

Research Paper

Antipsychotic Drug Poisoning in Children Under 12 Years Old in Loghman-Hakim Hospital During 2016-2022



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ABSTRACT

Background: Unintentional pediatric poisoning with antipsychotic medications represents an important clinical entity. This study aimed to evaluate the epidemiology, clinical manifestations, and outcomes of antipsychotic poisoning among children presenting to a referral hospital.

Methods: This descriptive, cross-sectional study reviewed medical records of children <12 years old hospitalized for antipsychotic drug poisoning at Loghman Hakim Hospital in Tehran from 2015-2016. Data extracted included demographic details, agent and dose ingested, clinical findings, treatments administered, and patient dispositions.

Results: 141 cases were identified, comprising 2.3% of all pediatric poisonings. Patient ages ranged from 6 months to 12 years (mean 5.5 years), with a male predominance (52.5%). The most common offending agents were risperidone (53.2%) and olanzapine (13.4%). Unintentional exposures accounted for 72.3% of cases. Central nervous system (CNS) effects like somnolence (61.7%) and dysarthria (19.1%) were most prevalent. Significant toxicity was infrequent; no fatalities occurred. Mean length of stay was 2 days for uncomplicated admissions.

Conclusion: Antipsychotic poisoning in children chiefly involves atypical agents with a largely benign course. Risperidone predominated due to prescribing patterns. Somnolence represented the principal clinical manifestation. With reasonable supportive care, favorable outcomes are achievable in the pediatric population.

Keywords:

Children, Antipsychotic, Acute poisoning

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Introduction

According to the annual report of the [American Association of Poison Control Center \[1\]](#), children under 6 years of age account for about half of all human poisonings. In addition, the highest number of emergency department visits for poisoning in children involved patients under 6 years of age [2, 3]. Specifically, there has been a significant increase in poisonings involving antipsychotic drugs in recent years, with around 8% of cases involving children under 6 years of age [4]. Among these cases, antipsychotic drugs account for 3 to 10% of pharmaceutical agents in various studies [5-7]. Antipsychotic drugs belong to a class of psychiatric medications primarily used to manage conditions, like schizophrenia, bipolar disorder, and obsessive-compulsive disorder [8]. There are two main types of antipsychotics: First-generation (typical) and second-generation (atypical) drugs. First-generation antipsychotics, such as chlorpromazine, haloperidol, and perphenazine, work by blocking the brain's dopamine D2 receptors. Second-generation antipsychotics, including clozapine, risperidone, olanzapine, and block D2 receptors exhibit additional effects on serotonin 5-HT_{2A} receptors [9, 10].

Antipsychotic drugs can cause a wide range of side effects that can be grouped into different categories. Central nervous system (CNS) effects include fatigue, drowsiness, dizziness, slurred speech, seizures, confusion, coma, lack of coordination, muscle stiffness and involuntary muscle twitches [11, 12]. Cardiopulmonary effects may include difficulty breathing, chest pain, rapid heartbeat, low blood pressure, and respiratory issues [13]. Anticholinergic effects consist of blurred vision, dry mouth, constipation, trouble urinating, and mild fever [14]. A common side effect of these medications is extrapyramidal symptoms (EPS), which involve physical and movement-related issues, like acute dystonia (involuntary muscle contractions and abnormal postures), Akathisia (restlessness and inability to sit still), Parkinsonism (tremors, rigidity and bradykinesia) and Tardive dyskinesia (repetitive and involuntary movements) [12, 15]. Cardiovascular effects include orthostatic hypotension (drop in blood pressure upon standing), prolonged QT interval (a heart rhythm disturbance that can lead to serious complications) and tachycardia (rapid heart rate) [16, 17].

Antipsychotic drug poisoning typically does not require specific laboratory testing for diagnosis or management [2, 12, 14], although, in certain instances, the levels of particular antipsychotics may be assessed in the blood

if the diagnosis is unclear. The patients' sodium levels may also be checked, especially if they exhibit signs of altered mental status or seizures, as some antipsychotics can cause low sodium levels [14]. Patients who have low blood pressure, muscle breakdown, prolonged difficulty urinating, or a condition called neuroleptic malignant syndrome may be susceptible to kidney injury, prompting regular monitoring of their kidney function and creatine kinase levels [18]. During the routine evaluation, the patient's blood sugar will be checked to rule out low blood sugar as the cause of the mental status changes and the levels of acetaminophen and salicylates will be measured to determine if the individual has ingested any other substances [2]. An electrocardiogram (ECG) will also be performed to assess any effects of the antipsychotic poisoning on the heart's electrical activity [14]. The initial treatment focuses on stabilizing the patient, ensuring their airway, breathing, and circulation are functioning properly, as administering the antidote naloxone does not aid in reversing the CNS depression caused by antipsychotic intoxication [12, 14]. If the patient develops acute movement disorders, like muscle spasms or restlessness as a result of the poisoning, diphenhydramine can be given at a dose of 25-50 mg IV in adults or 0.5-1 mg/kg in children, or benzotropine can be given at a dose of 1-2 mg IV in adults or 0.05 mg/kg in children over three years old with severe reactions [19].

Research into the use of antipsychotic medications in children is essential for several key reasons. Identifying risk factors that may predispose children to acute toxicity or adverse effects allows for the development of targeted monitoring and prevention strategies. Determining appropriate dosages and formulations for the pediatric population helps minimize the risk of adverse events while ensuring therapeutic efficacy. Research also informs the creation of evidence-based protocols for the prompt recognition, management and treatment of acute adverse events, thereby preventing serious complications. Evaluating the relative safety profiles of different antipsychotics guides clinicians in selecting the most appropriate and safest treatment option for each child. Collectively, this comprehensive research approach aims to optimize the safe and effective use of antipsychotics in children. This research examined the pediatric toxicity records involving antipsychotics from 2016 to 2022 at [Loghman Hakim Hospital](#).

Materials and Methods

In this descriptive cross-sectional study, we thoroughly examined the pediatric toxicity records involving antipsychotics from 2016 through 2022 at [Loghman Ha-](#)

kim Hospital, extracting and analyzing data that has informed our key findings. This data, entered by physicians, included age, sex, weight, ingested drug and dose, symptoms/signs/laboratory values, causal relationship, and therapeutic interventions.

Inclusion and exclusion criteria

The inclusion criteria were a documented history of antipsychotic drug poisoning, age <12 years and completion of the full course of inpatient treatment. Conversely, the exclusion criteria included age 12 years or older, cases involving multi-substance poisoning and those with incomplete treatment records or missing data. By applying these precise inclusion and exclusion parameters, the research was able to focus solely on the target population of pediatric patients who experienced isolated antipsychotic toxicity and received the full medical intervention. This approach ensured that the data was comprehensive and representative for analysis.

Statistical analysis was performed using SPSS software, version 29. Descriptive statistics were used to analyze the data. The correlation between patients' age and ingested dosages was tested using the Spearman rank correlation test, while the Wilcoxon test was employed to analyze the association between gender and ingested dose. Statistical significance was defined as $P < 0.05$.

Results

The study included 141 cases of antipsychotic drug poisoning, which accounted for 2.3% of all drug poisoning cases in children under 12 years old. Among these patients, 67 patients (47.5%) were female and 74 patients (52.5%) were male. The age range was six months to 12 years, with an average age of five years and six months. Concerning age distribution, 19 cases (13.4%) were under 3 years old, 69 cases (48.9%) were between 3 and 6 years old, 24 cases (17%) were between 6 and 9 years old and 29 cases (20.5%) were between 9 and 12 years.

Risperidone was the most commonly involved antipsychotic drug in poisoning cases, accounting for 53.2% ($n=75$) of the total. Other antipsychotic drugs were also implicated, but to a lesser extent: Olanzapine in 25.5% ($n=36$) of cases, quetiapine in 14.1% ($n=20$), chlorpromazine in 4.9% ($n=7$) and aripiprazole in 2.1% ($n=3$).

The average weight of the patients was 22.2 kg. The average dosages for the different antipsychotic drugs were as follows: 0.1 mg/kg for risperidone, 2.64 mg/kg

for quetiapine, 0.4 mg/kg for olanzapine, 1.57 mg/kg for chlorpromazine and 3.68 mg/kg for aripiprazole. However, in 18 cases, the dosage of the drug was unknown. No relationship was found between age and ingested dosages ($P > 0.05$) and there was no significant difference between males and females (Wilcoxon test, $P=0.38$).

The majority of the poisoning cases, 93 out of 141 (66%), did not have any underlying medical condition. However, 43 cases (30.4%) involved patients with attention-deficit hyperactivity disorder (ADHD). Among the ADHD cases, 32 were related to risperidone, 6 to olanzapine, 4 to chlorpromazine and 1 to aripiprazole. In three cases (2.1% of the total), the patients had an underlying tic disorder and all three cases involved intoxication with risperidone. Additionally, in 1 case (0.7% of the total), the patient had an underlying diagnosis of Autism, and this case also involved intoxication with risperidone (Table 1).

The study investigated the CNS manifestations of the poisoning cases from the time of admission throughout their hospitalization. The most common CNS symptom was drowsiness, which was observed in 87 cases (61.7%). Other CNS symptoms included stupor in five cases (3.5%), agitation in two cases (1.4%) and coma in one case (0.7%). The extrapyramidal side effects (dystonia, slurred speech, decrease in deep tendon reflexes, akathisia, and tardive dyskinesia) were observed in 58 cases (41.2%). The most common extrapyramidal symptom was acute dystonia, which occurred in 27 cases (19.1%). The majority of the acute dystonia cases (25 out of 27) were associated with risperidone poisoning, while one case each was linked to olanzapine and chlorpromazine. Slurred speech was observed in 22 cases (15.6%). The majority of these, 19 cases, were related to risperidone poisoning. The remaining three cases of slurred speech were associated with one case of olanzapine, one case of chlorpromazine, and one case of aripiprazole. A decrease in deep tendon reflexes was seen in 8 cases (5.6%), all of which were linked to risperidone poisoning. Akathisia was observed in six cases (4.2%), with four cases related to risperidone, one to olanzapine, and one to chlorpromazine. Finally, tardive dyskinesia was seen in five cases (3.5%), all of which were associated with risperidone poisoning. Using the Bazett formula (Equation 1):

$$1. QTc = QT / \sqrt{RR}$$

to calculate the corrected QT interval (QTc), QT interval prolongation was observed in 14 cases (10%). The majority of these cases, 12, were related to risperidone

Table 1. Patients' baseline characteristics

Variables	No. (%)						
	Total	Aripiprazole	Chlorpromazine	Olanzapine	Quetiapine	Risperidone	
Number of patients	141(100)	3(2.1)	7(4.9)	36(25.5)	20(14.1)	75(53.2)	
Sex							
Male	74(52.4)	2(1.4)	5(3.5)	17(12)	7(4.9)	43(30.5)	
Female	67(47.6)	1(0.7)	2(1.4)	19(13.8)	13(9.3)	32(22.7)	
Mean age (y/m)	5/6	9	5/6	5/1	3/7	6/4	
Age groups							
<3	19(13.4)	0	2(1.4)	11(7.9)	13(9.3)	13(9.3)	
3-6	69(48.9)	1(0.7)	3(2.1)	17(12)	3(2.1)	32(22.7)	
6-9	24(17)	1(0.7)	1(0.7)	5(3.5)	3(2.1)	11(7.9)	
9-12	29(20.5)	1(0.7)	1(0.7)	3(2.1)	1(0.7)	19(13.8)	
Underlying medical condition							
ADHD	43(30.4)	1(0.7)	4(2.9)	6(4.3)	-	32(22.6)	
Tic disorder	3(2.1)	-	-	-	-	3(2.1)	
Autism	1(0.7)	-	-	-	-	1(0.7)	

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Table 2. Observed symptoms and signs

Variables	No. (%)						
	Drugs						
	Total	Aripiprazole	Chlorpromazine	Olanzapine	Quetiapine	Risperidone	
Cardio-vascular system	Tachycardia (HR>110 bpm)	3(2.1)	-	-	1(0.7)	-	2(1.4)
	Prolonged QTc interval	14(9.8)	-	1(0.7)	1(0.7)	-	12(8.4)
Gastro-intestinal tract	Abdominal pain	3(2.1)	-	1(0.7)	-	1(0.7)	1(0.7)
	Vomiting	4(2.8)	-	-	1(0.7)	1(0.7)	1(0.7)
Level of consciousness at the time of admission	Agitation	2(1.4)	-	-	-	-	2(1.4)
	Coma	1(0.7)	-	-	-	-	1(0.7)
	Drowsiness	87(60.9)	-	5(3.5)	20(14)	7(4.9)	55(38.5)
	Stupor	5(3.5%)	-	-	-	-	5(3.5)
Nervous system	Acute dystonia	27(18.9)	-	1(0.7)	1(0.7)	-	25(17.5)
	Decreased deep tendon reflex (DTR)	8(5.6)	-	-	-	-	8(5.6)
	Slurred speech	22(15.4)	1(0.7%)	1(0.7)	1(0.7)	-	19(13.3)
	Tardive dyskinesia	5(3.5)	-	-	-	-	5(3.5)
	Akathisia	6(4.2)	-	1(0.7)	1(0.7)	-	4(2.8)
	Miosis	41(28.7)	1(0.7)	2(1.4)	11(7.7)	4(2.8)	23(16.1)

Abbreviations: HR: Heart rate; bpm: Beats per minute; QTc: QT Interval corrected for heart rate.

poisoning, while 1 case each was linked to olanzapine and chlorpromazine (Table 2).

Regarding respiratory manifestations, from the time of admission up to hospitalization, only one case of risperidone poisoning resulted in loss of consciousness, coma, and respiratory depression, necessitating intubation and transfer to the ICU. In all the remaining cases, no respiratory depression was observed during this period, and there were no changes in the patient's venous blood gases (VBG) and oxygen saturation. The average oxygen (O₂) saturation in patients was 95%, and the average pH in VBG was 7.42. No electrolyte disorder, kidney function decline (according to creatinine level), or acid-base disorder was observed in any of the patients throughout their hospitalization.

For all patients admitted with antipsychotic drug poisoning, the treatment approach included providing in-

travenous fluids and requesting a comprehensive set of tests. These tests, such as complete blood count (CBC), electrolytes, creatinine, blood sugar and VBG analyses, were performed multiple times from the time of admission throughout the child's hospitalization and all results were found to be normal. This suggests that the child did not develop any significant hematological, electrolyte, renal, metabolic, or acid-base abnormalities as a result of the antipsychotic toxicity. Cardiac monitoring and pulse oximetry were conducted for all patients, and an ECG was performed to assess the QTc interval (using the Bazett formula [Equation 1]) and check for other cardiac abnormalities. Patients with QT interval prolongation underwent more frequent vital sign monitoring and serial ECGs. Supplemental oxygen was provided to those who presented with loss of consciousness. Activated charcoal and gastric lavage were performed for most patients, except for six cases where it was not possible due to unconsciousness and two cases due to late hos-

pital presentation. Diphenhydramine was the preferred treatment for all extrapyramidal cases, and its administration continued after discharge for 30 of those patients (51.7%), based on expert opinion and the clinical situation, including the severity of symptoms. All patients were discharged from the hospital in stable condition, and there were no reported deaths.

Discussion

In this study, the peak incidence of poisoning was observed in children aged 3 to 6 years, which contrasts with the findings of Meli et al. [20], who reported the highest number of poisonings in the age group of 1 to 3 years, but is consistent with the study by Fakhernia et al. [21]. The effectiveness of family education in preventing poisoning in younger children has been proposed as a reason for this difference. No relationship was found between age and the number of pills ingested, and there was no clear relationship between gender and the occurrence of poisoning, which is consistent with studies by Meli and Manouchehri Far et al. [20, 22].

Our results showed that risperidone is the most common drug involved in antipsychotic poisoning, likely due to its availability, which is in accordance with the findings of previous studies [7, 23]. Accidental poisoning with atypical antipsychotics in children, who have typically taken 0.5 to 2 tablets, mainly results in a benign clinical course without consequences. However, significant toxicity has been described after taking just one tablet of this class of drugs [20, 24]. The toxic dose per kg body weight found in this study for olanzapine is similar to that described by Isbister et al. [23], while we found a much lower toxic dose for clozapine, indicating toxicity. To our knowledge, no toxic doses of quetiapine and risperidone have been previously described [20, 23].

CNS effects were the most common clinical manifestations, ranging from drowsiness and dysarthria in mild poisoning to deep coma in severe cases. Unlike in adults, no children with central anticholinergic syndrome due to quetiapine poisoning were observed in our study. Somnolence was the most common symptom, consistent with its common adverse effect at therapeutic doses, with clozapine appearing to be the most sedating agent. Acute EPS were less common with atypical antipsychotics but appeared to occur more frequently in children than in adults [25, 26]. In this study, 27 cases of EPS were reported, with 25 cases related to risperidone, one case following the use of chlorpromazine, and one case following the use of olanzapine.

Cardiovascular complications are also uncommon in atypical antipsychotic poisoning compared to poisoning with first-generation antipsychotics [13]. Tachycardia was the most common cardiovascular symptom in overdose, consistent with observations at therapeutic dose ranges. Although intoxication with atypical antipsychotics has been reported to be associated with ECG changes and QT prolongation with an inherent risk of torsade de pointes, no cases of torsade de pointes were observed in this study [16, 17].

The absence of reported deaths due to antipsychotic poisoning in children in this study aligns with the findings from previous research [4, 6, 20, 23], suggesting that fatal outcomes are rare in cases of pediatric antipsychotic toxicity. This favorable outcome may be attributed to several factors, including early detection of poisoning, effective therapeutic interventions, and the influence of the ingested dose and the specific antipsychotic agents involved.

Conclusion

This study showed that antipsychotic drug poisoning in children predominantly involved atypical agents, with risperidone being the most common due to its widespread availability. The clinical course was typically benign, with symptoms primarily affecting the CNS and cardiovascular system. Prompt recognition, comprehensive evaluation, and appropriate therapeutic interventions, such as obtaining an ECG, screening for concomitant poisoning, close monitoring for at least 24 hours, and the judicious use of activated charcoal and gastric lavage within 2 hours of ingestion, were found to be crucial in effectively managing these cases and minimizing the risk of adverse outcomes. Furthermore, the study underscores the importance of ongoing education and training for healthcare professionals in recognizing and effectively managing antipsychotic poisoning in pediatric populations.

Study limitations

The retrospective design and reliance on existing medical records can introduce biases, such as misclassification or recall bias, and incomplete data, which may affect the study's accuracy. Additionally, the absence of long-term follow-up means that the study may not capture the full spectrum of outcomes, particularly post-discharge effects. Since the study was conducted at a single center, the findings may not represent the patterns of pediatric antipsychotic toxicity in different healthcare settings or geographic areas.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of [Shahid Beheshti University of Medical Sciences](#) (Code: IR.SBMU.MSP.REC.1401.141). The present study was carried out with the informed consent of the patients, ensuring the confidentiality of the participants' personal data.

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Authors' contributions

Conceptualization, methodology, project administration and supervision: Fariba Farnaghi; Investigation, resources, data curation and writing the original draft: Pooya Eini; Formal analysis: Latif Gachkar; Visualization and software: Pooya Eini and Latif Gachkar; Validation: Fariba Farnaghi and Latif Gachkar; Review and editing: Pooya Eini and Fariba Farnaghi.

Conflict of interest

The authors declared no conflicts of interests.

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