

Analysis of hematinic formulations available in the Indian market

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ABSTRACT

Objectives: To analyze the hematinic formulations available in Indian market for their varieties of dosage forms, iron salts used, content of elemental iron, frequency of administration, additional nutrients, and cost. **Materials and Methods:** Hematinic formulations listed in Indian Drug Review (2009) were analyzed for the iron salts contained and the elemental iron content. Preparations containing iron $\pm$ folic acid $\pm$ vitamin C were considered as 'acceptable' formulations. For proper comparison, cost of 100 mg elemental iron in each formulation was calculated. Acceptable oral formulations containing iron with folic acid were further classified according to iron salts, and the median cost of various iron salts was compared. We also identified oral solid formulations that required administration more than three times a day. Prices of 'acceptable' iron preparations were compared with that of 'irrational' formulations. **Results:** Out of 621 formulations, 365 were oral solid formulations, 232 were oral liquids, and 24 were for parenteral administration. Formulations containing iron salts like ferrous sulphate, ferrous sulphate (dried), carbonyl iron, and ferrous fumarate are cheaper than formulations containing other iron salts. Among the 365 oral (solid) iron formulations, we found 60 that would require administration more than three times a day to provide a therapeutic dosage of elemental iron. As compared to irrational formulations, the cost of acceptable formulations was in a significantly narrow range; however, the median cost of acceptable products was significantly higher than that of the irrational ones, except in case of the parenteral preparations. **Conclusion:** The drug regulation authorities should tune the drug price in such a way that rational formulations cost less than the irrational ones.

Key words: Elemental iron, hematinic, irrational, acceptable

INTRODUCTION

Indian drug market is flooded with more than 70000 drug formulations, the majority of which are proprietary multi-drug combinations. The hematinics market in India is currently worth around Rs. 900 crores and is growing at 15% per

annum.^[1] The prescribing and buying of drugs is an issue of unparalleled peculiarity because the prescriber (the doctor) decides what to buy, but he is not the one who pays for the drug; the one who pays and benefits (the patient) has no say in what he/she buys. The law comes into the picture for the price control of only a limited number of drugs and formulations.

Hematinics are drugs used for the treatment and prevention of anemia. Hemopoiesis requires adequate supplies of minerals like iron and copper; vitamins like folic acid, vitamin B₁₂, vitamin C, pyridoxine, riboflavin; and various hematopoietic growth factors.^[2] Each of these is effective individually in specific types of anemias, but there is rampant and indiscriminate use of several of these agents simultaneously,

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without first determining their applicability to the case at hand. Why should a patient with pernicious anemia be given iron, folic acid, or ascorbic acid?^[3] Worse, many of these hematinic formulations contain several ingredients that have nothing to do with hemopoiesis! Most formulations marketed in India as hematinics contain not just iron, folic acid, vitamin B₁₂, and vitamin C, but also other B complex vitamins, trace elements like copper, cobalt, and zinc, and biological products like liver extract and hemoglobin from animals. The rationality of such combinations is questionable; for example, the addition of ascorbic acid in these formulations seems to have little advantage over increasing the amount of iron administered. It is inadvisable to use preparations that contain other compounds with therapeutic actions of their own, such as vitamin B₁₂, folate, or cobalt, because the patient's response to the combinations cannot easily be interpreted.^[2] Combination of iron with other nutrients like ascorbic acid, folic acid, and other vitamins increase the cost as well as the frequency of side effects and hence leads to noncompliance.^[4] The Drugs Technical Advisory Board (DTAB) of India has recommended that vitamin B complex and zinc should not be included in iron- and folic acid-containing hematinic preparations.^[5]

The objective of this study was to analyze the hematinic formulations available in Indian market for their varieties of dosage forms, iron salts used, content of elemental iron, frequency of administration required, presence of additional nutrients, and cost.

MATERIAL AND METHODS

Detailed information about hematinic formulations was obtained from the Indian Drug Review (IDR) issue 5, 2009. The formulations were classified into the following categories: (A) solid formulations, (B) liquid formulations, and (C) parenteral formulations. Each category was further subdivided into formulations containing:

- Iron salts only
- Iron salts with vitamins
- Iron salts with vitamins, minerals, and other chemicals
- Iron salts with minerals and other chemicals
- Iron salts with vitamin and essential amino acids
- Iron salts with vitamins, minerals, other chemicals, and essential amino acids
- Iron content (but without the salt being specified)
- Preparations available as a 'kit'
- Iron salts with miscellaneous contents

If information about the type of iron salt, quantity, cost were not available, such formulations were not included for the cost analysis. For comparison of cost, only the elemental iron content was taken into consideration since the element iron available from different iron salts differs significantly and the

response (increase in hemoglobin) depends on the elemental iron available. The recommended therapeutic dose of iron is 100–200 mg elemental iron daily in three divided doses^[5,6] and, hence, the cost of 100 mg of elemental iron available from each formulation was calculated.

We found that the formulations containing only iron salts were very few. Apart from deficiency of iron, deficiency of folic acid is also a common cause of anemia. Besides, vitamin C is known to increase absorption of iron^[2,3,5] and hence formulations having iron salts $\pm$ folic acid $\pm$ vitamin C were considered as acceptable formulations.

To find out whether the difference between the minimum and maximum cost value was due to differences in the iron salts present, we classified acceptable oral formulations according to the various iron salts present and calculated the median cost of the different iron salts.

To provide 100 mg of elemental iron per day in not more than three doses, the formulation should deliver approximately 33 mg elemental iron per dose. Hence, we also separated out those formulations which contained less than 33 mg elemental iron per dose.

The median cost of acceptable iron formulations was calculated and compared with that of irrational ones.

RESULTS

In all, 621 formulations were listed in the IDR as hematinics. Of these, 365 were oral solid formulations, 232 were oral liquid formulations, and 24 were parenteral formulations.

Several dosage forms are available for oral solid iron preparations, viz, capsules (222), tablets (121), powder (8), kit (5), spansules (4), caplet (1), and granules (1). The type of formulation was not mentioned in three cases. Among the oral liquids, the syrup form (146) was the most common, followed by drops (29), suspensions (21), and others (36).

As shown in Table 1, there was only one solid oral iron preparation containing iron alone. Among the liquid formulations the situation was better, with 33 options. As many as 81% of the solid oral preparations and 75% of the liquid oral iron preparations were classified as irrational even after allowing for the inclusion of folic acid and vitamin C as a compromise. Twenty nine percent of parenteral iron formulations were irrational.

Information about the type of iron salt, its amount or its price was not mentioned in the IDR for certain formulations and these were therefore not considered for the cost analysis. Thus, from category A (solid oral), 81 formulations were dropped

Table 1: Iron formulations: Acceptable vs irrational

Formulation	Contents	%
Oral – Solid (N=365)	Iron salts only (n=1)	0.27
	Iron salts with folic acid (n=61)	16.71
	Iron salts with folic acid and vitamin C (n=7)	1.92
	Iron salts with other ingredients (n=296)	81.10
Oral – Liquid (N=232)	Iron salts only (n=33)	14.22
	Iron salts with folic acid (n=25)	10.78
	Iron salts with folic acid and vitamin C (n=0)	0
	Iron salts with other ingredients (n=174)	75.00
Parenteral (N=24)	Iron salts only (n=17)	70.83
	Iron salts with folic acid and vitamin C (n=0)	0
	Iron salts with other ingredients (vitamin B12, sorbitol) (n=7)	29.17

and from categories B (liquid oral) and C (parental), 135 and 6 formulations were not included for cost analysis, respectively.

The range of cost (minimum and maximum cost value) of solid oral iron formulations for providing 100 mg elemental iron was Rs. 0.14 to Rs. 816.67, for liquid oral formulations it was Rs. 1.26 to Rs. 188.44, and for parenteral formulations it was Rs. 51.3 to Rs. 5000.

Among the acceptable solid oral formulations containing iron with folic acid, the cost ranged from Rs. 0.14 to Rs. 183.25 (1300-fold difference) and for those having iron with folic acid and vitamin C the range was Rs. 2.56 to Rs. 12.37. In the case of liquid oral formulations containing iron only, the cost ranged from Rs. 1.9 to Rs. 188.44, for those having iron with folic acid the cost was Rs. 5.67 to Rs. 77.76, and for parenteral formulations containing iron only the cost was Rs. 51.3 to Rs. 5000.

Comparison of the median cost of different iron salts of category-A formulations containing iron with folic acid shows that with salts like ferrous ascorbate, ferrous glycine sulphate, iron polysucrose, ferric hydroxide polymaltose complex, ferric hydroxide, and ferrous gluconate the cost ranges from Rs. 8.04 to Rs. 51.71, whereas with iron salts like ferrous sulphate, ferrous sulphate (dried), carbonyl iron, and ferrous fumarate the cost is between Rs. 1.24 to Rs. 5.

We found that 60 out of 365 oral (solid) iron formulations would require administration more than 3 times a day to provide the 100 mg of elemental iron necessary for therapeutic purposes.

Comparison of the median cost value of irrational iron formulations with that of acceptable ones is shown in Table 2

Table 2: Median cost of irrational and acceptable iron formulations

Formulations	Irrational	Acceptable
Oral – solid	4.50 (n=218)	11.25 (n=66)
Oral – liquid	8.40 (n=68)	9.95 (n=29)
Parenteral	984.00 (n=4)	264.00 (n=14)

DISCUSSION

As mentioned earlier, for comparison of cost, instead of the dose of iron salts, we considered only the elemental iron content since the elemental iron available from different salts varies widely.

The list of other nutrients added in the various hematinic formulations was quite long:

- Vitamins: Vitamin A, D, E, K, C, B-complex, pantothenic acid, biotin
- Minerals and other chemicals: zinc, copper, manganese, calcium, sodium, potassium, iodine, selenium, chromium, magnesium, phosphate, molybdate, boron, chlorine, vanadium, nickel, tin, silicon
- Essential amino acids like histidine, lysine, glycine, glutamic acid
- Miscellaneous nutrients like fat, protein, carbohydrate, spirulina, choline, carnitine, taurine, inositol, saffron, dioctyl sodium sulfosuccinate, lycopene, hemoglobin, succinic acid, liver extract, ashwagandha, ginseng, *Centella asiatica*, yeast, peptone, casein, caffeine, glycerophosphoric acid

The findings are alarming as the cost of solid oral formulations ranged widely from Rs. 0.14 to Rs. 816.67, a whopping 6000-fold difference between the cheapest and the costliest formulation! It is incomprehensible why any patient should be made to spend Rs. 816.67 for 100 mg of elemental iron. What would be the total cost of treating his/her anemia?

When we allowed for addition of folic acid and/or vitamin C as a compromise formula and excluded all other 'irrational' formulations, the cost range of acceptable formulations narrowed significantly. Among the acceptable solid oral formulations containing iron with folic acid, the cost for 100 mg elemental iron ranged between Rs. 0.14 to Rs. 183.25 (a 1300-fold difference).

Preparations of iron hydroxide polymaltose were 4–5 times costlier than other iron salts. Dissociable ferrous salts are inexpensive, have high iron content, and are better absorbed than ferric salts, especially at higher doses. A greater percentage of ingested iron is absorbed during iron deficiency states,^[5] which means that absorption of iron depends not only on type of iron salt, but also on the patient's iron deficient state.

We also analyzed the data to see if type of iron salt has any bearing on the cost of the formulations. From the results we can say that formulations containing iron salts like ferrous sulphate, ferrous sulphate (dried), carbonyl iron, and ferrous fumarate are cheaper than formulations containing other iron salts .

Formulations containing less than 33 mg elemental iron require more than three administrations per day, and this can adversely affect patient compliance.

When we compared the prices of acceptable iron preparations with that of irrational formulations, to our surprise we found that the acceptable products were costlier than the irrational ones to a significant extent, except in the case of parenteral preparations [Table 2] This is rather unfortunate and indicates a lack of awareness of the prescribers regarding the costs of medicines.

CONCLUSION

One of the major principles of rational use of drugs is to prescribe only those drugs that are really indicated; in other words, unnecessary drugs should not be prescribed. Only 24% of hematinic formulations fit into the definition of rational (or acceptable). Indian patients are being made to ingest totally

unnecessary drugs (in the garb of nutrients). It would not be out of place to urge the drug regulation authorities to tune the drug price regime in such a way that rational (acceptable) formulations cost less than the irrational ones. Until such action is taken, prescribers should be sensitive to the cost of iron therapy.

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