

Short Communication

Pharmacoeconomic Evaluation of Ferrous Ascorbate, Ferrous Fumarate and Iron Polymaltose Complex in 14 To 24 Weeks of Gestation

Angadi Eesha¹, Karandikar Yogita^{2*}, Talathi Manju^{3**}, Wagh Girija^{4**}, Pandit Vijaya^{4*}

¹First Year Resident, ²Associate Professor, ³Assistant Professor, ⁴Professor and Head,
*Dept. of Pharmacology, **Dept. of Obstetrics and Gynecology,
Bharati Vidyapeeth Deemed Medical University and Bharati Hospital, Pune.

Corresponding Author: Angadi Eesha

Received: 18/09/2015

Revised: 23/10/2015

Accepted: 23/10/2015

ABSTRACT

Objectives: This study was designed to compare efficacy and conduct cost effective analysis of three commonly used oral iron preparations among anemic women (n=150) of gestation (12-24 weeks) in tertiary hospital.

Methods: We conducted retrospective analysis of data collected from pregnant women in their second trimester (between 14-20 weeks) from antenatal clinic. The patients were divided into 3 groups (n=50) each and treated with Iron polymaltose complex, Ferrous fumarate, Ferrous ascorbate respectively. Hemoglobin gm%, were recorded after the interval of 30 days from baseline. Cost effectiveness ratio for different groups was calculated by dividing the cost of treatment by clinical outcome yielded the ratio in terms of rupees.

Data was analyzed using graph pad prism software. Efficacy variables between groups calculated using ANOVA followed by Tukey's test.

Results: We observed that patients treated with Ferrous ascorbate showed significant rise in Hb (1.569gm%) which was greater than that Ferrous fumarate (1.097gm%, p=0.005) and Iron polymaltose complex (0.48 gm%, p<0.0001). The average cost-effectiveness ratio (ACER) in patient's perspective of Iron polymaltose complex, Ferrous fumarate, Ferrous ascorbate was Rs. 281.125, Rs60.164 and Rs. 184.21 per increase in Hb gm%.

Conclusion: It can be concluded that, ferrous fumarate still can be considered best cost effective medication for treatment as well as prevention of Iron deficiency anemia in pregnancy.

Keywords: Ferrous Ascorbate, Ferrous Fumarate, Iron Polymaltose Complex.

INTRODUCTION

Iron deficiency is a major problem worldwide especially in women of reproductive age. Classification derived from an iron-supplemented population lists the following levels as anemic: Hb (g/dl) levels below 11 g/dl in the first trimester; 10.5 g/dl in the second trimester; and 11g/dl in the third trimester. [1] Anemia has significant impact on health of the foetus as well as that of mother. Increased need

of iron during pregnancy especially after 2nd trimester makes iron supplementation mandatory. [2] Ferrous fumarate and Ferrous Ascorbate has less gastrointestinal side effects and is readily absorbed than Ferrous sulfate therefore better patient compliance. [3] Iron polymaltose complex has no troublesome interactions with food or medications, excellent tolerability and long term safety. [4] IPC is distributed to gestational women as free government

supplies in various health care centers in Maharashtra state.

India drug market is flooded with more than 7000 drug formulations where majority of them are available in combination. In all, 621 formulations were listed in the IDR as hematinics. The range of cost (minimum and maximum cost value) of solid oral iron formulations with folic acid for providing 100 mg elemental iron was Rs. 0.14 to Rs.183.25. [5]

The prescribing and buying of drugs is an issue of unparalleled peculiarity because the prescriber (Physician) decides what medicine the patient should purchase, but he is not the one who pays for drugs. The one who pays and consumes (patient) has no say in what he/she purchases. Thus, there is a general misconception that Pharmacoeconomic Evaluation is merely a mean to find the least expensive alternative drug. Instead, it is a comparison tool, it will not always indicate a clear choice, but will evaluate options quantitatively and objectively based on a defined model which has not been studied for Iron preparations so far [6] Thus this study would throw a light on how to select a drug, keeping the cost, efficacy, tolerance and side effects in mind.

MATERIALS AND METHODS

The study was conducted after taking permission from institutional ethics committee. The prescriptions from Department of obstetrics and gynaecology were selected according the following inclusion and exclusion criteria. Inclusion criteria included pregnant women with gestational age between 14 -24 weeks baseline Hemoglobin level > 8gm% and patients with history of severe oral intolerance of oral Iron preparations, excessive emesis, bleeding piles, active peptic ulcer, Other GIT problem, high obstetric risks pregnancies like multifoetal pregnancy and any other anaemia other than Iron Deficiency Anemia e.g.

Megaloblastic Anemia thalassemia, etc. were excluded from the study. 150 prescriptions were categorized in the following 3 groups Group A: Ferrous Ascorbate 100mg + Folic acid 1.5 mg, Group B: Ferrous Fumarate 100mg + Folic acid 1.5 mg, Group C: Iron Polymaltose Complex 100mg + Folic acid 1.1 mg. The study is a retrospective cohort observational study of prescription.

Investigations: The parameter of Hb was noted at “day 0” (baseline), and then at the end of 30 days. Parameters used to evaluate Cost effectiveness: a) Cost effectiveness ratio: Cost effectiveness ratio for two groups was calculated by dividing the cost of treatment by its clinical outcome to yield the ratio in terms of rupees. b) Incremental cost effective ratio: This was measured by dividing difference in the cost between two groups to difference in benefit between two groups. [7]

Incremental Cost Effectiveness Ratio =
 $\frac{(\text{Cost of drug A} - \text{Cost of drug B})}{(\text{Benefit of drug A} - \text{Benefit of drug B})}$

Statistical analysis: The characteristics all treatment groups were compared for both demographic and efficacy variables. In all tests mean values of test groups (A and B) were compared. Students paired t test was used to test the significance of difference in overall efficacy of two treatments resulting in rise in Hb or change in other parameters. Data was analyzed using graph pad prism software.

RESULTS

We observed that patients treated with Ferrous ascorbate showed significant rise in Hb (1.569gm %) which was greater than that Ferrous fumarate (1.097gm%, p=0.005) and Iron polymaltose complex (0.48 gm%, p<0.0001).

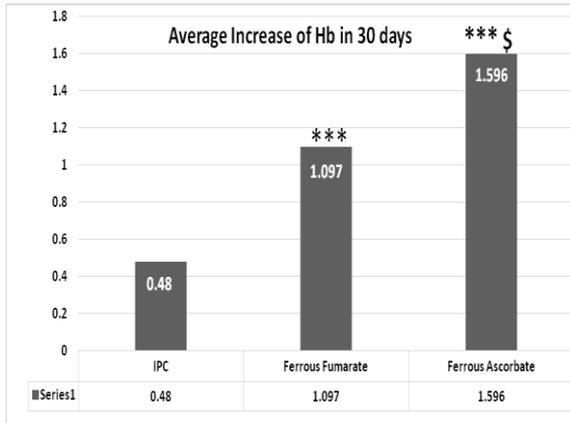


Fig 1: Showing rise in Hb by IPC, Ferrous fumarate and ferrous ascorbate in four weeks in pregnant women

Efficacy variables between groups calculated using ANOVA followed by Tukey's test.

*** P<0.001 when compared with IPC. § P<0.001 when compared with Ferrous Fumarate.

Table 1: Cost effectiveness ratio of Tab IPC, Ferrous fumarate and ferrous ascorbate

	IPC	Ferrous Fumarate	Ferrous Ascorbate
Cost of 30 tablets (In Rs.)	135	66	294
Cost of tabs. For 1 year. (In Rs.)	1620	792	3528
Cost effectiveness ratio	281.25	60.16	184.21

Ferrous fumarate is found to be the most Cost effective Iron preparation compared to IPC and Ferrous Ascorbate.

The average cost-effectiveness ratio (ACER) in patient's perspective of Iron polymaltose complex, Ferrous fumarate, Ferrous ascorbate was Rs. 281.12, Rs60.16 and Rs. 184.21 per increase in Hb gm%.

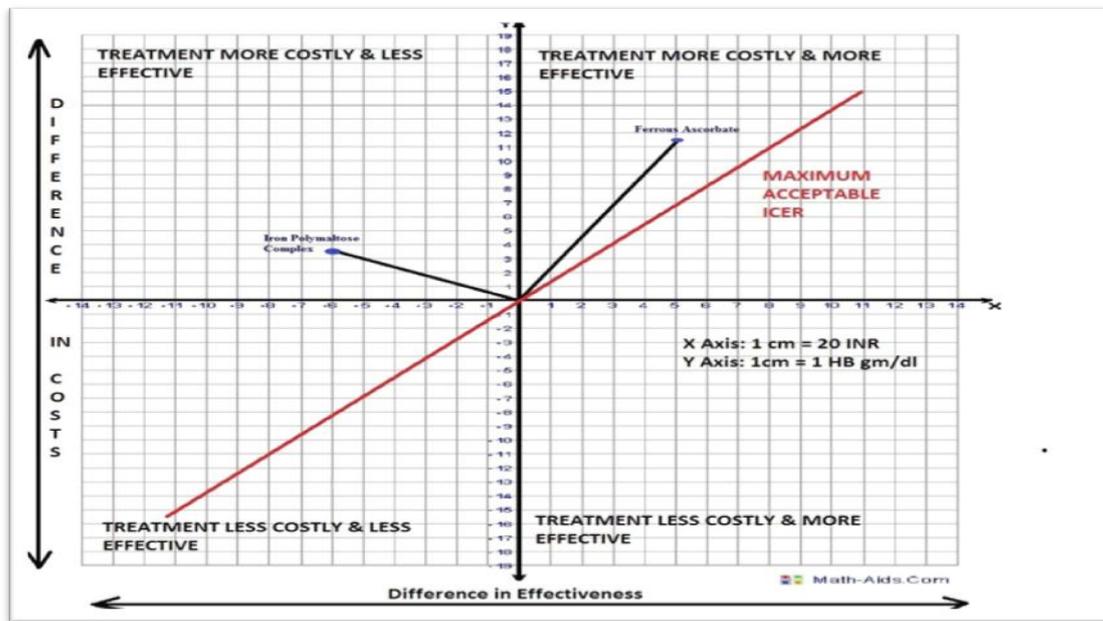


Fig 2: Incremental cost effectiveness ratio graph

- ❖ Ferrous Ascorbate fall in the quadrant where drug is fairly acceptable. IPC fall is the not acceptable quadrant of ICER graph.

DISCUSSION

We conducted retrospective analysis of data collected from pregnant women in their second trimester (between 14-20 weeks) from antenatal clinic.

Ferrous Ascorbate shows good bioavailability due to its Ascorbic acid molecules which reduces ferric iron into ferrous iron making it absorb thrice as much as other compounds, The greater absorption of iron in vivo from ferrous ascorbate as compared with other salts has been described both to retardation or

prevention of Fe (II) oxidation by ascorbate and to the existence of Fe(II) as a chelate with ascorbate resulting in fastest rise in iron which reflects in our study. But this preparation is 4-5 times costlier. [8] This is reflected in our study .We have observed a rise of 1.097 gm% over a period of 4 week. In a similar study Ferrous Ascorbate has shown a rise of 2.32gm% in duration of 4 weeks.

Iron-polymaltose complex (IPC), a combination of ferric iron with maltol (a food additive), was developed as a

molecule that is soluble at neutral pH and is not chelated by other substances. [9]

Despite the advantage of the IPC over ferrous salts, the efficacy of IPC has not been well established in pregnancy. Studies have shown that IPC is as effective as FS, or even more so. [9] But some studies contradict these results. [10]

Our results indicate that IPC causes least rise in Hb compared to other drugs (Table 1).

Lower efficacy due to extremely poor solubility of ferric iron in alkaline medium and need to transform into ferrous iron before being absorbed. Our results are similar to previous studies where efficacy of IPC is questionable and is 2-3times costlier than conventional iron salts. [10]

In our study, there was a rise of 1.097mg/dl Hb in 30days with Ferrous Fumarate. In a previous study (Perfect Trial) it was 0.73 mg/dl rise in Hb in duration of 4 weeks in Ferrous Fumarate group. [12] An iron salt like ferrous fumarate, which is already in the reduced state, does not depend upon gastric acidity for absorption and thus readily bioavailable. [11]

Pharmacoeconomic evaluation: There are very few studies regarding cost effective analysis and found that, there is vast difference in cost of various iron preparations. Conventional iron. Preparations are cheaper and newer iron preparations are 4 to 5 times costlier than conventional iron preparations. [5]

Cost is one of the determining factors for compliance of patient. This is particularly important in low socioeconomic developing country like India. Pregnant woman should take iron supplement for one year which can affect mortality and morbidity of mother as well as fetus

We conducted cost effective analysis considering both health results (rise in Hb) and the cost for medical care. Cost effective ratio was least with Ferrous Fumarate. This superiority of ferrous

fumarate group is due to better efficacy and less cost compared to other drugs.

The Cost Effective plane constructed using the mean-based ICERs. When the mean-based ICER is concerned, each pair on the CE plane represents the difference of the mean costs and the difference of the mean effectiveness. The South East quadrant represents the situation when the new treatment is less costly and more effective, hence it is highly favorable.

On the opposite side, in the North West quadrant, the new treatment is more costly and less effective, so it is highly unfavorable.

ICER for IPC falls in rejection quadrant (Fig 2). In the present study, the drugs (IPC) were given to the patient at no cost, but in our analysis, the cost was calculated as per the retail price. Even considering no cost to the patient it falls in third quadrant i.e. south west which is not preferred. [12]

The Indian Council for Medical Research (ICMR)'s district nutrition survey data also reported similar anemia prevalence of 84.2 %, with 13.1 % being in the severe anemia category. [13] In another survey, a total of 84 per cent pregnant and 92.2 per cent lactating women were anemic with severe anaemia in 9.2 and 7.3 per cent respectively. [14] National programmers' to control and prevent anemia have not been successful. Patients' compliance may be poor due to high cost of drugs. This may be one of the reasons for persistence of high prevalence of anemia in India. Anemic women coming to public health sector is in need of more iron supplement.

During our study period IPC was supplied for free not only in our institute but to all government hospital. The results in the present study can be extrapolated directly to public sector hospitals. Our result found out that IPC failed to raise Hb as compared to other two iron preparation. Early crucial weeks of pregnancy were

wasted which affect final outcome. It will also add to economic burden to patients when same patients required parenteral iron supplement at later stages in pregnancy. So IPC should be replaced with other iron preparations. Very recently the government has replaced IPC with Ferrous ascorbate as the free iron supplement salt. ICER of Ferrous Ascorbate falls in the North east quadrant where drug is fairly acceptable. Ferrous Ascorbate though costly can show maximum rise of Hb (1.59) among all group within one month.

In our opinion treatment of IDA in early pregnancy should be started with Ferrous Ascorbate for fast rise in Hb, and later on maintained with Ferrous Fumarate once patients Hb reaches upto 11 gm%. Since Government has started with free supply of ferrous ascorbate to gestational women visiting various ANC centers in the state, this step seems very promising and most beneficial to patient's health and also would reduce the economic burden of the society to a great extent.

Limitation: This study was a retrospective one, hence monitoring of drug related adverse effect and compliance of patient was not done.

In our study data was analyzed only for period of four weeks.

Serum Ferritin levels should be considered as it is indicator of iron storage .But we were not able to obtain data about Serum ferritin as this investigation is costly and routinely not advised to all patients.

CONCLUSION

It can be concluded that, *ferrous fumarate* still can be considered best cost effective medication for treatment as well as prevention of Iron deficiency anemia in pregnancy.

REFERENCES

1. Centers for Disease Control and Prevention (CDC): Recommendations to prevent and control iron deficiency

- in the United States. *Morb Mortal Wkly Rep* 1998; 47: 1-29
2. Saha L, Pandhi P, Gopalan S, Malhotra S, Shah PK. Comparison of Efficacy, Tolerability, and Cost of Iron Polymaltose Complex With Ferrous Sulphate in the Treatment of Iron Deficiency Anemia in Pregnant Women. *Med Gen Med* 2007; 9(1):1
3. Szarfarc, S. C., De Cassana, L. M., Fujimori, E., Guerra-Shinohara, E. M., & de Oliveira, I. M. Relative effectiveness of iron bis-glycinate chelate and ferrous sulfate in the control of iron deficiency in pregnant women. *Archivos Latinoamericanos De Nutricion (Sao Paulo university. Sa0 Paulo-Brazil)* 2001; supl vol.51 No.1:42-47.
4. Geisser P. Safety and efficacy of iron (111)-hydroxide polymaltose complex: A review of over 25 years experience. *ArzneimittelForschung (Drug Research)* 2007; 57(6a): 439-52.
5. Karelia BN, Buch JG. Analysis of hematinic formulations available in the Indian market. *Journal of Pharmacology & Pharmacotherapeutics*. 2012; 3(1):35-38. doi:10.4103/0976-500X.92504.
6. SAVING San Economic Analysis of Generic Drug Usage in the U.S., GPhA, September 2011; page1
7. Owens, D.K. Interpretation of Cost-Effectiveness Analyses. *Journal of General Internal Medicine*. 1998; 13(10):716-717. doi:10.1046/j.1525-1497.1998.00211.x.
8. Plug CM, Dekker D, Bult A. Complex stability of ferrous ascorbate in aqueous solution and its significance for iron absorption. *Pharm Weekbl Sci*. 1984 Dec 14; 6(6): 245-8.
9. Mehta BC. Iron hydroxide polymaltose complex –cause of persistent anemia at delivery. *Indian J Med Sci*. 2001; 55:616–620.
10. Sagaonkar S, Sukhija S, Tayal R, Sagaonkar PD. Pregnancy induced iron deficiency and the evaluation and comparison of the efficacy and safety of ferrous fumarate and carbonyl iron in its treatment - PERFECT trial. J

- Obstet Gynecol India 2009; 59 (6): 552-562
11. Bang H. Median-Based Incremental Cost-Effectiveness Ratio (ICER). Stat Theory Pract. 2012 ; 6(3): 428-442
 12. Toteja G, Singh P. Micronutrient deficiency disorders in 16 districts of India. Report of an ICMR Task Force Study -District Nutrition Project. Part 1. 2001
 13. Agarwal K. N., Agarwal D.K., Sharma A, Sharma K, Prasad K, Kalita M. C, et al. Prevalence of anaemia in pregnant & Lactating women in India. Indian J Med Res 2006;124:173-84
 14. Kapur D, Agarwal K.N, Agarwal D.K. Nutritional anemia and its control. Indian J Pediatr 2002; 69: 607-16.

How to cite this article: Eesha A, Yogita K, Manju T et al. Pharmacoeconomic evaluation of ferrous ascorbate, ferrous fumarate and iron polymaltose complex in 14 to 24 weeks of gestation. Int J Health Sci Res. 2015; 5(11):339-344.
