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CASE REPORT

An autopsy report with a diagnostic clinical profile on fatal overdose of life-saving iron supplement

N. Ramaswamy[1] · Sathish K.[1] · Bhawana Ashok Badhe[2]

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Abstract

Ferrous sulfate is a commonly prescribed drug for prophylaxis and treatment purposes, particularly in women and adolescent girls. However, its easy availability, potential toxicity at higher doses, and vague clinical presentation make it a drug of concern when evaluating a case of poisoning. We present the case of a 28-year-old female who allegedly consumed 60 ferrous sulfate (60 mg of elemental iron in 200 mg of ferrous sulfate) tablets in a suicidal attempt. She presented with gastrointestinal disturbances on the same day to a tertiary care health facility. Investigations revealed deranged liver function tests, serum iron levels ten times the normal range, and high levels of saturated transferrin. Despite treatment, she succumbed to the poisoning 4 days after the incident. Autopsy showed features of liver failure, which was confirmed by histopathology. Chemical examination detected free ferrous and chloride ions. This fatal case of adult iron toxicity highlights the different causes of death in various stages of iron toxicity, providing a wider perspective on clinical management and aiding in the determination of the cause of death during an autopsy. This article adds a rare fatal iron poisoning case in adults to the literature, emphasizing the necessity for regulating iron tablet supplementation and raising public awareness of the toxicity of iron, which could save millions of lives.

Keywords Poison · Suicide · Ferrous sulfate · Bilirubin · Liver toxicity

Introduction

Iron (ferrous sulfate) is frequently used for therapy and prophylaxis in women and children [1]. The liver plays a fundamental role in iron metabolism, serving as a significant iron storage site, absorbing transferrin- and non-transferrin-bound iron before releasing it into the bloodstream. The liver also acts as a sensor of the body's total iron levels, regulating intestinal absorption of dietary iron and the release of iron from macrophages in response to biochemical changes. The regulator protein hepcidin plays a vital role in all these functions of the liver. Furthermore, iron overload contributes to the etiology of several human liver diseases [1, 2].

While adults rarely intentionally overdose on iron supplements, people may falsely believe that iron supplements are harmless and use them as a suicide threat. Additionally, a lack of effort is made to keep them away from the pediatric population, making them easily accessible for accidental consumption [1]. Most cases of acute iron toxicity occur in children under the age of 5 due to inadvertent intake of iron supplements. The majority of literature reports iron overload in adults taking other hepatotoxic drugs, mainly paracetamol. Clinical outcomes vary depending on the amount of elemental iron consumed, other medications taken, and the length of time between diagnosis and treatment. The toxicity of some iron preparations, such as carbonyl iron, is influenced by their delayed absorption rate [1, 3]. Understanding these factors enables a forensic pathologist to provide an opinion on the cause of death and directs clinicians on treatment and precautions.

This report highlights a case where the deceased allegedly consumed iron (ferrous sulfate) and did not consume any

✉ Sathish K.
sathukumar91@gmail.com

N. Ramaswamy
nagappanramaswamy@gmail.com

Bhawana Ashok Badhe
bhawanabdh11@gmail.com

[1] Department of Forensic Medicine and Toxicology, Jawaharlal Institute of Postgraduate Medical Education & Research, Puducherry 605006, India

[2] Department of Pathology, Jawaharlal Institute of Postgraduate Medical Education & Research, Puducherry 605006, India

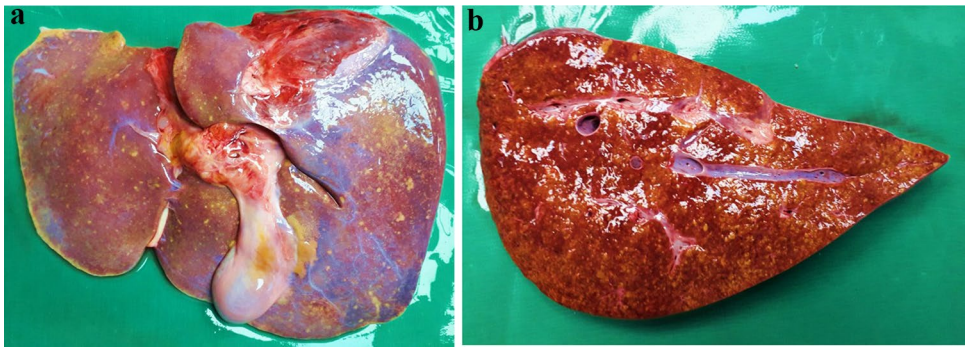

Fig. 1 **a** Patchy yellow discoloration of the surface of the liver. **b** Yellow discoloration of the parenchyma of the liver

other tablets which led to fatal direct hepatotoxicity. Pathological findings from autopsy, combined with a diagnostic clinical profile, provide insights into the pathophysiology of acute iron toxicity.

Case history

Following consumption of 60 ferrous sulfate tablets (60 mg of elemental iron in 200 mg of ferrous sulfate) or 3600 mg of elemental iron, with the purported purpose to threaten and assuming iron tablets are not toxic, a 28-year-old woman presented to a tertiary healthcare center on the same day with gastrointestinal symptoms. She had no history of hematemesis and her vitals were stable at admission. Blood tests within 24 h of consumption of ferrous sulfate tablets revealed a hemoglobin level of 11.5 g/dl, a total white blood cell (WBC) count of 15,083/cu mm, raised serum iron levels of 220.3 µg/dl, and higher overall iron binding capacity of 421 µg/dl. With an exponential rise in serum glutamic pyruvic transaminase (SGPT—7523 mg/dl) and serum glutamic oxaloacetic transaminase (SGOT—6112 mg/dl) as well as total bilirubin (4.83 mg %) and direct bilirubin (1.68 mg %), the liver function tests indicated hepatocellular injury. Serum iron was increased to 220.3 µg/dl (normal range: 110–130 µg/dl) and the total iron binding capacity (TIBC) was 421 µg/dl (normal range: 400 µg/dl) when measured at 12–24 h since consumption. Despite treatment, the patient continued to deteriorate and eventually developed liver failure, which worsened progressively, and she succumbed after 4 days.

At autopsy, it was noted that the conjunctiva, meninges, and scalp had a yellowish discoloration. The surface of the liver and parenchyma showed patchy yellow discoloration (Fig. 1). The kidneys showed distinct cortico-medullary differentiation. Free ferrous ions and sulfate ions were detected in the liver and kidney on chemical analysis. Confluent pan-lobular necrosis and feathery degeneration of the liver were confirmed by histopathology (Figs. 2 and 3). The opinion as to the cause of death was hepatic necrosis as a complication of ferrous sulfate poisoning.

Discussion

More cases of iron toxicity are reported in females than in males. This may be due to the increased use of iron prescriptions for treatment or prophylaxis in pregnant women

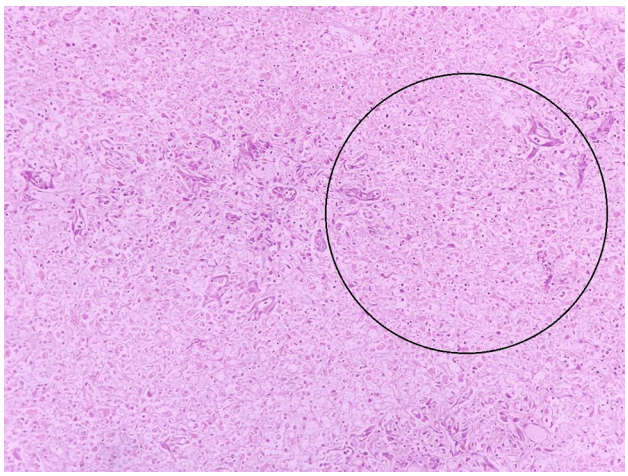

Fig. 2 Confluent pan-lobular necrosis of the liver (H&E, 200×)

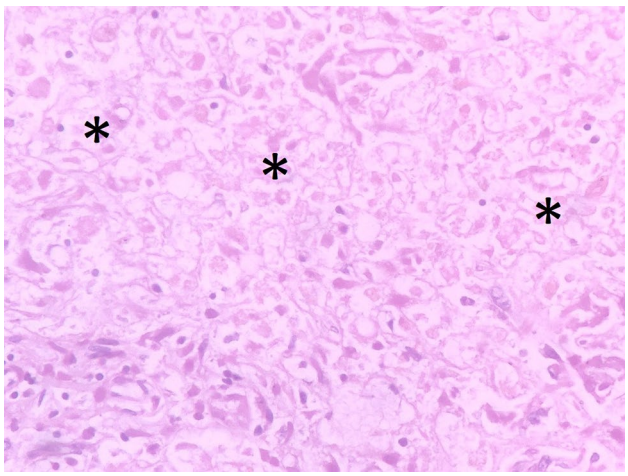

Fig. 3 Hepatocyte necrosis with feathery degeneration (H&E, 400×)

Table 1 Stages of liver toxicity [7–9]

Stages	Time since consumption	Pathology	Clinical presentation	Cause of death
I	< 6 h	Direct gastrointestinal injury	Vomiting, diarrhea, GI hemorrhage	Hypovolemic shock/metabolic acidosis
II	6–24 h	Phase of intracellular iron distribution	Resolution of symptoms	Metabolic acidosis
III	6–72 h	Cytotoxicity of iron	Unstable vitals	Cardiogenic shock
IV	12–96 h	Direct and indirect toxicity	Hyperbilirubinemia	Liver failure
V	2–8 weeks	Gastrointestinal fibrosis	GI obstruction	GI obstruction

and adolescent girls, making iron supplements more widely available in these populations [1, 4].

When the body has more iron than it needs, it is converted to the ferric form and stored in the iron storage protein ferritin. Hemosiderin, a membrane-enclosed complex that holds ferric iron, serves as a secondary storage location for iron. A disruption in the processes that control iron intake might result in an excessive deposition because there is no regulated method of iron excretion [2].

The ability of ferrous iron to combine with H_2O_2 and produce the extremely reactive hydroxyl radical is a key mechanism behind iron toxicity. Local gastrointestinal symptoms and systemic toxicity are the two main categories of iron toxicity. Uncontrolled iron absorption results from direct oxidative injury to the upper GI mucosa which leads to unregulated iron absorption. The number of free iron increases after transferrin saturation, causing toxicity [5]. The major mechanisms involved are direct oxidative damage, modification of oxidative phosphorylation, liver failure, and a direct impact on thrombin. These effects are dose-dependent. Significant systemic toxicity and shock occur at serum iron concentrations of 500–1000 (µg/dl). Serum iron concentrations above 1000 (µg/dl) are reported to cause considerable mortality [6]. The serum iron in our case did not fall within this toxic level, owing to cellular redistribution at 12–24 h. Based on time since consumption of a toxic dose of iron, there are five stages of toxicity (Table 1) [7–9].

Abhilash et al. reported GI hemorrhage and metabolic acidosis as causes of death within 24 h from ingestion in two adults [3]. This is in line with the GI and latent stage of iron toxicity. Crofton et al. showed GI symptoms to be the most common presenting symptoms and liver failure to be the most common fatal complication as in our case. In our case, the weight of the patient was 55 kg, and 3600 mg of elemental iron would be considered fatal. She died between 12 and 96 h from ingestion resulting in stage IV or hepatotoxic stage. All of this corroborates with our autopsy findings and thus the cause of death provides a complete arc of events in fatal iron (ferrous sulfate) toxicity [7].

The packaging of these medications in unit doses has significantly decreased child unintentional overdose [10]. However, presuming that iron tablets are nutritional supplements, the paucity of knowledge about their potential toxicity at greater doses is concerning in cases of intentional overdose in adults and adolescents.

Conclusion

To avoid future incidents of fatal ferrous sulfate poisoning in adults, regulation of the supply of iron pills and a concerted effort to raise awareness about toxicity are highly advised. The current literature emphasizes that the cause of death in iron toxicity should be approached based on stages of iron toxicity. A treating physician should constantly keep iron poisoning in mind in cases of acute liver failure or gastrointestinal hemorrhage of unknown origin, particularly in the vulnerable population. This case report adds to the literature and provides a complete arc of events in fatal iron toxicity, highlighting the importance of understanding the mechanisms of iron toxicity and its potential consequences.

Key points

1. Ferrous sulfate should be taken into account while evaluating or investigating a case of poisoning due to its availability, potential for toxicity at larger dosages, and ambiguous clinical presentation.
2. Major pathogenesis includes direct gastrointestinal injury, phase of intracellular iron distribution, cytotoxicity of iron, direct and indirect toxicity, and gastrointestinal fibrosis.
3. Clinical presentation, pathogenesis, and the cause of death vary based on the time since consumption and arrival to the healthcare facility.

Author contribution NR and KS conceived the idea of writing this paper. NR, KS, and BAB were involved in the design of the work, analysis, and interpretation of the case. NR wrote the initial draft of the manuscript. NR, KS, and BAB have read and approved the final version of the manuscript. All authors have equally participated in this work. All authors read and approved the final manuscript.

Availability of data and materials Not applicable.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication Obtained from the legally acceptable representative.

Competing interests The authors declare no competing interests.

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