



RETROSPECTIVE INVESTIGATION OF ACETAMINOPHEN POISONING IN CHILDREN AGED 0-18 YEARS

0-18 YAŞ ARASI ÇOCUKLARDA ASETAMİNOFEN ZEHİRLENMESİNİN RETROSPEKTİF OLARAK İNCELENMESİ

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ABSTRACT

Objective: Acetaminophen is widely used as an antipyretic and analgesic in children. Acetaminophen poisoning is one of the most common drug poisonings worldwide. Despite this, there is still no consensus on treatment. This study aims to evaluate the clinical characteristics, laboratory findings, and treatment approaches of pediatric patients aged 0-18 years who were hospitalized due to acute acetaminophen poisoning.

Method: In this retrospective study, medical records of children aged 0-18 years who were admitted to the Emergency Department of Kırşehir Training and Research Hospital with acetaminophen ingestion and subsequently hospitalized in the Pediatric Health and Diseases Department between January 2016 and January 2021 were reviewed. Patients' demographic characteristics, reasons for acetaminophen intake, symptoms, laboratory findings, and treatment processes were analyzed. Descriptive statistics such as number (n), percentage (%), median, and quartiles (Q1-Q3) were used for data analysis.

Results: Between January 2016 and January 2021, a total of 38 patients were admitted due to acetaminophen poisoning. Among them, 36.8% were aged 0-5 years, while 63.2% were in the 14-18 age group. There were no recorded cases in the 5-14 year age group. Clinical symptoms were rarely observed. A total of 63.2% of the cases involved suicidal ingestion, and 76% of these patients were female. Activated charcoal was administered to 73.7% of the patients, gastric lavage to 68.2%, and NAC to 23.7%. The median values for ALT, AST, and prothrombin time were 15.24, 19.50, and 12.60, respectively.

Conclusion: Our study demonstrates that acetaminophen poisoning in young children is usually accidental, whereas in adolescents, it primarily occurs with suicidal intent. The rate of drug ingestion for suicidal purposes was higher among female patients. The results are consistent with similar studies in the literature. To prevent poisoning cases, increasing parental awareness, ensuring safe medication storage, implementing restricted access interventions, and identifying at-risk individuals are necessary.

Key Words: Child, Acetaminophen Poisoning, Retrospective Study

ÖZ

Amaç: Asetaminofen, çocuklarda ateş düşürücü ve ağrı kesici olarak yaygın bir şekilde kullanılmaktadır. Asetaminofen zehirlenmesi, dünya genelinde en yaygın ilaç zehirlenmelerinden biridir. Buna rağmen, tedaviye yönelik hâlâ bir fikir birliği bulunmamaktadır. Bu çalışma, akut asetaminofen zehirlenmesi nedeniyle hastaneye yatırılan 0-18 yaş arasındaki pediatrik hastaların klinik özelliklerini, laboratuvar bulgularını ve tedavi yaklaşımlarını değerlendirmeyi amaçlamaktadır.

Yöntem: Bu çalışmada Ocak 2016-Ocak 2021 tarihleri arasında Kırşehir Eğitim ve Araştırma Hastanesi Acil Servisine asetaminofen alımı ile başvuran ve Çocuk Sağlığı ve Hastalıkları Servisine yatırılan 0-18 yaş arası çocukların dosyaları retrospektif olarak incelendi. Hastaların demografik özellikleri, asetaminofen alım nedeni, semptomları, laboratuvar bulguları ve tedavi süreçleri değerlendirildi. Verilerin analizinde tanımlayıcı istatistikler için sayı (n), yüzde (%), median ve çeyreklikler (Q1-Q3) kullanıldı.

Bulgular: Ocak 2016-Ocak 2021 tarihleri arasında toplam 38 hasta asetaminofen zehirlenmesi ile başvurmuştur. Hastaların %36.8'i 0-5 yaş, %63.2'si 14-18 yaş grubundaydı. 5-14 yaş aralığında herhangi bir vaka tespit edilmedi. %63.2'si intihar amacıyla ilaç almış, intihar amacıyla ilaç alanların da %76'sı kadındı. Klinik semptomlar nadiren gözlenmiştir. Hastaların %73.7'sine aktif kömür, %68.2'sine mide lavajı, %23.7'sine NAC uygulanmıştır. ALT, AST ve protrombin zamanı median değerleri sırasıyla 15.24, 19.50 ve 12.60 olarak bulundu.

Sonuç: Çalışmamız, küçük çocuklarda asetaminofen zehirlenmesinin genellikle kaza sonucu, ergenlerde ise intihar amacıyla meydana geldiğini göstermektedir. Kadın hastaların intihar amaçlı ilaç alım oranı daha yüksek bulundu. Sonuçlar literatürdeki benzer çalışmalarla uyumludur. Zehirlenmeleri önlemek için ebeveyn farkındalığının artırılmasına, ilaçların güvenli saklanması, erişimi kısıtlayan müdahalelere, risk altındaki bireylerin belirlenmesine yönelik çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Çocuk, Asetaminofen Zehirlenmesi, Retrospektif Çalışma

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INTRODUCTION

Acetaminophen (paracetamol) is one of the most widely used medications worldwide and is easily available over the counter in most countries [1]. It is included in the World Health Organization's (WHO) List of Essential Medicines [2]. It is recommended as a first-line treatment for most cases of pain and fever, and its use is considered safe in infants younger than one month and in pregnant women [3]. Acetaminophen is available in various forms, including oral tablets, capsules, liquid formulations, and rectal suppositories.

Acetaminophen is used as an antipyretic and analgesic in children. In children under 5 years of age, acute acetaminophen poisoning is mostly due to accidental ingestion, whereas in older children, poisoning is usually due to suicidal intent. In infants, poisoning rarely develops as a result of intentional administration of the drug [4]. Acetaminophen poisoning is commonly observed in children due to the perception of the drug as safe and its easy accessibility, as it can be obtained without a prescription. In addition, poisoning may also occur because parents do not dispose of the drugs safely and physicians make dosing errors [5].

Acetaminophen intake at a dose of 150 mg/kg in adults and 200 mg/kg and above in children can cause poisoning. Poisoning may occur due to intake of acetaminophen at a dose of 90 mg/kg/day for 1-2 days in children and over 4 g/day in adults [6]. The most important side effects of acetaminophen poisoning are due to its toxic effects on the liver. Hepatotoxicity develops due to microsomal enzyme induction and glutathione depletion [7]. When acetaminophen is taken at therapeutic doses, it is conjugated with glucuronyltransferase and sulfotransferase enzymes in the liver and converted into non-toxic metabolites and excreted from the body through the kidneys [5,8,9]. However, when acetaminophen is taken in high doses, it cannot be fully conjugated by glucuronyltransferase or sulfotransferases and the remaining acetaminophen is converted to N-acetyl-p-benzoquinonimine (NAPQI) by cytochrome-p450. NAPQI is an electrophilic metabolite toxic to the liver. NAPQI is detoxified by glutathione, and when glutathione stores are depleted, the remaining NAPQI binds to proteins in the cell, causing cell damage and cell death [5,9].

Acetaminophen is metabolized very rapidly in children and its elimination half-life is very short; therefore, serum levels should be monitored at 2-hour intervals in case of intoxication. However, acetaminophen metabolism in children over 12 years of age is similar to adult metabolism. Acetaminophen intoxication in children occurs in four stages. In the first few hours, the patient experiences loss of appetite, nausea, vomiting, weakness and sweating. In the second stage, the patient may not have any clinical symptoms. While symptoms disappear in some patients, others may have pain and tenderness in the right upper quadrant, hepatic enlargement and oliguria. Bilirubin levels increase, ALT and AST levels rise and prothrombin time is prolonged. In the third stage (usually after 2-3 days), the patient develops signs of acute hepatitis and symptoms of liver failure. Signs of liver failure such as anorexia, hypoglycemia, coagulopathy and encephalopathy, jaundice, nausea, vomiting and weakness are observed. The last stage covers a period of 7-10 days when symptoms disappear. Complete blood count, renal and liver function tests should be requested from the patient presenting with acetaminophen poisoning [5]. Severe hepatotoxicity in children has been reported to occur as a result of repeated ingestion of low doses of acetaminophen rather than acute intoxication due to a single high dose of acetaminophen [10]. Approximately 12-13% of acute overdoses result in hepatotoxicity even with treatment [11], 2-5% progress to liver failure, and 0.2-0.5% result in death [12]. Acute kidney injury can occur even in the absence of liver failure and may present in a delayed fashion [13,14].

Biomarkers help determine the risk of toxicity, the need for treatment, and the effectiveness of therapy. Common tests used to guide the management of acetaminophen overdose include serum acetaminophen concentration, liver function tests (particularly alanine

and aspartate aminotransferases, ALT & AST), and the international normalized ratio (INR).

Acetaminophen concentration is plotted against time since ingestion on the Rumack-Matthew nomogram [15]. This nomogram is used to predict the risk of liver toxicity and to determine whether acetylcysteine treatment should be administered [16].

ALT and AST are hepatic enzymes released into the bloodstream following hepatocellular injury and are used to diagnose or exclude acute liver damage [17,18]. After an acute overdose, ALT/AST levels may begin to rise after 8 hours [17], but they can remain within normal range for up to 24 hours before hepatotoxicity becomes evident [19]. INR levels are used to indicate the severity, prognosis, and duration of treatment with acetylcysteine [15].

Developing consistent global guidelines for the treatment of acetaminophen poisoning is challenging. Various countries have adopted alternative NAC regimens or even lower treatment thresholds based on the Rumack-Matthew nomogram [20]. Denmark, for example, has abandoned the use of these nomograms and treats all patients with a full course of NAC regardless of acetaminophen concentrations [21].

N-acetyl cysteine (NAC) is used in the treatment of acetaminophen poisoning. NAC protects the liver by reducing glutathione consumption in the liver. NAC should be given within the first 8-10 hours after poisoning. NAC can be given both orally and IV. If the patient vomits within 1 hour after NAC administration, the dose should be repeated. Metoclopramide (0.5-1 mg/kg) or ondansetron (0.15 mg/kg) is given IV to prevent vomiting. If vomiting is persistent, NAC should be given through a nasogastric tube [6]. Methionine is also used in treatment. Methionine is given orally. Hemofiltration, hemodialysis or hemoperfusion may be added to the treatment to accelerate the excretion of acetaminophen. If there is bleeding due to prolonged prothrombin time, vitamin K1 may be given IM or IV [6]. Acetaminophen poisoning is one of the most common drug poisonings worldwide. Despite this, there is still no consensus on treatment [22].

Despite its widespread use and general safety at therapeutic doses, acetaminophen poisoning remains a significant cause of morbidity and mortality worldwide, particularly among children. The variability in clinical presentation and the potential for severe hepatotoxicity necessitate timely diagnosis and appropriate management. However, challenges persist in establishing standardized treatment protocols globally, partly due to differences in healthcare resources and clinical guidelines.

The aim of our study is to investigate the demographic and clinical characteristics, and treatment approaches of pediatric patients who presented to the emergency department of Kırşehir Training and Research Hospital due to acetaminophen poisoning, with a particular focus on the differences between accidental and intentional ingestions.

METHOD

Study Design

This study was designed as a retrospective analysis of pediatric patients admitted to the Emergency Department of Kırşehir Training and Research Hospital due to acetaminophen intake. The study covered a five-year period from January 2016 to January 2021. Only cases that required hospitalization in the Pediatrics Department were included. Data were obtained from hospital records and patient files.

In the study, no exclusion criteria were applied other than missing records and ingestion of multiple drugs. No data were obtained regarding the measurement of patients' acetaminophen levels from medical records. Based on the records, the treatment plan was determined according to the history provided by the patient or their relatives.

Participants

The study included children aged 0-18 years who were admitted to the Emergency Department with a history of acetaminophen ingestion. Patients were included in the study if they required hospitalization for observation or treatment. Cases with incomplete medical records or co-ingestion of other substances were excluded from the analysis.

Data Collection

Demographic and clinical information were taken from patient records retrospectively. The following variables were recorded and analyzed:

Acetaminophen-Related Factors: Formulation (pediatric or adult), and reason for intake (accidental or intentional).

Clinical Presentation: Symptoms observed upon admission.

Laboratory Parameters: Liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT]), and prothrombin times (PT), kidney function tests (urea, creatinine).

Treatment and management: Medical interventions, including use of N-acetylcysteine (NAC) as an antidote and supportive treatments.

Ethical Approval

Ethical approval was obtained from Kırşehir Training and Research Hospital and Kırşehir Ahi Evran University Clinical Research Ethics Committee (date: 03.08.2021, approval number: 2021-13/149).

Statistical Analysis

Number (n), percentage (%), median and quartiles (Q1-Q3) were used for descriptive statistics. The dependent variable of the study was acetaminophen as the cause of poisoning, while the independent variables were age, taking more than one medicine, NAC receiving treatment, receiving activated charcoal treatment, receiving gastric gavage therapy, ALT, AST, PT. The compatibility of continuous variables with normal distribution was examined by Kolmogorov-Smirnov test. Mann Whitney U test was used to compare the numerical data. The Wilcoxon signed-rank test was used to evaluate the difference between participants' measurement values on day 0 and day 3. Pearson chi-square test and Fisher's exact test were used to compare categorical variables. $P < 0.05$ was considered statistically significant. SPSS v26.0 package program was used for the analyses (SPSS Inc., Chicago, IL, USA).

RESULTS

This study examined the clinical and demographic characteristics of pediatric patients with acetaminophen poisoning. Among all poisoning cases, drug-related intoxications were the most frequent, accounting for 271(47.6%). Acetaminophen alone was responsible for 38(6.7%) of all cases, while other drugs accounted for 233(40.9%). Chemical substances represented the second most common cause, seen in 243(42.7%) of cases. Specific chemical agents included pesticides 18(3.2%), carbon monoxide 14(2.5%), alcohol or cologne 8(1.4%), plant or fungal toxins 4(0.7%), and petroleum derivatives 3(0.5%). In 8(1.4%) of the cases, the source of poisoning was unknown (Table 1).

Of the 38 patients with acetaminophen poisoning, 14(36.8%) were between 0-5 years of age, and 24(63.2%) were between 14-18 years. No cases were observed between the ages of 5-14. The majority of patients were female 25(65.8%), and suicidal ingestion was reported in 24(63.2%) of the cases. Activated charcoal was administered to 28(73.7%), gastric lavage was performed in 22(68.2%), and NAC treatment was given to 9(23.7%) (Table 2).

Among the 25 female patients, 19(76%) had ingested acetaminophen with suicidal intent, whereas 5(38.5%) of the 13 male patients had taken the drug for suicide purposes. This difference was statistically significant ($p=0.035$) (Table 3). The male-to-female ratio was 1:1.92.

Table 1. Substances that cause poisoning (0-18 ages)

Variables	Patient (n)	Percentages (%)
All drugs	271	47.6%
Acetaminophen	38	6.7%
Other drugs	233	40.9%
Chemical substances	243	42.7%
Carbon monoxide	14	2.5%
Pesticide	18	3.2%
Alcohol-cologne	8	1.4%
Plant-fungus	4	0.7%
Petroleum derivatives	3	0.5%
Unknown	8	1.4%
Total	569	%100.00

Table 2. Descriptive statistics in acetaminophen poisoning

Variable	Category	n	%
Age	0-5 years	14	36.8
	6-13 years	0	0
	14-18 years	24	63.2
Sex	Female	25	65.8
	Male	13	34.2
Reason for ingestion	Other causes (accident, misuse)	14	36.8
	Suicide	24	63.2
	Suspension	15	39.5
Formulation of the drug	Tablet	23	60.5
	Intravenous (IV) form	0	0
Symptoms	Positive	2	5.3
	None	36	94.7
Activated Charcoal	Given	28	73.7
	Not given	9	23.7
Gastric Lavage	Done	22	68.2
	Not done	15	29.2
NAC Treatment Status	Received	9	23.7
	Did not receive	28	73.7

NAC: N-acetyl cysteine.

Multiple drug ingestion was reported in 14(36.8%) of the cases. Among these, 12(85.7%) were suicide attempts ($p=0.028$). Activated charcoal was administered to 73.68% of patients, gastric lavage was performed in 68.2%, and 23.9% received N-acetylcysteine (NAC) treatment (Table 4).

The median ALT and AST values were 15.24 U/L (8.00-18.00) and 19.50 U/L (14.75-28.20), respectively, both showing statistically significant differences between accidental and intentional ingestion ($p=0.023$ and $p<0.001$, respectively). The median PT value was 12.60 seconds (10.55-12.90), with no significant difference observed ($p=0.372$) (Table 4).

Table 3. Causes of poisoning by sex

Sex	Reason for Intake		Total	p*
	Accident	Suicide		
Female	n	6	19	0.035
	%	24	76	
	Total	15.80	50.00	
Male	n	8	5	
	%	61.50	38.50	
	Total	21.10%	13.20	
Total	n	14	24	
	%	36.80	63.20	

*Pearson chi-square test.

Table 4. Median values in acetaminophen poisoning

Variable	Value
Number of patients (n)	38
Age- median (Q1- Q3)	15.00 (3.75- 17.00)
Sex (Female)	25 (65.79%)
Male: Female Ratio	1: 1.92
Reason for ingestion	
Accident	14 (36.84%)
Suicide	24 (63.16%)
Taking more than one medicine	14 (36.84%)
Activated charcoal treatment	28 (73.68%)
Gastric lavage treatment	22 (68.2%)
NAC treatment received	9 (23.9%)
ALT- median (Q1- Q3)	15.24 (8.00- 18.00)
AST- median (Q1- Q3)	19.50 (14.75- 28.20)
ALT (after 3 days) -median (Q1-Q3)	11.00 (10.00-15.25)
AST (after 3 days) -median (Q1-Q3)	20.00 (15.00-27.25)
Urea-median (Q1-Q3)	24.50 (18.75-28.00)
Creatine-median (Q1-Q3)	0.51 (0.40-0.68)
Urea (after 3 days)-median (Q1-Q3)	18.00 (16.00-23.00)
Creatine (after 3 days)-median (Q1-Q3)	0.54 (0.41-0.70)
PT-median (Q1-Q3)	12.60 (10.55-12.90)

All accidental ingestions presented to the emergency department within the first 8 hours. Among patients with suicidal ingestion, 79.1% arrived within the same timeframe. All suicide-related ingestions occurred in the 14-18 age group, and 19 (79.17%) of these patients were female (Table 5).

The median age of patients who ingested acetaminophen with suicidal intent was 16 years, whereas the median age in accidental ingestion cases was 3.36 years ($p<0.001$). Among patients with suicidal ingestion, the male-to-female ratio was 1:3.8. Combined drug use was significantly more frequent in the intentional group (50.00% vs. 14.29%, $p=0.028$). Initial ALT and AST levels were significantly lower in the intentional group ($p=0.023$ and $p<0.001$, respectively), and AST levels on the third day remained lower ($p=0.025$).

Additionally, creatinine levels on admission were significantly higher in the intentional group ($p<0.001$) (Table 6).

Table 5. Acetaminophen ingestion period according to age groups

Age range	0-5	5-14	14-18	Total	p
	n %	n %	n %		
Ingestion	Accident	-	Suicide		
Period	14 (36.8)	-	24 (63.2)	38 (100)	
0-2 h	9 (64.2)	-	14 (58.3)	23 (60.5)	2.247
2-8 h	5 (35.8)	-	5 (20.8)	10 (26.3)	
8-24 h	0	-	4 (16.7)	4 (10.5)	
>24 h	0	-	1 (4.2)	1 (2.5)	

*Pearson chi-square test

Table 6. Descriptive statistics by reason for acetaminophen intake

Variables	Suicide (n=24)	Accident (n=14)	p*
Age-median (Q1-Q3)	16.00 (15.00-17.00)	3.36 (3.00-4.00)	<0.001
Gender			
Female	19 (79.17)	6 (42.86)	0.035
Male	5 (20.83)	8 (57.14)	
Male: Female ratio	1:3.8	1:0.75	
Combined drug use	12 (50.00)	2 (14.29)	0.028
Received activated charcoal	18 (75.00)	10 (71.43)	0.639
Received gastric lavage	15 (62.50)	7 (50.00)	0.361
Received NAC treatment	8 (33.33)	1 (7.14)	0.057
ALT-median (Q1-Q3)	10.50 (8.00-15.00)	17.50 (12.75-22.50)	0.023
AST-median (Q1-Q3)	17.00 (13.25-19.75)	29.50 (25.50-35.00)	<0.001
ALT (after 3 days)-median (Q1-Q3)	11.00 (10.00-13.75)	12.50 (11.00-25.00)	0.377
AST (after 3 days)-median (Q1-Q3)	18.50 (14.25-27.00)	20.50 (16.00-29.00)	0.025
Urea-median (Q1-Q3)	22.00 (18.25-26.75)	26.00 (22.50-32.25)	0.106
Creatinine-median (Q1-Q3)	0.67 (0.57-0.79)	0.36 (0.32-0.42)	<0.001
Urea (after 3 days)-median (Q1-Q3)	18.00 (16.00-21.50)	18.00 (14.75-26.00)	0.907
Creatinine (after 3 days)-median (Q1-Q3)	0.53 (0.41-0.69)	0.60 (0.39-0.70)	0.881
PT-median (Q1-Q3)	12.25 (10.27-12.85)	12.60 (11.15-13.20)	0.372

*Mann-Whitney U test

A statistically significant difference was observed in AST levels between the first and third day among patients who ingested the substance accidentally. Similarly, a significant difference was also

found in creatinine levels between the first and third day in the same group (Table 7).

Table 7. Group comparison of 1. day and 3.day measurements

Reason for admission	Variable	Day 1- Median (Q1-Q3)	Day 3- Median (Q1-Q3)	Z	p*
Accident (n=14)	ALT	15.00	12.50	0.134	0.894
		(11.75-22.00)	(11.00-25.00)		
		27.75	20.50		
	AST	(19.00-34.25)	(16.00-29.00)	-2.424	0.015
		26.00	18.00		
		(22.25-32.25)	(14.75-26.00)		
	Urea	0.36	0.60	-1.728	0.084
		(0.32-0.42)	(0.39-0.70)		
Suicide (n=24)	ALT	11.50	11.00	-0.693	0.489
		(8.00-17.00)	(10.00-13.75)		
		16.00	18.50		
	AST	(13.00-25.50)	(14.25-27.00)	0.718	0.473
		22.00	18.00		
		(18.25-26.75)	(16.00-21.50)		
	Urea	0.67	0.53	-1.514	0.130
		(0.57-0.79)	(0.41-0.69)		

*Wilcoxon signed-rank test

DISCUSSION

Acetaminophen is a widely used analgesic and antipyretic in children, and its misuse can lead to serious health problems. It is a common cause of poisoning in children due to its easy accessibility and the fact that many parents do not realize how dangerous it can be. In this study, we analyzed the prevalence, risk factors, and clinical outcomes of acetaminophen poisoning across different age groups, comparing our findings with previous research.

Parents often underestimate the potential dangers of acetaminophen and ibuprofen. They frequently fail to store these medications safely, leaving them within easy reach of children, which contributes to the prominent role of analgesics in pediatric poisonings [23]. Extended-release formulations, containing higher doses of active ingredients and increasingly used, can lead to unpredictable clinical outcomes in overdose cases [24].

In our study, half of all poisoning cases were drug-related, and among these, 6.7% were identified as acetaminophen poisonings. Similar results were reported in a study conducted in Qatar, where analgesic and antipyretic medications, particularly acetaminophen, were identified as the most commonly ingested substances by children [25]. Koh et al. also found that analgesic/antipyretic agents and antihistamines were the drugs most frequently involved in poisoning incidents [26]. In Northwestern Romania, anticonvulsants, non-steroidal anti-inflammatory drugs (NSAIDs), and acetaminophen were the main drugs involved in poisonings [27]. The frequent use of

acetaminophen and ibuprofen in poisonings aligns with findings by Zakharov et al. [28]. Their widespread use is likely due to their availability in nearly every household. Adolescents can purchase these medications over the counter, as acetaminophen is sold without prescription in pharmacies and non-pharmacy outlets throughout the European Union [23]. Nguyen et al. identified five main substance groups responsible for acute poisoning in children. Non-drug chemicals accounted for 42.9% of exposures, medications for 37.6%, with acetaminophen (20.7%) and sedatives (13.8%) being the most common pharmaceuticals [29]. In our study, children under five years old were at high risk of accidental acetaminophen ingestion, while most cases among 14-18-year-olds involved intentional ingestion related to suicide attempts. The majority of intentional ingestions occurred in females (76%). Acute acetaminophen poisoning in children under five is usually accidental, whereas in older children and adolescents, it is more commonly due to intentional overdose for suicidal purposes [1]. Among our cases, 63.16% were due to suicidal ingestion, with a female-to-male ratio of 3.8:1. Conversely, accidental ingestions were more common in males. Marona et al. similarly reported that young children (median age 2.5 years) frequently ingested acetaminophen accidentally. In their study, 21.1% of cases were suicidal, with a female-to-male ratio of 1:17.5 among those attempting suicide [30]. Compared to their findings, our study shows a significantly higher proportion of females involved in suicide attempts. Consistent with previous research, symptomatic cases after acetaminophen ingestion were relatively low. In our study, 5.2% of cases were symptomatic, compared to 7.4% reported by Marona et al. Symptoms included chills, shivering, headache, and vomiting in two patients. The mean age for accidental ingestion in our study was 3.36 years, while for suicidal ingestion it was 16 years. Matalova et al. reported mean ages of 4.43 and 14.36 years, respectively [31]. Another study by Roversi et al. analyzed 267 adolescent patients hospitalized for acute poisoning. Of these, 85.8% were female, with a mean age of 15.8 years. Symptomatic presentation occurred in 44.2% of cases; 71.1% had at least one psychiatric comorbidity, and 79.6% required hospitalization. Antidote therapy was administered in 16.6%, and a minority needed intensive care. Acetaminophen (28.1%) was the most commonly ingested drug, followed by ibuprofen (10.1%) and aripiprazole (10.1%). Antipsychotics were the most frequently misused drug group (33.1%) [32]. A study by Shadman et al. found that in the United States, 9,935 out of every 100,000 children aged 0-19 were hospitalized due to acetaminophen poisoning. Both accidental and suicidal ingestions were more frequent among females [33]. In our study, 63.16% of cases were suicidal ingestions, while 36.84% were accidental. Activated charcoal was administered in 73.68% of cases, gastric lavage was performed in 68.2%, and N-acetylcysteine was given in 23.9%. Shekunov et al. reviewed 110 acetaminophen overdose cases, with 89 females and 21 males. Suicidal ingestion accounted for 88% of cases, while 12% were accidental. N-acetylcysteine was administered in 59%, 89% underwent psychiatric evaluation, and 73% were admitted to psychiatric services [34].

In our study, none of the 38 patients developed liver failure and kidney failure. A meta-analysis found that in acetaminophen poisoning, when N-acetylcysteine is administered early (generally within 10 hours of ingestion), the incidence of liver injury is low for both oral and intravenous (IV) administration [11]. Our results are in agreement with earlier research that found acetaminophen to be the most often poisoned medicine in children. Intentional intake was more prevalent than accidental ingestion, according to our study. Intentional ingestion was more common in adolescence, with most of these instances being female, whereas accidental ingestion was more common in young children. While the majority of cases were asymptomatic, some patients had headaches, nausea, and chills. Treatment methods included gastrointestinal lavage, activated charcoal, and the administration of N-acetylcysteine.

Limitations

Our study's retrospective design is one of its limitations, which could have resulted in inconsistent or underreported data, particularly with regard to the timing of the intervention and the amount of medication taken. Although we looked at the files within five years, our study's limitations include the fact that our study site is small in size and that there were 38 cases of acetaminophen poisoning overall. The lack of long-term follow-up for patients prevents us from assessing potential delayed effects of poisoning.

CONCLUSION

Our study demonstrates that acetaminophen poisoning is a significant public health issue in children. While poisoning in young children usually occurs accidentally, in adolescents, it is predominantly due to suicidal intent. Notably, suicidal drug ingestion was more common among adolescent females. Most patients did not develop severe toxicity, and symptoms were rarely observed. To prevent acetaminophen poisoning, parental awareness should be increased, medications should be stored safely, and physicians should pay attention to accurate dose calculations. Additionally, providing psychosocial support to adolescents is essential to prevent suicide attempts. NAC administration, gastric lavage, and activated charcoal are effective treatment methods, but a personalized approach based on clinical and laboratory findings is necessary.

Acetaminophen poisoning remains a global concern, and there is still no definitive consensus on treatment strategies. Therefore, large-scale prospective studies are needed to standardize management and treatment protocols.

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REFERENCES

- Brune K, Renner B, Tiegs G. Acetaminophen/paracetamol: a history of errors, failures and false decisions. *Eur J Pain*. 2015;19(7):953-965.
- WHO. WHO Model List of Essential Medicines-22nd List. Geneva: World Health Organization; 2021.
- Australian Medicines Handbook Pty Ltd. Australian Medicines Handbook. Adelaide: Australian Medicines Handbook; 2020.
- Penna A, Buchanan N. Paracetamol poisoning in children and hepatotoxicity. *Br J Clin Pharmacol*. 1991;32(2):143-149.
- Sia J, Chan Y. Case Report: Paracetamol poisoning in a 2-year-old child-from international overview to the role of the Hong Kong Poison Information Centre. *Hong Kong J Emerg Med*. 2006;13(4):225-231.
- Republic of Turkey Ministry of Health. Diagnostic and Treatment Guidelines for Primary Care. Ankara: Ministry of Health; 2012.
- Jones AL, Dargan PI. What's new in toxicology? *Curr Paediatr*. 2001;11(6):409-413.
- Shah AD, Wood DM, Dargan PI. Understanding lactic acidosis in paracetamol (acetaminophen) poisoning. *Br J Clin Pharmacol*. 2011;71(1):20-28.
- Corcoran G, Mitchell JR, Vaishnav YN, Horning EC. Evidence that acetaminophen and N-hydroxyacetaminophen form a common arylating intermediate, N-acetyl-p-benzoquinoneimine. *Mol Pharmacol*. 1980;18(3):536-542.
- Rivera-Penera T, Gugig R, Davis J, McDiarmid S, Vargas J, Rosenthal P, et al. Outcome of acetaminophen overdose in pediatric patients and factors contributing to hepatotoxicity. *J Pediatr*. 1997;130(2):300-304.
- JL Green JL, Heard KJ, Reynolds KM, Albert D. Oral and intravenous acetylcysteine for treatment of acetaminophen toxicity: a systematic review and meta-analysis. *West J Emerg Med*. 2013;14(3):218-226.
- Buckley N, Calear A, Cairns R, Reily N, Tang S, McCallum S, Christensen H. Independent expert report on the risks of intentional self-poisoning with paracetamol. Canberra: Therapeutic Goods Administration; 2022. Therapeutic Goods Administration; 2022.
- Waring W, Jamie H, Leggett G. Delayed onset of acute renal failure after significant paracetamol overdose: a case series. *Hum Exp Toxicol*. 2010;29(1):63-68.
- Eguia L, Materson BJ. Acetaminophen-related acute renal failure without fulminant liver failure. *Pharmacotherapy*. 1997;17(2):363-370.
- Chiew AL, Reith D, Pomerleau A, Wong A, Isoardi KZ, Soderstrom J, et al. Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand. *Med J Aust*. 2020;212(4):175-183.
- Wong A, Graudins A. Risk prediction of hepatotoxicity in paracetamol poisoning. *Clin Toxicol (Phila)*. 2017;55(8):879-892.
- Gloor Y, Schwartz D, Samer CF. Old problem, new solutions: biomarker discovery for acetaminophen liver toxicity. *Expert Opin Drug Metab Toxicol*. 2019;15(8):659-669.
- Dear JW, Antoine DJ. Stratification of paracetamol overdose patients using new toxicity biomarkers: current candidates and future challenges. *Expert Rev Clin Pharmacol*. 2014;7(2):181-189.
- Chiew AL, James LP, Isbister GK, Pickering JW, McArdle K, Chan BS, et al. Early acetaminophen-protein adducts predict hepatotoxicity following overdose (ATOM-5). *J Hepatol*. 2020;72(3):450-462.
- Bateman DN, Dear JW. Acetylcysteine in paracetamol poisoning: a perspective of 45 years of use. *Toxicol Res (Camb)*. 2019;8(4):489-498.
- Schmidt L, Dalhoff K. Risk factors in the development of adverse reactions to N-acetylcysteine in patients with paracetamol poisoning. *Br J Clin Pharmacol*. 2001;51(1):87-91.
- Heubi JE, Barbacci MB, Zimmerman HJ. Therapeutic misadventures with acetaminophen: hepatotoxicity after multiple doses in children. *J Pediatr*. 1998;132(1):22-27.
- Mund ME, Quarcoo D, Gyo C, Brüggmann D, Groneberg DA. Paracetamol as a toxic substance for children: aspects of legislation in selected countries. *J Occup Med Toxicol*. 2015;10:1-7.
- Rakovcová H. Drug poisoning in children. *Pediatric Pro Praxi*. 2013;14(2):126-129.
- Ahmed A, AlJamal AN, Mohamed Ibrahim MI, Saleh K, AlYafei K, Zaineh SA, et al. Poisoning emergency visits among children: a 3-year retrospective study in Qatar. *BMC Pediatr*. 2015;15:1-7.
- Koh SH, Tan KHB, Ganapathy S. Epidemiology of paediatric poisoning presenting to a children's emergency department in Singapore over a five-year period. *Singapore Med J*. 2018;59(5):247-250.
- Nistor N, Frasinariu OE, Rugina A, Ciomaga IM, Jitareanu C, Streanga V. Epidemiological study on accidental poisonings in children from northeast Romania. *Medicine (Baltimore)*. 2018;97(29):e11469.
- Zakharov S, Navratil T, Pelcova D. Non-fatal suicidal self-poisonings in children and adolescents over a 5-year period (2007-2011). *Basic Clin Pharmacol Toxicol*. 2013;112(6):425-430.
- Nguyen SN, Vu LT, Nguyen HT, Nguyen LMT. Childhood acute poisoning at Haiphong Children's Hospital: a 10-year retrospective study. *Int J Pediatr*. 2023;2023(1):2130755.
- Marano M, Roversi M, Severini F, Memoli C, Musolino A, Pisani M, et al. Adverse drugs reactions to paracetamol and ibuprofen in children: a 5-year report from a pediatric poison control center in Italy. *Ital J Pediatr*. 2023;49(1):20.
- Matalova P, Buchta M, Drietomska V, Spicakova A, Wawruch M, Ondra P, et al. Acute drug intoxication in childhood: a 10-year retrospective observational single-centre study and case reports. *Biomol Pap Med Fac Univ Palacky Olomouc Czech Repub*. 2023;167(3):294-302.
- Roversi M, Martini M, Musolino A, Pisani M, Zampini G, Genuini L, et al. Drug self-poisoning in adolescents: a report of 267 cases. *Toxicol Rep*. 2023;10:680-685.
- Shadman KA, Edmonson MB, Collier RJ, Sklansky DJ, Nacht CL, Zhao Q, et al. US hospital stays in children and adolescents with acetaminophen poisoning. *Hosp Pediatr*. 2022;12(2):e60-e67.
- Shekunov J, Lewis CP, Vande Voort JL, Bostwick JM, Romanowicz M. Clinical characteristics, outcomes, disposition, and acute care of children and adolescents treated for acetaminophen toxicity. *Psychiatr Serv*. 2021;72(7):758-765.

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