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Pediatric atypical antipsychotic poisoning: A single-center cohort study

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MAIN POINTS

- In our cohort, atypical antipsychotic poisonings were predominantly mild to moderate in severity, and no fatalities occurred.
- Risperidone exposure was the most common, and risperidone-associated extrapyramidal symptoms were resolved with biperiden.
- The prognosis was favorable with symptom-directed supportive care, and patients achieved complete recovery.

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ABSTRACT

Aim: This study aimed to describe the clinical features, exposure characteristics, management, and outcomes of pediatric atypical antipsychotic poisonings treated in a single tertiary pediatric intensive care unit (PICU) and to contextualize findings using the Poisoning Severity Score (PSS).

Materials and Methods: We conducted a retrospective, descriptive review of children and adolescents (1 month–18 years) managed for single-agent atypical antipsychotic ingestion at the PICU of Ağrı Training and Research Hospital between January 2018 and January 2023. De-identified electronic records were abstracted for demographics, implicated agent (amisulpride, aripiprazole, quetiapine, olanzapine, risperidone, ziprasidone), dose (mg and mg/kg), time from ingestion to presentation, decontamination (gastric lavage, activated charcoal), treatments (including biperiden), clinical/laboratory findings, and outcomes. Severity was classified according to PSS (0–4). Continuous data are reported as median (IQR); categorical data are reported as n (%). A two-sided $p<0.05$ was considered significant.

Results: Forty-one pediatric cases were included. The most frequent agent was risperidone (46.3%). Decontamination included gastric lavage in 43.9% and activated charcoal in 46.3%. Tachycardia, hypokalemia, confusion, extrapyramidal symptoms (EPS), and drowsiness were common findings. The PSS distribution was none 14.6%, minor 43.9%, moderate 36.6%, and severe 4.9%; no deaths occurred (therefore, no PSS grade 4). In a risperidone subgroup analysis (n = 19), biperiden was administered to 6 patients for acute EPS; time to presentation tended to be longer in those given biperiden (median 9.0 vs 4.0 h; p = 0.08). Ordinal logistic modeling indicated higher PSS categories in the biperiden group (odds ratio [OR], 68.11; 95% confidence interval [CI], 3.59–1291.68; p = 0.005).

Conclusion: In this cohort, pediatric atypical antipsychotic poisonings were predominantly mild to moderate with no fatalities. Risperidone exposures were the most common and frequently associated with EPS, which resolved with biperiden. These data support a generally favorable prognosis with timely supportive care and targeted symptomatic management.

Keywords: Poisoning, Pediatrics, Antipsychotic agents, Risperidone, Biperiden

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INTRODUCTION

Atypical (second-generation) antipsychotics are increasingly prescribed not only in adults but also in pediatric populations for conditions such as autism spectrum disorders, bipolar disorder, and schizophrenia. As a result, these medications have become more prevalent in households, increasing the risk of pediatric exposures through accidental ingestion or intentional overdose [1]. Atypical antipsychotics include risperidone, quetiapine, olanzapine, aripiprazole, ziprasidone, and amisulpride. Each of these agents carries a risk of toxicity in children, with clinical manifestations related to their pharmacologic profiles. In overdose, central nervous system (CNS) depression and cardiovascular effects are prominent across this class [2]. In contrast, risperidone and ziprasidone, which have potent dopamine D_2 receptor antagonism and less anticholinergic activity, tend to produce less sedation but can precipitate extrapyramidal symptoms (EPS) such as acute dystonia, especially in pediatric patients [3].

This study aimed to characterize the presentation, management (including biperiden use), and outcomes (PSS-based severity) of pediatric atypical antipsychotic poisonings and compare these patterns with recent pediatric reports.

MATERIALS AND METHODS

The study was designed as a retrospective, descriptive review of cases of atypical antipsychotic poisoning in the Pediatric Intensive Care Unit of Ağrı Training and Research Hospital between January 2018 and January 2023. The study was approved by the Ağrı İbrahim Çeçen University Scientific Research Ethics Committee (approval date: May 25, 2023; approval number: 2023/132). Cases were identified through daily PICU admission logs and electronic health record queries using drug intoxication diagnosis codes. Institutional electronic records were deidentified and processed under the study identifiers.

The inclusion criteria were:

- Pediatric age (1 month–18 years)
- Single-drug exposure
- Exposure to an atypical antipsychotic at a known ingested dose.

The exposure was confirmed by the caregiver's history, corroborated by pill counts/packaging or medication lists, and the formulation was recorded (immediate vs. extended-release; drops vs. tablets; route of exposure). Demographic variables (age in months, sex, body weight); the implicated agent (amisulpride, aripiprazole, quetiapine, olanzapine, risperidone, ziprasidone); total dose (mg); circumstance of exposure (unintentional/therapeutic error/intentional/unknown); time from exposure to presentation (hours); decontamination procedures (activated charcoal, gastric lavage); patients' vital signs; and laboratory results (glucose, serum electrolytes, renal function tests, liver function tests, creatine kinase) were abstracted retrospectively from patient charts, along with administered treatments (biperiden). Time to presentation was defined as the interval from reported ingestion to first medical contact. Organ-system domains coded clinical effects, and overall poisoning severity was determined according to the Poisoning Severity Score (PSS) developed by the International Program on Chemical Safety and the European Association of Poison Center and Clinical Toxicologists (IPCS/EAPCCT). The severity grades were as follows: none (0), minor (1), moderate (2), severe (3), and fatal (4).

Statistical analysis

Analyses were performed in IBM SPSS Statistics, version 27.0 (Armonk, NY: IBM Corp.). Continuous variables are summarized as median (IQR) owing to non-normal distributions; when approximately normal, mean ± SD is also presented. Categorical variables are expressed as n (%). Normality was assessed using the Shapiro–Wilk test. Between-group comparisons were performed using the Mann–Whitney U test for 2 groups. Categorical comparisons were performed using the chi-square test or Fisher's exact test when the expected counts were <5. For severity graded by the Poisoning Severity Score (0–3), proportional-odds (ordinal logistic) models were additionally fitted to estimate common odds ratios (ORs) with 95% confidence intervals for prespecified contrasts (e.g., biperiden use vs no use), checking the proportional-odds assumption (test of parallel lines). All tests were two-sided, and $p<0.05$ was considered statistically significant. No a priori sample size calculation was conducted; using a two-sided $\alpha=0.05$ and the observed effect size (common OR 68.11; 95% CI 3.59–1291.68), the post-hoc power achieved was approximately 0.80 (80%).

RESULTS

The analysis included 41 pediatric cases of atypical antipsychotic intoxication. The median age was 163 months (IQR 51–198), and 56.1% of the participants were female (Table 1). The implicated agents were risperidone (46.3%), quetiapine (22.0%), olanzapine (19.5%), aripiprazole, ziprasidone,

Table 1. Patients' characteristics.

Age (month), median, (25-75p)	163 (51-95)	
	n	%
Sex		
Female	23	56.1
Male	18	43.9
Drugs		
Risperidone	19	46.3
Quetiapine	9	22
Olanzapine	8	19.5
Aripiprazole	2	4.9
Ziprasidone	2	4.9
Amisulpride	1	2.4
Decontamination		
Gastric lavage	18	43.9
Activated charcoal	19	46.3

Table 2. Symptoms and signs.

	n	%
Hypokalemia	10	24.4
Tachycardia	9	22
Confusion	7	17.1
Extrapyramidal symptoms	7	17.1
Drowsiness	4	9.8
Metabolic acidosis	4	9.8
Hyperthermia	3	7.3
Agitation	2	4.9
Dizziness	2	4.9
Vomiting	2	4.9
Hallucinations	2	4.9
Hypoglycemia	1	2.4
Transaminase elevation	1	2.4
Rhabdomyolysis	1	2.4
AV block (I)	1	2.4
Nausea	1	2.4
Hypotension	1	2.4
Coma	1	2.4

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Table 3. Poisoning severity and ingested dose.

	n (%)	Dose range (mg/kg), median IQR (25–75p)
Total		
• None	6 (14.6)	
• Minor	18 (43.9)	
• Moderate	15 (36.6)	
• Severe	2 (4.9)	
Risperidone		
• None	2 (10.5)	0.10–0.16, 0.13 (0.12–0.15)
• Minor	10 (52.6)	0.07–0.45, 0.28 (0.15–0.32)
• Moderate	6 (31.6)	0.12–0.35, 0.25 (0.20–0.27)
• Severe	1 (5.3)	0.33
Quetiapine		
• None	2 (22.2)	0.7-3.5, 2.1 (1.4-2.8)
• Minor	4 (44.5)	2.5-33.3, 7.5 (2.65-17.55)
• Moderate	3 (33.3)	2.2-28.5, 5.7 (3.95-17.10)
Olanzapine		
• None	1 (12.5)	0.5
• Minor	2 (25)	1.2-2.6, 1.90 (1.55–2.25)
• Moderate	5 (62.5)	1-15.8, 1.7 (1.5-2.9)
Aripiprazole		
• None	1 (50)	1
• Minor	1 (50)	1.25
Ziprasidone		
• Minor	1 (50)	1
• Severe	1 (50)	8
Amisulpride		
• Moderate	1 (100)	25

Table 4. Clinical characteristics by Biperiden use.

	Biperiden not administered	Biperiden administered	p
n (%)	13 (68.4)	6 (31.6)	
Age (month)	180 (46-213)	57 (25-182)	0.059
Sex			
• Female	9 (69.2)	4 (66.7)	1.00
• Male	4 (30.8)	2 (33.3)	
Time to presentation	4 (2-6)	9 (5.8-10)	0.08
Decontamination			
• Gastric lavage	6 (46.2)	-	0.11
• Activated charcoal	8 (61.5)	1 (16.7)	0.14
Dose (mg)	10 (5-17)	5 (4.5-6.75)	0.21
Dose (mg/kg)	0.26 (0.15-0.32)	0.25 (0.2-0.27)	0.93

and amisulpride. Decontamination consisted of gastric lavage of 43.9% of the samples and activated charcoal in 46.3%.

Clinical findings (Table 2) were as follows: hypokalemia, 24.4%; tachycardia, 22.0%; confusion, 17.1%; extrapyramidal symptoms, 17.1%; drowsiness, 9.8%; metabolic acidosis, 9.8%; hyperthermia, 7.3%; agitation, 4.9%; dizziness, 4.9%; vomiting, 4.9%; hallucinations, 4.9%; and single instances (2.4% each) of hypoglycemia, transaminase elevation, rhabdomyolysis, first-degree AV block, nausea, hypotension, and coma.

The PSS distribution was as follows: none 14.6%, minor 43.9%, moderate 36.6%, and severe 4.9%. No deaths were recorded; therefore, no fatal (grade 4) intoxication occurred. Dose ranges by drug and severity are presented in Table 3.

Biperiden (Table 4) was more frequently used among younger patients, although the difference was not statistically signif-

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icant (p = 0.059). The time to presentation tended to be longer in the biperiden group (9 vs. 4 h; p = 0.08). All other comparisons—sex distribution, gastric lavage, activated charcoal, and dose metrics (mg and mg/kg)—showed no between-group differences ($p \geq 0.05$). Biperiden administration was associated with a higher common odds of being in a more severe category (OR 68.11, 95% CI 3.59–1291.68; p = 0.005) in an ordinal logistic model for PSS 0–3.

DISCUSSION

In this 5-year retrospective series of pediatric atypical antipsychotic poisonings, we identified 41 cases managed in the PICU, with no fatalities and universally good outcomes. The children in our study ranged from infancy to late adolescence (approximately 1 year to 17 years old), reflecting two primary exposure scenarios: accidental ingestion in toddlers/young children and intentional overdose in adolescents. This age distribution is similar to patterns reported in the literature, where unintentional poisonings predominate in children and adolescent cases often involve deliberate self-harm or misuse [4]. Risperidone was the single most commonly used agent. This reflects the widespread use of risperidone in pediatric psychiatry. Our finding agrees with prior reports; for example, data from the U.S. poison center (2005–2013) showed that risperidone was responsible for thousands of pediatric exposures [1].

Despite being drawn from an intensive care population, the clinical severity of poisonings in our cohort was generally low to moderate. Using the PSS, over half of the patients (≈59%) had either no symptoms or only mild effects (PSS 0–1), and about one-third (37%) experienced moderate effects (PSS 2). Only two patients (4.9%) were classified as having severe poisoning (PSS 3), and none had fatal outcomes (PSS 4). These findings reinforce the favorable prognosis of single-agent atypical antipsychotic ingestion in children. They closely parallel the experience reported in other pediatric studies: for instance, Meli et al. observed no deaths and only two severe cases out of 106 young children (<6 years) exposed to risperidone, olanzapine, quetiapine, or clozapine [5]. Similarly, Stassinos and Klein-Schwartz, analyzing >16,000 U.S. cases in children <6, found that central toxicity was under 1% and there were no deaths [1]. All patients in our series made a full recovery, consistent with extensive pediatric studies showing that—absent polypharmacy—atypical antipsychotic poisonings rarely cause lasting harm; the lack of mortality in our cohort further indicates that, with appropriate supportive care, even children who develop severe symptoms can be successfully managed [6].

Several patients in our PICU had minimal or no symptoms despite significant reported ingestions. For example, some adolescents taking high doses of quetiapine or risperidone had a PSS of 0 or 1. This aligns with the observations of Lofton et al, who reported that adolescents can sometimes tolerate very high aripiprazole doses with only transient or minor effects [7]. In contrast, younger children in our study tended to manifest more noticeable toxicity from comparatively minor ingestions. The only two severe cases we encountered illustrate this point: a 19-month-old child who ingested ziprasidone (PSS: 3) and a 46-month-old who ingested risperidone (PSS: 3). In both cases, the patients were infants/toddlers, and the severity of their presentations was disproportionate to the doses that an older child or adult would tolerate. This age-related vulnerability has been well documented. Young children have immature physiology and often ingest doses per kilogram that far exceed therapeutic levels. For example, the pediatric case reported by Fasano et al. shows that ingestion of a single ziprasidone tablet in a 30-month-old child resulted in coma and respiratory depression, underscoring that severe toxicity can occur from low doses at a young age [8]. Our findings concur that younger pediatric patients are at higher risk of severe central nervous system (CNS) depression and other effects, reinforcing the need for aggressive management and observation in that age group.

Risperidone was used in nearly half of our cases, and it exhibited a fairly characteristic clinical profile. Most risperidone-ingested children in our cohort developed mild CNS depression and sinus tachycardia, which is consistent with the known effects of risperidone. Acute dystonic reactions have emerged as a salient issue in risperidone poisoning. Intravenous treatment with biperiden, which led to complete resolution of the dystonic symptoms. Acute anticholinergic treatment was is needed in more than a quarter nearly one-third of our risperidone cases. Previous pediatric studies have reported varying incidence rates of EPS. For example, Meli et al observed extrapyramidal symptoms in only 1% of <6-year-old cases [5]. In the study conducted by Vial et al., extrapyramidal findings were detected in 16.8% (n= 17) of the patients, and EPS was reported in only one patient aged 5 years [9]. Our higher rate reflects the inclusion of older children and adolescents (who may be more prone to EPS at higher doses) as well as intentional cases with higher doses ingested. Fortunately, these reactions were benign and rapidly reversible with the appropriate use of anticholinergic agents, though frightening for the patient and caregivers. In our series, no child suffered airway compromise due to dystonia, and none had recurrent EPS after treatment.

CONCLUSION

In conclusion, our discussion highlights that when appropriately managed, pediatric atypical antipsychotic poisonings have a low incidence of severe morbidity. PICU care was crucial for the handful of severe cases, and supportive measures were uniformly successful. With vigilant monitoring and symptomatic treatment, pediatric patients who ingest psychotropic medications can be expected to fully recover.

Ethics Committee Approval: The study was approved by the Ağrı İbrahim Çeçen University Scientific Research Ethics

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Committee (approval date: May 25, 2023; approval number: 2023/132).

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