Comparison of Deferoxamine, Activated Charcoal, and Vitamin C in Changing the Serum Level of Fe in Iron Overloaded Rats

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ABSTRACT

Background: Iron is an essential mineral for normal cellular physiology but its overload can lead to cell injury. For many years, deferoxamine injection has been used as an iron chelator for treatment of iron overload. The aim of this study is to compare oral deferoxamine, activated charcoal, and vitamin C, as an absorbent factor of Fe, in changing the serum level of iron in iron overload rats.

Methods: In this experimental study, all groups were administered 150 mg iron dextran orally by gavage. After eight hours, rats in the first group received oral deferoxamine while those in the second and third groups received oral activated charcoal 1 mg/kg and oral vitamin C 150 mg, respectively. Then, serum levels of iron were measured in all rats.

Results: The mean serum level of iron in rats that received oral deferoxamine was 258.11±10.49 µg/dl, whereas mean levels of iron in charcoal and vitamin C groups were 380.88±11.21 µg/dl and 401.22±13.28 µg/dl, respectively. None of the measurements were within safety limits of serum iron.

Conclusion: It seems that oral deferoxamine per se may not help physicians in the management of cases presented with iron toxicity. Activated charcoal did not reduce serum iron significantly in this study and further investigations may be warranted to assess the potential clinical utility of its mixture with oral deferoxamine as an adjunct in the clinical management of iron ingestions.

Keywords: Ascorbic Acid, Charcoal, Deferoxamine, Iron, Poisoning, Rats.
24 hr/day, 5-6 days/week) and it is expensive [13].

In cases of excessive iron ingestion, prevention of gastrointestinal (GI) absorption (GI decontamination) with activated charcoal can also be used [14]. It is produced through heating wood paste at 900°C and then rinsing with water. Then charcoal becomes activated by strong acids. Each gram of this substance has approximately 1000 m² surface area which can sop up numerous drugs and poisons and prevent their absorption into systemic circulation. If it is administered within 1 hour after ingestion of certain poisons, it would effectively prevent their absorption. Constipation is the most notable side effect of activated charcoal [15].

On the other hand, initial evidence suggests that ascorbic acid can enhance iron absorption. It has been emphasized in several studies that ascorbic acid increase Fe absorption from 3.7 to 10.4% [16, 17]. Hence, the aim of this study was to compare oral deferoxamine, activated charcoal, and vitamin C as an absorbent factor of Fe in changing serum levels of Fe after ingestion of iron in rats.

MATERIALS AND METHODS

This experimental study included 27 Sprague–Dawley rats weighing 250-300 g randomly divided into three groups. The animals were fed with a standard rat pellet diet for 2 weeks as acclimation period. During this period, they had access to water ad libitum, with alternate 12-h dark/light cycle; and the ambient temperature held constant between 21 and 25°C. None of the rats were excluded and there was no mortality.

All animals were administered 150 mg iron dextran orally by gavage. Immediately, rats in the first group received oral deferoxamine while those in the second and third groups received oral activated charcoal 1 mg/kg and oral vitamin C 150 mg. For blood sampling, nearly 1.8 ml of blood was collected through iliac vein from each rat. Then, after eight hours, serum levels of iron were measured in all rats.

This study was approved by the local Ethics Committee of Arak University of Medical Sciences, Arak, Iran. The collected data were analyzed by student’s t-test using SPSS statistical software version 16.0.

RESULTS

Serum concentration of Iron was evaluated in all three groups. The mean serum level of Fe in rats that received oral deferoxamine was 258.11±10.49 µg/dl while in charcoal and vitamin C groups, this value was 380.88±11.21 µg/dl and 401.22±13.28 µg/dl, respectively. Details of measurements are presented in Table 1.

Table 1. Serum concentration of Fe in groups (µg/dl).

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean±SD</th>
</tr>
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<tbody>
<tr>
<td>Deferoxamine</td>
<td>258.11±10.49 µg/dl</td>
</tr>
<tr>
<td>Charcoal</td>
<td>380.88±11.21 µg/dl</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>401.22±13.28 µg/dl</td>
</tr>
</tbody>
</table>

Mean serum level of iron in the deferoxamine group was significantly lower than the other two groups. The paired sample t-test showed that there was a statically significant difference between the mean concentrations of Fe between the deferoxamine group and activated charcoal group (P<0.0001) and also vitamin C group (P<0.0001).

The comparison between the other two groups also revealed that the mean serum levels of iron in charcoal group were significantly lower than the vitamin C group (P=0.006).

DISCUSSION

The results of the present study showed that oral deferoxamine significantly lowers the amounts of serum Fe in comparison to oral activated charcoal. Although serum levels of Fe in the deferoxamine group were lower than the other groups, the iron concentration achieved in the present study was not within safety limits [18, 19].

Although these findings were consistent with those in previous studies [20], they contradict the findings of Gomez et al. who reported the prevention of iron absorption by...
a slurry containing deferoxamine and activated charcoal [13].

Deferoxamine is a drug that is created by the bacterial fermentation of Streptomyces pilosus species [21]. One molecule of this compound can bind to a three-valence iron ion and form ferrioxamine complex which is biologically inactive [21]. In cases of oral administration of deferoxamine, this complex forms in the gut and because of its low gastrointestinal absorption [15], its excretion increases [22]. GI absorption of deferoxamine is too low and the small amount that is absorbed is rapidly eliminated from the blood stream [21]. Since the mechanism of iron absorption from the digestive tract is similar in humans and in rats [19], the results of the present study have comparable bearing in humans.

Trials to substitute oral deferoxamine instead of subcutaneous infusion have shown that oral administration can be effective in removing iron from GI tract [18]; however, it should be noted that systemic absorption of oral deferoxamine is very low and, as a result, the excretion of absorbed iron as compared to infusion form of deferoxamine is very low [18]. In laboratory trials with guinea pigs, oral deferoxamine therapy was successful in preventing or delaying death, depending on the elapsed time of administration following ingestion [23]. However, the efficacy of oral deferoxamine in humans for iron poisoning has not been established [24].

Activated charcoal has been used to adsorb ingested iron and is likely to be effective especially in ferrous sulfate overdose but it is not used often because of the widely-held belief that it binds poorly to iron [25]. In contrast, Eshel et al. reported that activated charcoal had no effect on iron absorption in rats. In their study, deferoxamine and activated charcoal did not alter iron absorption from the digestive tract [19]. They found that serum iron concentrations measured 1 hour after treatment were as high as those found in the untreated control groups. Despite the fact that most studies using deferoxamine or activated charcoal did not show any significant effect on iron excretion, Gomez et al. found that a premixed deferoxamine and activated charcoal slurry could decrease GI absorption of ferrous sulfate [14].

CONCLUSION

In summary, it seems that oral deferoxamine may help physicians in management of cases presented with iron toxicity. In the present study, activated charcoal did not reduce serum iron significantly and further investigations may be warranted to assess the potential clinical utility of its mixture with oral deferoxamine as an adjunct in the clinical management of iron ingestions.

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REFERENCES