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A pilot study on effect of intravenous iron sucrose on oxidative stress and antioxidant status of pregnant women with iron deficiency anemia

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ABSTRACT

Objectives: Iron deficiency anemia (IDA) is the most common nutritional deficiency among pregnant women in India. Iron can be supplemented orally or intravenously to treat IDA. Intravenous supplementation of iron can be risky as there is more possibility for the production of free iron in circulation. The role of free iron in the generation of free radicals and thereby oxidative stress is well known. The present study tends to evaluate oxidative stress and antioxidant status of intravenous iron sucrose treated pregnant women.

Materials and Methods: This prospective study was conducted in ACS Medical College and Hospital, Chennai. Twenty pregnant women with moderate IDA (Hb: 7–9.9 g/dl) were included in the present study. Blood samples were collected before and after the treatment with intravenous iron sucrose to measure antioxidants such as reduced glutathione, catalase and superoxide dismutase, and lipid peroxidation marker such as malondialdehyde.

Results: In the present study, plasma malondialdehyde levels were increased significantly after the treatment with intravenous iron sucrose. No significant alterations were observed in the levels of reduced glutathione and activities of catalase and superoxide dismutase.

Conclusion: In the present study, intravenous iron sucrose infusion was associated with oxidative stress as evidenced by increased lipid peroxidation in antenatal women with IDA. Hence, treatment with antioxidants during iron infusions can be considered.

Keywords: Anemia, Antioxidants, Intravenous iron-sucrose, Oxidative stress, Pregnancy

INTRODUCTION

Iron deficiency anemia (IDA) is the most common nutritional deficiency among pregnant women. According to the WHO, the prevalence of IDA is about 38% among pregnant women.[1] In India, the prevalence is around 84%.[2] About half of the maternal deaths globally occur due to anemia in South Asian countries and India contributes to about 80% of this mortality ratio.[3] The main causative factors for iron deficiency during pregnancy are poor intake and low bioavailability. IDA is classified based on hemoglobin levels as mild (10–10.9 g %), moderate (7–9.9 g %), severe (4–6.9 g %), and very severe (<4 g %) (Good clinical practice 2011). The first line of treatment for mild IDA in pregnancy is oral iron therapy. However, in the case of moderate and severe anemia, it requires longer treatment duration and compliance issue also occurs. For moderate anemia, better treatment modality will be parenteral iron therapy.[4]

Various parenteral (intravenous and intramuscular) iron preparations are available in the market such as iron dextran, iron sucrose, iron sorbitol, and iron citrate of which iron sucrose has been reported to be safe and effective during pregnancy.[4] Intravenous iron-sucrose appears to be a treatment of choice with no serious side effects which is indicated in the rapid correction of anemia in pregnancy or restoring maternal iron stores because the total iron stores can be administered within a short period of time.[5] Therefore, intravenous iron sucrose transfusion is an effective treatment strategy for pregnant women with severe anemia during late pregnancy and in patients non-compliant to oral therapy.

Both iron overload and iron deficiency could promote the generation of free radicals and result in cellular damage.[6] The iron-transporting protein and transferrin are normally kept at around 30% of iron saturation to ensure that no

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free iron is available to catalyze the formation of dangerous radicals such as OH ion. High percentage transferrin saturation was found to be associated with the presence of non-transferrin-bound, potentially redox-active iron.[7] Redox-active iron, potent pro-oxidant levels were increased in hemodialysis patients on intravenous iron sucrose therapy.[8] Although intravenous iron is effective in correcting anemia during pregnancy, its consequence on the oxidative stress status of pregnant women is not known. Hence, the present study aims at determining the oxidative stress and antioxidant status of iron-deficient pregnant women on intravenous iron sucrose therapy.

MATERIALS AND METHODS

The present study is a prospective study conducted in the Department of Biochemistry in collaboration with Department of Obstetrics and Gynecology in ACS Medical College and Hospital, Chennai. About 20 pregnant women with moderate anemia (Hb: 7–9.9 g/dl) were included in the present study. Pregnant women having gestational diabetes mellitus, heart diseases, liver and renal disorders, peptic ulcer, allergy, asthma, inflammation, and anemia due to causes other than iron deficiency were excluded from the present study.

Dosage of iron sucrose

The dose of total iron sucrose to be administered was calculated and rounded up to the nearest multiple of 100 mg.

Total dose = weight in kg × (target Hb in g/L–Actual Hb in g/L) × 0.24 + 500 mg. The calculated dose of iron sucrose complex was administered as 200 mg in 100 ml 0.9% sodium chloride intravenously over 20–30 min. This was given on alternate days with a maximum of 600 mg/week up to the total dose. Oral administration of iron was excluded during this period. Target hemoglobin was 120g/L.[9]

Blood collection

After taking informed consent from the patients, about 2 ml each of blood was collected in EDTA coated tubes before and after administration of intravenous iron sucrose. The following biochemical analyses were carried out. Hemoglobin content of the blood was analyzed using ERBA H 360 cell count analyzer and the erythrocyte reduced glutathione[10] catalase,[11] superoxide dismutase,[12] and malondialdehyde[13] were determined by standard procedures.

Statistical analysis

Results were analyzed by SPSS version 16.0. Student's paired t-test was used to assess the significance of difference before and after the treatment. All results were presented as mean ± SD. P <0.05 was considered significant.

RESULTS

Patients' baseline characteristics

A total of 20 pregnant anemic women took part in the present study. The baseline characteristics such as age of the participants, hemoglobin levels, and average gestational period of the participants are shown in [Table 1].

Oxidative stress and antioxidant status of the antenatal women before and after intravenous iron sucrose treatment are shown in [Table 2]. There was no significant difference in the levels of glutathione before and after the treatment with I.V. iron sucrose. Catalase activities were not significantly different before and after the treatment.

Superoxide dismutase activity shown before and after the treatment (with intravenous iron sucrose) was not significant. There was a statistically significant increase in malondialdehye (MDA) values after the treatment with intravenous iron.

DISCUSSION

In the present study, we did not find any significant difference in the levels of blood glutathione after infusion compared with basal level, that is, before infusion. An intravenous iron infusion did not alter the reduced glutathione to oxidized glutathione ratio in anemic patients up to 6 h in contrast to healthy volunteers where the above mentioned ratio is decreased.[14] This may explain why glutathione is not altered in our study.

In the present study, plasma levels of MDA, an end product of lipid peroxidation, were significantly elevated after intravenous iron sucrose infusion. According to a study done by Zager *et al*., various iron preparations including iron sucrose increased lipid peroxide levels in cell culture. The authors also revealed that the cell viability was least with iron sucrose compared with other preparations.[15] Increased MDA levels were demonstrated in dialysis patients treated with intravenous iron sucrose.[16] In addition to this, Roob *et al*. demonstrated the generation of

Table 1: Baseline characteristics of the study participants.

Parameter	Variables
Age (Years)	26.4±4.3
Gestational period (weeks)	28.5±4.5
Hemoglobin (g/dl)	9±0.9

Table 2: Comparison of oxidative stress and antioxidant status of the study participants before and after the treatment.

Parameters	Before treatment (n=20)	After treatment (n=20)
Glutathione (mg/g Hb)	1.49±0.37	1.44±0.36
Catalase (U/ml)	15.03±4.64	15.58±5.00
SOD (U/ml)	9489±1020	9181±993
MDA (nmoles/ml)	8.86±1.89	10.49±0.3.24*

MDA, and its peaking after 30 min of the start of an intravenous iron sucrose infusion. They also illustrated a rapid increase in redox-active iron a mediator of oxidative stress after infusion.[8]

A randomized and controlled trial showed that the effect of iron supplementation during the third trimester of pregnancy on iron status and lipid peroxidation and this study supported the hypothesis that high doses of iron might induce lipid peroxidation.[17] Excess iron intake has deleterious effects due to induction of direct intestinal damage, oxidative stress, cell toxicity, endothelial dysfunction, or growth of pathogens.[18,19]

In the present study, the antioxidant enzymes catalase and superoxide dismutase were not altered significantly, this may be due to immediate sample collection. Being enzymes, the regulatory mechanism has to be activated which may take more time. The present study was conducted with smaller sample size. Studying oxidative stress, in larger populations and, for longer duration (start of infusion and end of infusion), will provide more insight.

CONCLUSION

In the present study, intravenous iron sucrose infusion was associated with oxidative stress as evidenced by increased lipid peroxidation in antenatal women with IDA. Further study with more number of samples may help us to understand the role of intravenous iron sucrose on oxidative stress and antioxidant status.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. World Health Organization. The Global Prevalence of Anaemia in 2011. Geneva, Switzerland: World Health Organization; 2011.
2. Toteja GS, Singh P, Dhillon BS, Saxena BN, Ahmed FU, Singh RP, *et al*. Prevalence of anemia among pregnant women and adolescent girls in 16 districts of India. Food Nutr Bull 2006;27:311-5.
3. Sectorial Policies and Programs. Tenth Five Year Plan 2002-2007. Nutrition Planning Commission. New Delhi: Government of India; 2002. Available from: https://www.planningcommission.nic.in/plans/planrel/fiveyr/10th [Last accessed on 2021 Mar 4].
4. Gomathi V, Kumaresan K, Sivankumar K. Parenteral iron therapy for treatment of moderate to severe anemia in pregnancy. Int J Contemp Med Res 2016;3:2853-5.
5. Gupta A, Rathore AM, Manaktala U, Gupta A, Gupta S. Role of intravenous iron sucrose in correction of anemia in antenatal women with advanced pregnancy. Indian J Hematol Blood Transfus 2015;31:251-4.
6. Toxqui L, De Piero A, Courtois V, Bastida S, Sánchez-Muniz FJ, Vaquero MP. Iron deficiency and overload. Implications in oxidative stress and cardiovascular health. Nutr Hosp 2010;25:350-65.
7. Luo Y, Han Z, Chin SM, Linn S. Three chemically distinct types of oxidants formed by iron-mediated fenton reactions in the presence of DNA. Proc Natl Acad Sci USA 1994;91:12438-42.
8. Roob JM, Khoschsorur G, Tiran A, Horina JH, Holzer H, Winklhofer-Roob BM. Vitamin E attenuates oxidative stress induced by intravenous iron in patients on hemodialysis. J Am Soc Nephrol 2000;11:539-49.
9. Baird-Gunning J, Bromley J. Correcting iron deficiency. Aust Prescr 2016;39:193-9.
10. Beutler E, Kelley BM. The effect of sodium nitrate on RBC Glutathione. Experimentia 1963;19:96-7.
11. Beers RF Jr., Sizer IW. A spectrophotometric method for measuring the breakdown of hydrogen peroxide by catalase. J Biol Chem 1952;195:133-40.
12. Marklund S, Marklund G. Involvement of superoxide anion radical in the autoxidation of pyrogallol and a convenient assay for superoxide dismutase. Eur J Biochem 1974;47:469-74.
13. Niehaus WG Jr., Samuelsson B. Formation of malonaldehyde from phospholipid arachidonate during microsomal lipid peroxidation. Eur J Biochem 1968;6:126-30.
14. Lasocki S, Piednoir P, Couffignal C, Rineau E, Dufour G, Lefebvre T, *et al*. Does IV iron induce plasma oxidative stress in critically ill patients? A comparison with healthy volunteers. Crit Care Med 2016;44:521-30.
15. Zager RA, Johnson AC, Hanson SY, Wasse H. Parenteral iron formulations: A comparative toxicologic analysis and mechanisms of cell injury. Am J Kidney Dis 2002;40:90-103.
16. Eiselt J, Racek J, Opatrny K Jr., Trefil L, Stehlik P. The effect of intravenous iron on oxidative stress in hemodialysis patients at various levels of Vitamin C. Blood Purif 2006;24:531-7.
17. Lachili B, Hininger I, Faure H, Arnaud J, Richard MJ, Favier A, *et al*. Increased lipid peroxidation in pregnant women after iron and Vitamin C supplementation. Biol Trac Elem Res 2001;83:103-10.
18. Schümann K, Ettle T, Szegner B, Elsenhans B, Solomons NW. On risks and benefits of iron supplementation recommendations for iron intake revisited. J Trace Elem Med Biol 2007;21:147-68.
19. Maruyama Y, Nakayama M, Yoshimura K, Nakano H, Yamamoto H, Yokoyama K, *et al*. Effect of repeated intravenous iron administration in haemodialysis patients on serum 8-hydroxy-2'-deoxyguanosine levels. Nephrol Dial Transplant 2007;22:1407-12.

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