



Evaluation of Children Presenting to the Emergency Department with Iron Intoxication

Acil Servise Demir Zehirlenmesi İle Başvuran Çocuk Vakalarının Değerlendirilmesi

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ABSTRACT

Purpose: Intoxications is a common and preventable cause of childhood morbidity and mortality. Acute iron intoxication usually occurs in children under 5-year-old due to accidental ingestion, and composes 2% of all intoxication cases in children and adolescents. In this study, demographic, epidemiological, clinical features, treatments, and complications of the patients admitted to our emergency department with acute iron intoxication were evaluated.

Material and Method: Patients admitted to a Pediatric Emergency Service of the Faculty of Medicine diagnosed with iron intoxication between 2018 and 2020 were retrospectively investigated. The patients' demographic characteristics, information about intoxication, and laboratory results were recorded, and statistical analyzes were performed.

Results: Of the 12 patients included in the study, 66.7% were female, and 33.3% were male. The mean age was 81.3±83.52 months. When separated by age group, 66.6% of the patients were younger than 5-year-old. Those who came to the hospital via an ambulance were only 25%. All patients were transported to the hospital within an average of 40±15 minutes. While there was no life-threatening risk in 7 patients, the condition of 5 patients was severe. Only 2 of the patients took it to suicide. All cases received iron orally. One patient presented abdominal pain, and 2 patients presented nausea and vomiting. Activated charcoal was administered to 4 of the patients. In the laboratory follow-ups of the patients, all mean results, excluding iron, were normal. In addition, the blood gases of the patients at the time of admission were compensated metabolic acidosis.

Conclusion: As a pediatric emergency, iron intoxication in children remains important as one of the preventable morbidity and mortality causes. We believe that iron preparations are packaged in a single-dose form and do not have an attractive taste and appearance for children, have protective caps in medicine boxes, and when physicians prescribe iron drugs to adult patients, warning them about toxicity in children will reduce mortality and morbidity.

Keywords: Children, iron intoxication, emergency

ÖZ

Amaç: Bu çalışma ile oral demir alımı sonrası intoksikasyon nedeniyle başvuran hastaların; demografik, epidemiyolojik, klinik özellikleri, tedavileri ve komplikasyonlarının geriye dönük olarak değerlendirilmesi neticesinde ülkemiz çocukluk çağı demir zehirlenmeleri verilerine katkı sağlamak amaçlandı.

Gereç ve Yöntem: 2018-2020 yılları arasında demir intoksikasyonu tanısı ile bir Tıp Fakültesi Çocuk Acil Polikliniği'ne başvurmuş hastalar retrospektif olarak tarandı. Hastaların demografik özellikleri, intoksikasyona ait bilgiler ve laboratuvar tetkik sonuçları kayıt altına alınarak istatistiksel analizleri gerçekleştirildi.

Bulgular: Çalışmaya dahil edilen 12 hastanın %66,7'si kadın %33,3'ü erkekti. Ortalama yaş 81,3± 83,52 aydı. Yaş gruplarına göre ayrıldıklarında olguların %66,6'sı 5 yaşından küçük çocuklar olarak gözlemlendi. Hastaneye bir ambulans yardımı ile gelenler sadece %25'ini oluşturmaktaydı. Ortalama 40±15 dk içerisinde tüm hastaların hastaneye nakli gerçekleştirilmiştir. 7 hastanın hayati bir riski bulunmazken, 5 hastanın durumu ciddi idi. Hastalardan sadece 2 tanesi suisid amaçlı zehirlenmişti. Tüm vakalar demiri oral yoldan almıştır. 1 hastada karın ağrısı, 2 hasta da bulantı, kusma oluşmuştur. Hastalardan 4'üne tedavide aktif kömür uygulandı. Hastaların laboratuvar takiplerinde demir dışındaki diğer tüm değerlerin ortalama sonuçları normal bulundu. Ayrıca hastaların başvuru esnasındaki kan gazları kompanse metabolik sendrom şeklindedir.

Sonuç: Pediatrik acil olarak; çocuklarda demir intoksikasyonu, önlenilebilir morbidite ve mortalitenin nedenlerinden birisi olarak halen önemini korumaktadır. Demir preparatlarının tek doz şeklinde paketlenmesinin yanı sıra çocukların cezbedici tat ve görünümünde olmaması, koruyucu kapakların ilaç kutularında mutlaka kullanılması, hekimlerin demir ilaçlarını reçete ettiği yetişkin hastalarını çocuklardaki toksisite açısından uyararak gerekli bilgileri vermesi mortalite ve morbiditeyi azaltacağı kanaatindeyiz.

Anahtar Kelimeler: Demir, zehirlenme, acil servis

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INTRODUCTION

Intoxications, a common and preventable cause of childhood morbidity and mortality, are among the most important reasons for admission to pediatric emergency services and hospitalizations in our country, including in developed countries worldwide(1).

Acute iron intoxication usually occurs in children under 5-year-old due to accidental ingestion, and it is less common in adolescents and adults. The American Association of Poison Control Centers reported in 2004 that 2% of all intoxication cases in children and adolescents are iron poisoning (2). The main reasons are the widespread availability of iron-containing dietary supplements, the tablets' sugar-like appearance, and parents' lack of potential toxicity awareness (1-4). A study showed that only one-third of parents keep their iron-containing drugs in areas out of reach of children (5).

The excess amount of iron taken orally affects the gastrointestinal system barrier via its direct caustic effect. As a result, massive iron absorption occurs. When the serum iron level exceeds the binding capacity, free radicals emerge, and lipid peroxidation and cell destruction occur. Although toxicity mainly affects the liver, kidney, heart, lungs, and hematological system are also adversely affected (4-6). The toxicity severity depends on the amount of iron taken. The toxicity risk is generally low, below 20 mg/kg. Decontamination is recommended, with patient monitoring for 6 hours. There is a moderate toxicity risk in iron intake of 20-40 mg/kg. Chelation therapy should be considered in addition to decontamination. Doses above 60 mg/kg are regarded as high risk, and chelation therapy should be started in addition to decontamination (6).

In this study, we aimed to contribute to the data on childhood iron intoxication with the retrospective evaluation of demographic, epidemiological, clinical features, treatments, and complications of the patients who applied due to intoxication after oral iron intake in our emergency department.

MATERIAL AND METHOD

The study was carried out with the permission of Selçuk University Ethics Committee (Date: 29.03.2022, Decision No: 2022/151). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study is retrospective. Patients between 1 month and 18 years who were diagnosed with iron intoxication and followed up in the Pediatric Emergency Service of Selçuk University Faculty of Medicine between January 1, 2018, and June 30, 2020, were examined and included. Patients with missing data, incomplete diagnostic codes, and intoxication with non-ferrous and/or other drugs were excluded from the study. Ethics committee approval was obtained.

In addition to demographic characteristics of the patients such as age, gender, presence of chronic diseases, many intoxication-related factors such as the year, season, admission time to the hospital, the way and duration of admission, the presence of additional comorbidities, intoxication types (suicide, accident, substance, etc.), consciousness status were included in the examination. In addition to this, laboratory examinations and the treatments administered are included.

Statistical Analysis

All data were evaluated using the SPSS 21.0 statistical package program. The normal distribution of the variables was studied using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/ Shapiro-Wilk tests). Descriptive analyzes were given using mean and standard deviation values for normally distributed variables and median values for non-normally distributed variables. The results were evaluated at the 95% confidence interval, and the significance level was $p < 0.05$. Number, percentage, mean and standard deviation were used to assess the data.

RESULTS

Of 12 patients who met the criteria of our study between 2018 and 2020 and applied to the pediatric emergency department due to acute iron intoxication, 66.7% were female, and 33.3% were male. The mean age was 81.3 ± 83.52 (12-215) months. When separated by age group, 66.6% of the patients were children younger than 5-year-old. Sociodemographic characteristics of iron intoxication patients are shown in **Table 1**.

It was observed that the patients mainly applied in the spring (41.6%) of the year. Intoxication occurred mainly between 16:00-23:59 hours. Those who came to the hospital via an ambulance were only 25%. All patients were transferred to the hospital within an average of 40 ± 15 minutes (**Table 1**).

While the reason for the admission of three patients was the presence of the symptom, the other 9 patients were admitted as forensic cases. As a result, 7 (58.3%) patients were discharged after patient monitoring in the emergency department. 4 patients were hospitalized, and 1 patient was referred (**Table 1**).

Headache, dizziness, fainting, convulsions, palpitations, arrhythmias, respiratory distress, cough, fever, color change in the mouth, bruising, bleeding, paresthesia, and arrest were not observed. In addition, CK-MB and troponin markers were evaluated in a normal range. All patients were conscious at the time of admission. Again, no changes in consciousness were observed in all of them. According to the previous medical records, only 1 of the patients had a history of hematological disease.



There was no life-threatening risk in 7 patients, but, 5 patients were severe. Only 2 of the all patients were poisoned to suicide. All cases received iron orally. One patient presented abdominal pain, and 2 patients presented nausea and vomiting. Activated charcoal was administered to 4 patients.

When we examined the laboratory results of our study, the average results of all values except iron were normal. In addition, when the blood gas was analyzed, the pH was 7.40 ± 0.04 . According to these results, the patients' blood gases were compensated metabolic acidosis at the admission. The laboratory findings of the patients applying to the pediatric emergency department after iron intoxication are shown in **Table 2**.

DISCUSSION

Acute iron intoxication is one of the most important toxicities in childhood. Patients may be hypovolemic due to fluid loss and GI bleeding due to irritation. As a result of iron absorption, systemic toxicity findings may occur with the formation of free radicals. Free radicals causing disruption in oxidative phosphorylation, mitochondrial dysfunction, and cell death can be observed in severe poisonings (7).

In patients with digestive system symptoms, gastric lavage with ample hydration and gastrointestinal decontamination methods should be applied. In addition to iron intake, there are symptoms and signs such as lethargy, hypovolemia, persistent vomiting, shock, diarrhea, metabolic acidosis, or a serum iron level of 500 µg/dl and above. Chelation therapy with desferrioxamine should be applied (6-8). Since all patients in our study had a serum iron level of less than 500 µg/dl and had mild signs of poisoning, the patients were usually discharged after being kept under monitoring for 48 hours.

In many studies, it has been reported that poisoning is observed mainly between 1-5-year-old. A survey conducted on 2482041 poisoning cases in the USA in 2007 reported that 51.23% of them were children younger than five-year-old (9). In a study conducted in Greece, poisoning cases under five-year-old were 93% of the patients (10). The survey conducted by Sümer et al. on 233 patients who applied to the emergency department reported that 73.8% were children under 5-year-old (11). In addition to the low consciousness level in this age group, children are curious and try to recognize the world, especially with their sense of taste, which is why poisoning is more common before 5-year-old. The result of our study is similar to studies in Turkey and other countries, with 66.6% of poisonings occurring in children under 5-year-old.

In drug intoxication studies conducted in adults, the cause of intoxication is suicide in over 80%, while this rate drops below 50% in children (9,11,12). As a matter of fact, in our study, iron intake to suicide was very low (16.6%).

Table 1. Sociodemographic Characteristics of Iron Intoxication Patients

Parameters	(N)	(%)
Gender		
Female	8	66.7
Male	4	33.3
Categorical age (month)		
Between 0-60 months	8	66.6
Between 121-180 months	2	16.7
180 months and older	2	16.7
Admission season		
Spring	5	41.6
Summer	2	16.7
Fall	2	16.7
Winter	3	25
Time of cases		
08:00-15:59	2	16.7
16:00-23:59	8	66.6
00:00-07:59	2	16.7
First applied hospital		
Yes	9	75
No	3	25
Admission type		
Without ambulance	9	75
With ambulance	3	25
Activated charcoal application		
Yes, administered	4	33.3
No, not administered	8	66.7
Application result		
Discharge after patient monitoring in emergency service	7	58.3
Hospitalized	4	33.3
Referring	1	8.4

Table 2: Laboratory Findings of the Patients Presenting to the Pediatric Emergency Department after Iron Intoxication

Parameters	Mean±standart deviation (min. – max.)
Iron (µg.dl ⁻¹)	223.25±167.33 (37-411)
Alanine transaminase (U/L)	18.08±8.36 (9-34)
Aspartatetransaminase (U/L)	33.75±10.38 (16-47)
Hemoglobin (g/dL)	12.78±1.62 (10.90-15.80)
Hemotocrit (%)	38.13±4.70 (32.40-46.80)
Leukocyte (mm ³)	10.34±2.52 (6.30-14.40)
Lymphocyte (K/uL)	3.92±1.73 (2.30-8.28)
Thrombocyte (K/uL)	310.83±84.33 (177-477)
Glucose (mg/dL)	95.40±16.66 (78-128)
Urea (mg/dL)	27.84±7.58 (13.0-40.0)
Creatinin (mg/dL)	0.37±0.16 (0.22-0.69)
Uric acid (mg/dL)	4.18±1.05 (3.10-6.40)
Aptt (sec)	30.96±6.86 (26.00-41.40)
PT-INR (INR)	1.01±0.04 (0.96-1.06)
Sodium (mEq/L)	137.00±1.65 (134-140)
Potassium (mmol/L)	4.11±0.34 (3.46-4.83)
Calcium (mg/dL)	9.94±0.43 (9.30-10.70)
Magnesium (mg/dL)	2.22±0.14 (2.02-2.47)
Sedimentation (mm/saat)	5.20±5.21 (2.0-14.0)
C-reactive protein (mg/L)	1.85±1.73 (0.11-5.12)

Aptt: Activated partial thromboplastin time, PT-INR: Protrombin time- International Normalized Ratio

66.3% of our patients are girls. While all of the cases over 5-year-old were girls, if they were under 5-year-old, this ratio was equal for boys and girls. According to the literature, it was seen that accidental intoxication cases were more common in boys, and self-destructive intoxications were more common in girls. In addition, our results are compatible with the literature as we mainly observe accidental intoxication cases under the age of 5 years (12-14).

In their study, Akin et al. demonstrated that 96.1% of poisonings occur at home, and 96.1% occur orally (15). On the other hand, Ödek et al. found that 91.3% of poisonings occurred orally, and 89.1% occurred at home (12). We also found that all patients in our study had iron poisoning either orally or at home. This situation was considered that iron drugs at home and taken orally caused most of the poisonings.

The effects of iron poisoning are examined in four stages in the clinic. The first stage is gastrointestinal irritations such as nausea-vomiting. It occurs approximately 6 hours after ingesting the drug. Hypotension and metabolic acidosis develop with increased capillary permeability in the second stage. In the third stage, due to the cytotoxic effects of iron, organ failures such as kidney and liver failure are observed. Patients in the fourth stage, the last stage, have a higher risk of gastrointestinal bleeding. (16) In the first 6 hours of patient monitoring, if the patient's iron level is below 20 mg/kg and the patient is asymptomatic, there is usually no need for treatment. (17) The patients in our study had normal blood values and showed mild symptoms. Thus, the average blood gas results of the patients were compensated metabolic acidosis.

After admission to the pediatric emergency department, diagnosis and treatment of poisoning cases are usually carried out (15-42%) in pediatric emergency services. In our study, 33.3% of the patients were hospitalized and continued treatment in the pediatric emergency department (12-14). As the patients in our study did not have high-risk iron intoxication and the poisoning symptoms were mild, an intensive care unit was not required.

Activated charcoal administration is recommended for patients with an early diagnosis of iron intoxication. Activated charcoal was administered to 33.3% of the cases in our study. It was found that oral activated charcoal was administered at 42.7% to 48% in the study of Akgül et al., while this rate was 72.8% in the study of Ödek et al. (12,13). The relatively lower rate in our study was attributed to the fact that the admission time to the emergency department after poisoning was longer than 60 minutes on average.

Limitations

Our study has a relatively small sample size, and larger sample size will be much more meaningful in terms of results. One of the most important reasons for

the small sample size may be excluded patients with multiple drug intakes and iron-containing nutritional supplements from our study. In addition, the retrospective nature of our research and the inability to adequately determine the time between iron intake and transportation to the emergency room are other significant limitations.

CONCLUSION

As a pediatric emergency, iron intoxication in children still maintains its importance as one of the preventable morbidity and mortality causes. We believe that iron preparations are packaged in a single-dose form and do not have an attractive taste and appearance for children, have protective caps in medicine boxes, and when physicians prescribe iron drugs to adult patients, warning them about toxicity in children will reduce mortality and morbidity.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Selçuk University Ethics Committee (Date: 29.03.2022, Decision No: 2022/151).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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REFERENCES

1. Nistor N, Frasinariu OE, Rugina A, Ciomaga IM, Jitareanu C, Streanga V. Epidemiological study on accidental poisonings in children from northeast Romania. *Medicine*. 2018;97:29(e11469).
2. Watson WA, Litovitz TL, Rodgers GC Jr et al. 2004 Annual report of the American association of poison control centers toxic exposure surveillance system. *Am J Emerg Med* 2005;23:589-666.
3. Proudfoot AT, Simpson D, Dyson EH. Management of Acute Iron Poisoning. *Med Toxicol* 1986;1:83-100.
4. Tenenbein M. Hepatotoxicity in Acute Iron Poisoning. *J Toxicol Clin Toxicol* 2001;39:721-26.
5. Smolinske SC, Kaufman MM. Consumer perception of household hazardous materials. *Clin Toxicol* 2007;45:522-5.
6. Baranwal AK, Singhi SC. Acute Iron Poisoning: Management Guidelines. *Indian Pediatr* 2003;40:534-40.
7. American Academy of Clinical Toxicology, European Association of Poison Centres and Clinical Toxicologists. Position Paper: Whole Bowel Irrigation. *J Toxicol Clin Toxicol* 2004;42:843-54.
8. Audimoplam VK, Wendon J, Bernal W, Heaton N, O'Grady J, Auzinger G. Iron and Acetaminophen a Fatal Combination? *Transpl Int* 2011;24:85-8.



9. Bronstein AC, Spyker DA, Louis R, et al. 2007 Annual Report of The American Association of Poison Control Centers National Poison Data System (NPDS): 25th Annual Report. *Clinical Toxicology* 2008; 46: 927-1057.
10. Petridou E, Kouri N, Polychronopoulou A, et al. Risk factors for childhood poisoning: a case control study in Greece. *Injury Prevention* 1996; 2: 208-11.
11. Sümer V, Güler E, Karanfil R, Dalkıran T, et al. Gürsoy H. Evaluation of the poisoning cases who applied to the pediatrics emergency unit. *Turk Arch Ped* 2011; 46: 234-240.
12. Ödek Ç, Erol M, Demir R, Tunç M et al. Retrospective Analysis of Demographic, Epidemiologic, and Clinical Characteristics of Poisoning Cases Followed in Pediatric Intensive Care Unit. *J Pediatr Emerg Intensive Care Med* 2019;6(2).
13. Akgül F, Er A, Çelik FÇ, Çağlar A, Ulusoy E, ve ark. Çocukluk çağı zehirlenmelerinin geriye dönük olarak incelenmesi. *J Pediatr Emerg Intensive Care Med*. 2016;3:91-6.
14. Azab SMS, Hirshon JM, Hayes BD et al. Epidemiology of acute poisoning in children presenting to the poisoning treatment center at Ain Shams University in Cairo, Egypt, 2009-2013. *Clin Toxicol*. 2016;54:20-6.
15. Akin Y, Ağzıkuru T, Cömert S. et al. Hospitalizations for pediatric intoxication: a study from İstanbul. *Turk J Pediatr*. 2011;53:369-74.
16. Mills KC, Curry SC. Acute iron poisoning. *Emerg Med Clin North Am* 1994;12:397-413.
17. Curry SC, Braitberg G. Poisoning in pregnancy. In: Foley MR, Strong T, eds. *Obstetric Intensive Care*. Philadelphia, WB Saunders; 1997:347-67.