increasing national burden of AED poisonings, including the absence of childproof medication packaging and broader access to medications, as well as gaps in structured caregiver education and follow-up (16, 17). Moreover, the higher rate of intentional ingestions among girls aged ≥12 years is consistent with the epidemiology of adolescent suicide-related poisonings and age-specific risk behaviors reported in prior studies (18, 19). In cases of poisoning, it is imperative that parents undergo evaluation by specialists in psychiatry and social services. If deemed necessary, these parents should be furnished with psychological and social support.

A salient finding of our study is the marked disparities between patients under 12 years of age and those 12 years and older. Among patients aged 12 years and older, the majority were female, most cases were intentional poisonings, and more than half involved multiple drug ingestion.

This observation may be attributed to the fact that accidental poisoning is more common in younger children, whereas intentional poisoning is more prevalent during adolescence. Studies on risk-taking behaviors have indicated that boys tend to engage in risk-taking behaviors more frequently than girls. This tendency has been shown to increase during middle adolescence (16, 18, 19)

As pediatricians, our foremost responsibility is to avert potential risk factors before they manifest. In cases of antiepileptic drug (AED) poisoning, the dearth of well-defined toxidromes, targeted treatments, and antidotes constitutes a substantial impediment to diagnosis and treatment. The utilization of drugs such as sodium valproate and carbamazepine for indications other than epilepsy, the absence of childproof caps on antiepileptic drugs in our country, the capacity to obtain more medication than prescribed even with a report, and the limited use of epilepsy education nursing services are significant concerns. From an epidemiological perspective, there is a continuous relationship between accidental and intentional ingestions. While numerous side effects have been documented at certain doses and plasma levels of certain antiepileptic drugs, these effects are not typically drug-specific and are not associated with plasma drug concentrations.

Limitations

This is a single-center study. Sociocultural data for the children and families are not available. Long-term data, particularly for patients with intentional ingestion, regarding potential mortality and morbidity, are lacking.

Conclusion

Antiepileptic drug poisonings remain a clinically important problem in childhood and arise from both unintentional and intentional ingestions, with risk patterns varying by age and sex. Our findings stress

several modifiable, prevention-focused targets: secure home storage, child-resistant packaging, caregiver counseling, and judicious prescribing that avoids keeping excess quantities in the household may reduce accidental exposures, while adolescents—particularly those with suspected intentional or polysubstance ingestion—should routinely undergo psychosocial screening and obtain timely mental health referrals. Early recognition and active management may help limit morbidity, mortality, and hospitalization length. Finally, multicenter studies are needed to better inform health policy, including packaging redesign strategies and structured prevention programs (e.g., epilepsy-focused education delivered by dedicated nursing staff) to reduce pediatric antiepileptic drug exposures.

Disclosures

Ethical Approval: Ethical approval was obtained from the Clinical Research Ethics Committee of the University of Health Sciences, Ankara Pediatric Health and Diseases Hematology Oncology Training and Research Hospital, in accordance with the ethical standards of the 2024 Declaration of Helsinki (approval date: March 25, 2019, no: 2019-064).

Use of AI-Assisted Technologies in Visualization: During the preparation of this manuscript, the author(s) utilized Google NotebookLM Pro to enhance Figure 2, the graphical representation of the study. The underlying data, context, and prompts input into the tool were solely provided by the authors and derived from the original research. The author(s) have rigorously reviewed and verified the enhanced visual for scientific accuracy and take full responsibility for the integrity of the final published figure.

Peer-review: Externally peer-reviewed.

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