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# EVALUATION OF EFFICACY AND COMPLIANCE OF FERROUS SULFATE OF NATIONAL NUTRITIONAL ANEMIA PROPHYLAXIS AND CONTROL PROGRAMME IN COMPARISON WITH OTHER IRON PREPARATIONS IN ANTENATAL FEMALES

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**ABSTRACT** **Aim:** to compare efficacy and compliance of ferrous sulfate of national anemia prophylaxis programme with other oral iron preparations in antenatal female

**Introduction:** Anemia is defined as decreased hemoglobin level or circulating RBCs resulting in decreased iron carrying capacity of blood. It is the most common hematological disorder during pregnancy. According to Ministry of health and family welfare, 100 mg of elemental iron and 500 mcg of folic acid recommended for 100 days in pregnancy. National nutrition anemia prophylaxis programme was launched in 1970 to prevent nutritional anemia in mother and children. Even after 48 years, anemia is still a major concern for maternal mortality and morbidity in India. Side effects of oral iron therapy are a common problem in treatment of patients with oral iron preparations resulting in poor adherence to the therapy. Keeping all these facts in view, the current study was designed to compare ferrous sulphate with other iron preparations in terms of efficacy and compliance. Ferrous sulfate tablets provided under national nutritional anemia prophylaxis programme has very poor compliance despite of free government supply due to number of undesirable effects. This study gives us insight into changing oral iron preparation to a form with more efficacy and better patient compliance.

**Method:** Total 300 patients were included in this study and were randomly allocated into 7 groups: group 1, 2, 3, 4, 5, 6, and 7, according to the medication (oral iron preparation) given. Group 1 is ferrous sulphate given under National Programme, group 2 is ferrous sulphate-sustained release, group 3 is ferrous fumarate, group 4 is ferrous ascorbate, group 5 is colloidal iron, group 6 is ferric ammonium citrate suspension and group 7 is ferrous ascorbate suspension. Baseline hematological parameters were recorded and patients called up of follow up on day 30, day 60 and day 90. Compliance was ensured.

**Results:** elemental iron content of ferrous sulfate is comparable to that of other iron preparations, but por efficacy in improving hematological parameters due to poor compliance despite of free hospital supply owing to higher no.of side ffects whereas ferrous ascorbate and colloidal iron provide better alternative.

**KEYWORDS :** iron deficiency anemia, antenatal female, ferrous sulfate, national nutritional anemia prophylaxis programme, compliance

## INTRODUCTION

Anemia is defined as decreased hemoglobin level or circulating RBCs resulting in decreased iron carrying capacity of blood. It is the most common hematological disorder during pregnancy. As per WHO, anemia is defined as hemoglobin level less than 11 gm/dl[1]. According to WHO estimated prevalence of anemia in pregnant women is 14% in developed and 51% in developing countries and 65-75% in India[2]. Maternal anemia is often associated to increased maternal and fetal morbidity and mortality[2]. In India, anemia is the most common direct and indirect cause of maternal deaths. There is 8-10 fold increase in maternal mortality when haemoglobin falls below 5g/dl. India contributes to 80% of maternal deaths in south Asia caused due to anemia[3].

The additional iron requirements for pregnancy are estimated to be around 1000mg, of which 0.8mg/day of elemental iron is during the first trimester, 4-6mg/day in the second trimester increasing to as high as 8-10mg/day in the last 6 weeks of pregnancy[4]. So, it becomes mandatory to supplement pregnant women with iron preparation.[5,6,]

According to Ministry of health and family welfare, 100 mg of elemental iron and 500 mcg of folic acid recommended for 100 days in pregnancy[7]. Iron supplementation is advisable in pregnant females especially in developing countries where females enter in pregnancy with a low iron reserve.[8]

Iron deficiency anemia is most common type of anemia in pregnancy. Study of hematological parameters in pregnancy helps to differentiate iron deficiency anemia and physiological anemia of pregnancy. Iron deficiency anemia manifests as worsened quality of life, impaired physical and cognitive function, breathlessness and generalized body swelling in extreme[9]. Hematologically it appears as a hypochromic, microcytic anemia with low hemoglobin and hematological indices (MCV, MCH, MCHC).

National nutrition anemia prophylaxis programme was launched in 1970 to prevent nutritional anemia in mother and children. Even after 48 years, anemia is still a major concern for maternal mortality and morbidity in India. Side effects of oral iron therapy are a common problem in treatment of patients with oral iron preparations resulting in poor adherence to the therapy Keeping all these facts in view, the current study was designed to compare ferrous sulphate with other iron preparations in terms of efficacy and compliance.

## MATERIALS AND METHODS

This prospective study was conducted at obstetrics & gynecology department, GSVM Medical College, Kanpur, U.P. from January 2015 to November 2016. All antenatal cases of 13 to 28 weeks of gestational age attending OPD in our hospital with mild to moderate anemia (according to WHO criteria) having hemoglobin (7-10g/dl) were included in the study irrespective of gravida, parity. All pregnant women intolerant to oral iron preparations, bleeding piles, active peptic ulcer were excluded from the study.

High risk pregnancy associated with hypertension, diabetes, cardiac disease, hepatic and renal diseases and other GIT problems, tuberculosis, HIV, antepartum hemorrhage, pre- eclampsia, history of eclampsia or pregnancy induced hypertension were not included in this study. After taking informed consent of patient, detailed history and examination was done of each patient and routine investigations were advised. The patients attended our OPD; hemoglobin (Hb) by prick was done to know the baseline hemoglobin. Patients with severe anemia and normal Hb level were excluded from the study. The blood samples taken for hematological parameters (Hb, PCV, MCV, MCH, MCHC) at day 0 (before staring iron) to know baseline values and then after third month of starting iron therapy i.e. 90 days.

Total 300 patients were included in this study and were randomly allocated into 7 groups: group 1, 2, 3, 4, 5, 6, and 7, according to the medication (oral iron preparation) given. Group 1 is ferrous sulphate under National Programme, group 2 is ferrous sulphate - sustained release, group 3 is ferrous fumarate, group 4 is ferrous ascorbate, group 5 is colloidal iron, group 6 is ferric ammonium citrate suspension and group 7 is ferrous ascorbate suspension. The patients asked for regular

follow up and hemoglobin was done monthly but hematological parameters (PCV, MCV, MCH, MCHC) were done only after 3 months. Any adverse event like metallic taste, nausea, vomiting, dyspepsia, diarrhea and constipation were recorded on case record form. Compliance was checked by verbal enquiry and verified by checking empty or used packet of the drug brought by the patients. Some patients were lost to follow up and at the end of 3 months, total 182 patients, who continued their follow up, were studied for outcomes.

**Statistical analysis -**

Statistical analysis was done to analyse the difference in between the groups using percentages and chi-square test for categorical variables. Mean, standard deviation, paired 't'- test and ANOVA test for quantitative variables and results obtained by applying data using SPSS16 software.

## OBSERVATIONS

Table 1 shows distribution of antenatal patients in different oral iron preparations group and total elemental iron, dose of all iron preparations. We started the study with total 300 pregnant women, but at day 90, only 182 women came for follow up and maximum number of drop out occurred at day 90. Mean rise in Hemoglobin was found to be significant on day 90 in all preparation groups under study and it was found to be more with colloidal iron in comparison to other preparations. Mean rise in PCV, MCV, MCH, MCHC was found to be significant and comparable on day 90 in all preparation groups under study and it was found to be more with colloidal iron in comparison to other preparations (Table 2). Table 3 shows compliant and non-compliant patients during 90 days follow up.

## DISCUSSION

The present study was a prospective, comparative study which has been conducted to determine the effect of different oral iron preparations on hematological parameters in antenatal patients who were mild and moderate anaemic (according to WHO) and attended our hospital during January 2015 to November 2016. In our study, majority of patients belonged to age group of 20 – 30 years and were multiparous. The majority of the patients were illiterate, from rural population and of low socio-economic status which again reflects that the majority of patients were from underprivileged sector of society who had inadequate dietary intake and more caloric requirement.

In most of studies done earlier, only 2-3 iron preparations were compared but in study we tried to compare 7 iron preparations. In our study, it was found that ferrous sulphate followed by ferrous sulphate sustained release showed minimum rise in hemoglobin (Hb%) on day 90 whereas maximum rise was seen with colloidal iron.

In a observational prospective study by **Panchal Pavan J et al** they concluded that ferrous ascorbate increased haemoglobin more and better tolerated by patients as compared to ferrous sulfate[10].

A study by **Yeung et al** showed that regardless of iron status, ferrous ascorbate showed highest percentage uptake, followed by ferrous bis-glycinate, whereas uptake from all other forms of iron(including ferrous sulfate) was significantly lower[11].

In a study by **Guinea JM et al**, it was shown that ferrous ascorbate is batter tolerated than ferrous sulfate plus addetives[12].

In prospective, randomized, comparative clinical study done by **Singhal et al** compared the efficacy of ferrous sulphate, fumarate, ascorbate, sodium feredetate and ferrous bis-glycinate in the treatment of iron deficiency anaemia in pregnancy as ferrous ascorbate and ferrous bis-glycinate showed significantly ($p<0.05$) more rise in hemoglobin as compared to ferrous sulphate[13].

**Gogoi et al** noticed that oral ferrous ascorbate had treatment of iron deficiency anemia in pregnancy and concluded that ferrous ascorbate and bis-glycinate are more effective than ferrous sulphate in the shown more mean rise in the hemoglobin level than that of oral ferrous sulphate which was significant also[14].

**Szarfarc et al** also found that ferrous bisglycinate was significantly more effective than ferrous sulphate[15].

The mean rise in PCV was found maximum with colloidal iron and minimum with ferrous fumarate followed by ferrous sulphate (sustained release) respectively.

**Leslie (1979)** also supported the study and found four times more rise in PCV with ferrous glycine sulphate than ferrous sulphate (slow release preparation).

**G.S. Black(1981)** had done a single blind cross-over study with ferrous glycine sulphate and ferrous sulphate and found greater rise in Hb% and PCV with ferrous glycine sulphate but it was not statistically significant ($p>0.05$). They concluded that both tablets were equally efficacious but the total amount of iron ingested in the case of ferrous sulphate tablets was almost twice in comparison with ferrous glycine sulphate tablets.

In our study, maximum rise in mean MCV was found with colloidal iron and minimum with ferrous fumarate followed by ferrous sulfate (sustained release). Ferrous sulphate (National Programme) also showed a comparable rise in MCV.

**A. Aronstam et al (1982)** had done a cross-over comparative study with a controlled release preparation of ferrous glycine sulphate and ferrous fumarate and found a significant increase in MCV, similar with both preparations.

In this study, the mean rise in MCH was found significant and comparable on day 90 in all the groups ($p<0.0001$) but it was maximum with colloidal iron and minimum with ferrous sulphate.

Like our study, **Pavan Jagdishbhai Panchal et al 2014** also compared the efficacy and safety of oral ferrous ascorbate and ferrous sulphate in patients of anemia in chronic kidney disease (CKD) and at the end of study (after 12 weeks), ferrous ascorbate and ferrous sulphate had significantly improved mean hemoglobin and anemia indices however, mean increase in hemoglobin was more and significant with ferrous ascorbate (3.45 g/dl) as compared to ferrous sulfate (3.3 g/dl)[16]

## CONCLUSIONS

The National Nutritional Anaemia Prophylaxis Programme (NNAPP) in India was launched in 1970. However, after 48years, anaemia still continues to be a major public health problem. Partial coverage of the population, inadequate dose of the iron supplement, defective absorption due to intestinal infestations and problems with formulation have been recognized as factors responsible for its failure. Tab ferrous sulphate is given to pregnant women under national programme. In our study we found that ferrous sulphate of our National Programme had maximum total iron content and was comparable with other oral iron preparations but poor efficacy in improving hematological parameters as patients were least compliant to it in spite of free availability in government hospital because of its non-tolerable side effects. This is high time to introduce a new iron salt with better compliance, higher efficacy and lesser side effects in benefit of antenatal patients for which ferrous ascorbate and colloidal iron preparation provide a good option.

**Table 1**

| GROUPS | IRON PREPARATIONS | GENERIC NAME | COMPOSITION | ELEMENTAL IRON/DOSE | RECOMMENDED DOSE | ELEMENTAL IRON/DAY | NO. OF PATIENTS |
|---|---|---|---|---|---|---|---|
| 1 | FERROUS SULPHATE | NATIONAL PROGRAM | FeSO4 335 mg<br>folic acid .5mg | 100mg | OD | 100 mg | 46 |
| 2 | FERROUS SULPHATE SUSTAINED RELEASE | HEPP SR(HOSP SUPPLY) | FeSO4 150mg<br>folic acid .5mg<br>ZnSO4 61.6mg | 50mg | BD | 100 mg | 38 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 3 | FERROUS FUMARATE | AUTRIN | FF 300 mg<br>Folic acid 1.5 mg<br>Vit B12 7.5micro g | 98.6mg | OD | 98.6mg | 42 |
| 4 | FERROUS ASCORBATE TAB | CHERI- XT | FA 100mg<br>folic acid 1.5mg | 100mg | OD | 100mg | 44 |
| 5 | COLLOIDAL IRON | SYP TONOFERON | Each 5 ml<br>Iron 250mg<br>Folic acid .5mg<br>Vit B12 5 micro g | 50mg/ml | 1 tsp once a day | 250mg | 50 |
| 6 | FERRIC AMMONIUM CITRATE | SYP DEXORANGE | Each 15ml<br>Iron 160 mg<br>Folic acid .5mg<br>Vit B12 7.5micro g | 32.8mg/15 ml | 2 tsp thrice a day | 66mg | 40 |
| 7 | FERROUS ASCORBATE SUSP | SYP OROFER XT | iron 30mg<br>folic acid 550mcg | 6mg/ml | 1 tsp thrice a day | 90mg | 40 |

**different oral iron preparations studied**

**Table 2 mean rise in hematological parameters by 90 days of therapy**

| S no | Compound | Mean rise in Hemoglobin(g%) | Mean rise in PCV(%) | Mean rise in MCV(fl) | Mean rise in MCH(pg) | Mean rise in MCHC(g/dl) | Mean rise in S.Ferritin(ng/dl) |
|---|---|---|---|---|---|---|---|
| 1 | Ferrous sulfate(N) | 3.93±0.59 | 10.75±1.77 | 10.82±1.13 | 3.76±0.49 | 3.4±0.49 | 14.01±2.02 |
| 2 | Ferrous sulfate(SR) | 3.96±0.78 | 10.45±1.88 | 11.57±0.61 | 4.06±0.35 | 3.6±0.29 | 14.4±0.45 |
| 3 | Ferrous fumarate | 4.06±0.54 | 10.44±1.83 | 9.3±0.38 | 4.05±0.17 | 3.48±0.19 | 13.51±0.32 |
| 4 | Ferrous ascorbate | 4.29±0.66 | 11.7±1.73 | 10.93±0.38 | 4.36±0.21 | 4.04±0.07 | 14.23±0.18 |
| 5 | Colloidal iron | 5.18±0.49 | 14.54±1.22 | 11.96±0.63 | 5.2±0.31 | 5.23±0.14 | 18.34±0.25 |
| 6 | Ferrous ammonium citrate syrup | 4.51±0.43 | 12.3±0.67 | 11±1.12 | 4.67±0.93 | 4.47±0.93 | 15.42±0.36 |
| 7 | Ferrous ascorbate suspension | 4.93±0.91 | 13.42±1.04 | 11.33±1.06 | 4.98±0.94 | 5.08±1.22 | 16.08±1.07 |
| | p-value | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

**Table 3 compliance of patients for different oral iron preparations**

| | IRON PREPARATIONS | COMPLIANT (REGULAR INTAKE) | NON COMPLIANT (IRREGULAR INTAKE) | | | |
|---|---|---|---|---|---|---|
| | | | SIDE EFFECTS | COST | FORGET FULL | OTHERS |
| 1 | FERROUS SULPHATE (N) | 19 (41.54%) | 24 (52.31%) | NA | 1 (1.54%) | 2 (4.62%) |
| 2 | FERROUS SULPHATE (SR) | 21 (56.67%) | 15 (36.67%) | NA | 1 (3.33%) | 1 (3.33%) |
| 3 | FERROUS FUMARATE | 24 (58.73%) | 16 (38.1%) | 0 (0.00%) | 1 (1.59%) | 1 (1.59%) |
| 4 | FERROUS ASCORBATE | 23 (53.22%) | 20 (45.16%) | 1 (1.61%) | 0 (0.00%) | 0 (0.00%) |
| 5 | COLLOIDAL IRON | 32 (65.71%) | 14 (28.57%) | 1 (1.43%) | 1 (1.43%) | 2 (2.86%) |
| 6 | FERRIC AMMONIUM CITRATE | 20 (51.67%) | 14 (33.33%) | 2 (5.00%) | 3 (6.67%) | 1 (3.33%) |
| 7 | FERROUS ASCORBATE SUSPENSION | 18 (43.33%) | 17 (42.50%) | 3 (7.50%) | 1 (3.33%) | 1 (3.33%) |

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