Acute Iron Poisoning in Children: An Ongoing Important Pediatric Emergency

Çocuklarda Akut Demir Zehirlenmesi: Devam Eden Önemli Bir Pediatrik Acil

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ABSTRACT

Objective: Iron containing drugs are one of the most commonly prescribed drugs in our country and accidental or suicidal poisoning continues to be an important pediatric emergency. Our aim was to evaluate the clinical, laboratory, radiologic findings, and treatment approaches of children hospitalized with acute iron poisoning.

Material and Methods: The clinical, laboratory, and radiologic findings of and treatment approaches for 17 patients aged 14 months-15 years hospitalized with acute iron poisoning were reviewed.

Results: The mean age was 37±35.2 months. Iron poisoning was accidental in 16 patients. The mean duration between drug intake and hospital admission was 177±149 minutes. The mean ingested amount of iron was 35.4±19 mg/kg. The mean blood iron level was 232±136 mcg/dl. There was no significant relationship between the reported dose of ingested iron and the blood iron level (p>0.05). There was no significant relationship between blood iron level and ingestion time (p>0.05). Laboratory results revealed metabolic acidosis in 3 patients, respiratory acidosis in one patient, leucocytosis in one patient, and prolonged activated partial thromboplastin time in one patient. The patients' findings were not consistent with blood iron levels. Whole bowel irrigation and IV deferoxamine were used in 3 patients. There was no death. The mean hospitalization duration was 2.8±1.1 days.

Conclusion: Accidental iron poisoning continues to be an important pediatric emergency. There are no correlations between blood iron levels and the amount of ingested iron or the ingestion time. There was also no correlation between the blood iron levels and the clinical, laboratory and radiographic findings in our study.

Key Words: Iron, Fe+2, Fe+3, Poisoning

ÖZ

Amaç: Demir içeren ilaçlar ülkemizde en sık reçete edilen ilaçlardandır. Dolayısıyla kaza ya da suisidal zehirlenmeler önemli bir pediatrik acil olmaya devam etmektedir. Amacımız, akut demir zehirlenmesi ile hastaneye yatırılan çocukların klinik, laboratuvar, radyolojik bulgularını ve tedavi yaklaşımlarını değerlendirmektir.

Gereç ve Yöntemler: Akut demir zehirlenmesi nedeniyle hastaneye yatırılan 14 ay-15 yaş arası 17 hastanın klinik, laboratuvar, radyolojik bulguları ve tedavi yaklaşımları incelendi.

Bulgular: Ortalama yaş 37±35.2 aydı. Demir zehirlenmesi 16 hastada kazara gerçekleşmişti. İlaç alımı ile hastaneye başvuru arasındaki süre 177±149 dakikaydı. Ortalama alınan demir miktarı 35.4±19 mg/kg'dı. Ortalama kan demir düzeyi 232±136 mcg/dl'di. Alındığı söylenen doz ile kan demir düzeyi arasında anlamlı ilişki yoktu. (p>0.05). Kan demir düzeyi ile ilaç alma zamanı arasında da anlamlı ilişki yoktu (p>0.05). Laboratuvar incelemede; 3 hastada metabolik asidoz, 1 hastada respiratuar asidoz, 1 hastada lökositoz ve 1 hastada da uzamış aktive parsiyel tromboplastin zamanı (aPTT) görüldü. Hastaların bulguları ile kan demir düzeyleri uyumlu değildi. Tüm bağırsak yıkama ve IV desferrioxamine 3 hastada uygulandı. Ölüm olmadı. Ortalama hastanede kalım süresi 2.8±1.1 gündü.

Sonuç: Kaza ile demir zehirlenmesi önemli bir pediatrik acil olmaya devam etmektedir. Çalışmada kan demir düzeyleri ile alınan demir miktarı ve alınma zamanı arasında ilişki bulunmamıştır. Yine kan demir düzeyleri ile klinik, laboratuvar, radyolojik bulgular arasında da uyumluluk saptanmamıştır.

Anahtar Sözcükler: Demir, Fe+2, Fe+3, Zehirlenme

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INTRODUCTION

Acute iron poisoning generally occurs by accident in children whereas it is usually intentional in adolescents and adults. The wide availability of iron-containing nutritional supplements and iron tablets in the household, the candy-like appearance, and the lack of recognition of the potential toxicity by parents and the general public are the major risks for iron poisoning (1-5). Smolinske et al. (2) reported that only one-third of parents kept iron-containing drugs out of the reach of children. Iron in the free state disrupts multiple cellular processes by catalyzing redox reactions with lipid peroxidation and free radical formation. An ingested iron dose of 20 mg/kg can be potentially toxic. Ingestion of > 60mg/kg can be associated with severe toxicity including death (3,4).

Most of data for management of acute iron poisoning is based on case reports, expert consensus, animal studies, and adult volunteer studies (3). There is scarcity of literature about every aspect (clinical, laboratory, radiologic findings and treatment approaches) of pediatric acute iron poisoning. We aimed to evaluate the clinical, laboratory, radiologic findings and treatment approaches of children with acute iron poisoning.

MATERIAL and METHODS

The records of 17 patients aged 14 months to 15 years who were hospitalized due to witnessed acute iron poisoning by oral iron formulations between January 2006 and December 2015 were evaluated in this study. The age, gender, reason of iron intake (accidental/suicidal), duration between drug intake and hospital admission, level of consciousness, hospitalization duration, laboratory results and treatment approaches were recorded. The mean ingested iron was calculated according to the empty pills or space on the preparation and the reported dose. Patients with acute iron poisoning were included in the study. Patients with multidrug poisoning or iron-containing nutritional supplements were excluded from the study.

SPSS (Statistical Package For Social Sciences for Windows v. 15.0 SPSS Inc.; Chicago, IL, USA) was used to analyse the data. Results are presented as numbers and percentages. Mean±standard deviation was used for parametric values. Pearson's chi-square test was used to discover a relationship between two categorical variables. A P-value <0.05 was considered as significant.

RESULTS

Ten (59%) girls and 7 (41%) boys were enrolled in the study. The mean age was 37±35.2 (14-168) months. There were 6 patients aged under 2 years, and 10 patients aged 2-5 years. One patient was 15 years old. The reason of poisoning was a suicide attempt in the 15-year-old patient and accidental in the other 16 patients. All the patients ingested iron preparations orally. The mean duration between iron intake and hospital admission was 177±149 (30-600) minutes. The mean ingested iron was 35.4±19 mg/kg (16-95 mg/kg) in 16 patients. The mean ingested iron could not be detected in the patient who had attempted suicide because the amount of ingested drugs was not known exactly. Blood iron levels were checked between 2-8 hours after iron ingestion in 16 patients. Blood iron levels were checked at the time of hospital admission in one patient who had been transferred to our hospital from another hospital 10 hours after gastric lavage. The mean blood iron level was 232±136 (23-424) mcg/dl. Blood iron levels were <350 mcg/dl in 12 patients and 350-500 mcg/dl in 5 patients. There was no patient with a blood iron level above 500 mcg/dl. The highest iron level was found to be 424 mcg/dl in one patient who had ingested 95 mg/kg elementary iron. There was no significant relationship between ingested elementary iron (mg/kg) and blood iron levels (p= 0.158). There was no significant association between blood iron level and ingestion time (p= 0.274).

The most common symptom was vomiting (n=5). The laboratory test results revealed metabolic acidosis in 3 patients, respiratory acidosis in one patient, leucocytosis (>15.000/mm^3) in one patient, and prolonged activated partial thromboplastin time (39 seconds; range 23-35 sec) in one patient. None of the patients needed intensive care during their hospitalization. There was no sign and/or symptom in 8 (47%) patients. Abdominal plain film was obtained in 10 patients. Radio-opaque tablets were not detected in any of the patients.

There was no major outcome and no death. Gastric lavage was performed in 16 patients. Total bowel irrigation with polyethylene glycol (GoLytely®) and deferoxamine were used in 3 patients. Deferoxamine was given in 15 mg/kg/h doses by intravenous infusion for 24 hours. The mean duration of hospitalization was 2.8±1.1 days (1 day - 6 days). The demographic and clinical characteristics of the patients were shown in Table I.

DISCUSSION

The clinical effects of acute iron poisoning appear in 5 stages. The first stage is the initial 6 hour period in which the gastrointestinal system is affected. The second stage is the latent period occurring 6 to 24 hours after iron ingestion. A transient and misleading recovery could be seen. The third stage is the mitochondrial toxicity stage and is seen 12 to 48 hours after iron ingestion. Hypovolemic or cardiogenic shock, acidosis, coagulopathy, hyperglycemia and acute tubular nephritis can be seen. The fourth stage is hepatotoxicity and is seen after 48 hours. Pyloric or duodenal obstruction, which progresses to scarring at 2-8 weeks, is seen in the fifth stage (3-5).

Determination of blood iron levels is important to confirm acute iron poisoning. Measurement 2-6 hours after poisoning is suggested (4,5). A peak blood iron level of <350 mcg/dl causes minimal toxicity, 350-500 mcg/dl iron level causes mild or intermediate gastrointestinal symptoms, iron level >500 mcg/dl causes severe systemic toxicity, and iron level >1000 mcg/dl may lead to high morbidity and mortality (3-6). In fact, the blood iron level can be found to be normal even when iron is taken in high doses because of rapid cellular shifts (3). It is reported that there is no significant association between the serum iron

Table I: Characteristics of patients with acute iron poisoning.

Patient	Age (month)	Iron amount (mg/kg)	Signs	Time between drug intake and hospital admission (minute)	Serum iron level (mcg/dl)	Detection time of iron level (hour)	Abdominal X-ray	Treatment	Iron formulation
1	50	20	Leucocytosis (18.400/mm^3)	420	397	7	Normal	GL*	Ferrous sulfate (tablet)
2	21	30	Respiratory acidosis (pH:7.24, HCO3:23 mmHg, pCO2:53 mmHg)	120	23	6		GL	Ferrous glycine sulfate (Capsular)
3	20	37	Increased aPTT	180	38	3	Normal	GL	Ferri hydroxide (tablet)
4	14	16		60	147	6	Normal	GL	Ferrous glycine sulfate (Capsular)
5	18	20		90	355	2		GL*	Ferrous glycine sulfate (syrup)
6	21	20		30	106	2	Normal	GL	Ferri hydroxide (tablet)
7	46	95	Vomiting	180	424	3	Normal	GL*, D, P	Ferrous sulfate (tablet)
8	168	?		120	400	4		GL, D, P	Ferrous sulfate (Dragee)
9	25	30		90	97	2	Normal	GL*	Ferri hydroxide (tablet)
10	30	50	Vomiting, Metabolic acidosis (pH:7.30, HCO3:17 mmHg, pCO2:35 mmHg)	120	345	4		GL	Ferrous glycine sulfate (Drop)
11	48	34		210	130	4		GL*	Ferri hydroxide (syrup)
12	34	30	Vomiting, Metabolic acidosis (pH:7.32, HCO3:18mmHg, pCO2:35mmHg)	600	259	10		GL*	Ferrous glycine sulfate (Drop)
13	32	27		180	243	2		GL*	Ferrous glycine sulfate (syrup)
14	24	36		120	109	4	Normal	GL*	Ferri hydroxide (tablet)
15	30	53	Vomiting	90	340	4	Normal	GL*	Ferrous sulfate (tablet)
16	27	26	Vomiting	50	183	4	Normal		Ferrous sulfate (Dragee)
17	25	43	Metabolic acidosis (pH:7.33, HCO3:17 mmHg pCO2:33mmHg)	360	350	6	Normal	GL*, D, P	Ferrous sulfate (Dragee)

***Patients referred to our hospital after gastric lavage*
***GL:** Gastric lavage, **D:** Desferrioxamine, **P:** polyethylene glycol.*

level and clinical, laboratory and radiographic abnormalities in children (7). In this study, there was no correlation between the blood iron level and the amount of ingested iron (mg/kg). In a patient with 20 mg/kg iron ingestion, the white blood cell (WBC) count was increased to 18.400/mm³ after 8 hours (Table I). There was no significant association between serum iron level and ingestion time. Gastric lavage being carried out previously and differences in patient metabolism may have resulted in the lack of an association between serum iron level and the amount of ingested iron and ingestion time. Similarly, patients' findings were not consistent with the blood iron levels. Respiratory acidosis was seen in a patient with a blood iron level of 23 mcg/dl. Prolonged activated partial thromboplastin time was detected in the patient with a blood iron level of 38 mcg/dl. The blood iron levels of three patients with metabolic acidosis were 345, 259 and 350 mcg/dl, respectively.

An abdominal plain film may reveal pill fragments in the GI tract to confirm an uncertain diagnosis and may guide decision making for whole-bowel irrigation (WBI) which is an enteral decontamination method of choice for iron intoxication. A negative plain film does not absolutely rule out acute iron poisoning (3). Abdominal plain film was performed in 10 patients and radio-opaque iron tablets were not detected. However, the absence of radiopacities does not rule out a significant or even potentially lethal ingestion.

There have been no randomized clinical trials using WBI with iron poisoning; however, there are several case reports that have documented the successful use of WBI in various ingestions (8,9). Intravenous deferoxamine is used as an antidote in acute iron poisoning. Deferoxamine is recommended for those patients with severe symptoms (hemodynamic instability, impaired consciousness, persistent vomiting or diarrhea), metabolic acidosis, peak serum iron concentration >500 mcg/dL (90 micromol/L), and multiple tablets on abdominal radiography (4).

In this study, IV deferoxamine and whole bowel irrigation with polyethylene glycol were used in 3 patients. The first patient who was treated with WBI and deferoxamine had ingested 95 mg/kg iron and the blood iron level was found to be 424 mcg/dl. The second patient had ingested an unknown amount of iron in a suicide attempt and the blood iron level was found to be 400 mcg/dl. The third patient (25 months old) had metabolic acidosis with an ingestion of 43 mg/kg iron. The blood iron level was found to be 350 mcg/dl in that patient. There are few case reports about using deferoxamine in patients aged under 3 years (10,11). No adverse effects were seen with deferoxamine in any of our patients, including the 25-month-old infant.

It has been reported that blood exchange and hemodialysis can be successfully used in patients with severe iron poisoning (10,12).

Limitations

The sample size is relatively small and it would have been better if the sample size was larger. This may be due to the exclusion of patients with multidrug poisoning or iron-containing nutritional supplements from our study. The retrospective nature of the study is another limitation.

CONCLUSION

There was no correlation between the reported amount of ingested iron and the blood iron level. There was no correlation between blood iron level and ingestion time. There was also no correlation between blood iron levels and the clinical, laboratory, and radiographic findings. Accidental iron poisoning continues to be an important pediatric emergency.

REFERENCES

1. Jayashree M, Singhi S. Changing trends and predictors of outcome in patients with acute poisoning admitted to the intensive care. J Trop Pediatr 2011;57:340-6
2. Smolinske SC, Kaufman MM. Consumer perception of household hazardous materials. Clin Toxicol 2007;45:522-5.
3. Chang TP, Rangan C. Iron poisoning: A literature-based review of epidemiology, diagnosis, and management. Pediatr Emerg Care 2011;27:978-85.
4. Baranwal AK, Singhi SC. Acute iron poisoning: Management guidelines. Indian Pediatr. 2003;40:534-40.
5. Madiwale T, Liebelt E. Iron: Not a benign therapeutic drug. Curr Opin Pediatr 2006;18:174-9.
6. Skoczynska A, Kwiecinska D, Kielbinski M, Lukaszewski M. Acute iron poisoning in adult female. Hum Exp Toxicol 2007;26:663-6.
7. Porter JB. Concepts and goals in the management of transfusional iron overload. Am J Hematol 2007;82:1136-9.
8. Sipahi T, Karakurt C, Bakirtas A, Tavil B. Acute iron ingestion. Indian J Pediatr 2002;69:947-9.
9. Phillips S, Gomez H, Brent J. Pediatric gastrointestinal decontamination in acute toxin ingestion. J Clin Pharmacol 1993;33:497-507.
10. Carlsson M, Cortes D, Jepsen S, Kanstrup T. Severe iron intoxication treated with exchange transfusion. Arch Dis Child 2008;93:321-2.
11. Sankar J, Shukla A, Khurana R, Dubey N. Near fatal iron intoxication managed conservatively. BMJ Case Rep 2013; doi:10.1136/bcr-2012-007670.
12. Gumber MR, Kute VB, Shah PR, Vanikar AV, Patel HV, Balwani MR, et al. Successful treatment of severe iron intoxication with gastrointestinal decontamination, deferoxamine, and hemodialysis. Renal failure 2013;35:729-31.