Safety, efficacy and acceptance of parenteral iron sucrose therapy in anemia of pregnancy in rural area

Archana V. Daddenavar, Vikas M. Daddenavar
Department of OBG[1] and Surgery[2]
S. N. Medical College, Bagalkot. Karnataka, India

Abstract

Background: The impact of anemia in pregnancy affects both mother and fetus. Antenatal care should be concerned with its early detection and management. The aim of this study was to evaluate the safety, efficacy and acceptance of parenteral iron sucrose complex therapy in iron deficiency anaemia in pregnancy in rural area.

Material and Methods: This prospective clinical trial included 800 pregnant women between 16 to 32 weeks of gestation diagnosed as cases of Iron deficiency anaemia with Haemoglobin (Hb) level 5-8 gm%, who were seen from January 2013 to January 2015 in S N Medical College Hospital Bagalkot consulting department of Obstetrics and Gynaecology. All the patients received Iron Sucrose Complex (ISC) in infusion form. The aim was to bring her Hb level to 10gm% as well as to replenish the iron stores. All patients were monitored for laboratory response and adverse effects. Results were analyzed in terms of the safety, efficacy and acceptance by patients.

Results: Intravenous (IV) iron sucrose is effective in achieving target Hb of 10g/dl in 72% of patients. It shows that IV iron sucrose significantly ($P<0.001$) increases Hb levels within 4 weeks. There were no adverse reactions. All women stated that they found the treatment acceptable to them. Iron Sucrose Injection was found to be safe and well tolerated.

Conclusion: Iron sucrose complex is safe and effective in the treatment of iron deficiency anemia during pregnancy. It was well tolerated and acceptable by patients. It can be used safely in peripheral health centers and in rural areas as adverse reactions were absolutely nil in the presnt study.

Key words: Pregnancy, Iron Deficiency Anaemia (IDA); Iron Sucrose Complex

Introduction

Reducing maternal mortality is one of the eight health related Millennium Development Goals (MDG5) adopted at the Millennium Summit in 2000. Within this framework, the international community is committed to reduce Maternal Mortality by three quarters between 1990 and 2015[1]. Hemorrhage is the leading cause of maternal mortality[2]. Anemia is one of the world's leading causes of hemorrhage and disability[3] and thus is one of the most serious global public health problems. The impact of anemia in pregnancy affects both mother and fetus[4-8]. Because anemia is the most frequent maternal complication of pregnancy, antenatal care should be concerned with its early detection and management[9].

The routine treatment in majority of the institutions is oral iron and blood transfusion reserved for severe or emergency cases. Blood transfusion has its own hazards, including transfusion of mismatched blood and deadly infections like HIV, CMV, hepatitis and anaphylaxis. Thus, there is a need for a safe and effective alternative to oral iron or blood transfusion in the treatment of anemia. Iron dextran, the first parenteral iron used, lost its popularity due to anaphylaxis. Iron sucrose was then discovered as a parenteral iron that could be safe and effective.

The aim of this study was to evaluate the safety, efficacy and acceptance of parenteral iron sucrose complex therapy in iron deficiency anaemia in pregnancy in rural area.

Address for Correspondence
Dr. Archana V. Daddenavar
Assistant Professor Department Of OBG, S. N. Medical College, Bagalkot, Karnataka, India.
E-mail: drarchanavd@gmail.com

Materials and methods

800 consecutive consulting pregnant women between 16-32 weeks of gestation diagnosed as cases of Iron deficiency anaemia with Hb level 5-8 gm%, which were seen from January 2013 to January 2015 at our institute were recruited in study. After admission in hospital wards, written informed consent was taken prior to screening enrolment. All the patients received ISC in infusion form with the aim to correct the iron deficiency as well as to replenish the iron stores. The aim was to bring her Hb level to 10gm%. Estimation of hemoglobin was done using double chamber sysmax cell counter for all the patients.

Formulae were used to calculate the iron requirement of the patient to fulfill the deficit as well as to replenish the iron stores and were calculated as follows:

Amount of iron deficit (mg) = Body wt (Kg) × Hb deficit (gm%) × 0.24 + 500

ISC was administered as 200 mg elemental iron in 100 ml of 0.9% Normal Saline infusion over 15 to 20 minutes, on thrice a week basis, up to the total calculated dose. A test dose of one ml of Iron Sucrose infusion was given and followed by a 10 minutes window period, during which no infusion was given and patient was observed for any allergic reactions. If no reactions occurred, the rest of the infusion was given. Hb level was done on 1 month post treatment day.

A set of observations (BP, pulse, temperature) were taken before the start of the infusion, after 10 minutes and at the end of the infusion. Similar clinical observations were taken as and when required during blood transfusion i.e. looking for symptoms or signs of an adverse reaction. The subjects were allowed to go home four hours after the infusion if all observations were stable. No allergic reactions were noted during administration of ISC. Hb level and MCV were done after one month. Mean values of Hb and MCV were used to compare pre and post treatment parameters. A "p value" of less than 0.5 was considered to be significant. The data was compiled and standard tests of significance (p value) were applied.

Results

The total number of selected patients during the study period was 800. The age of subjects ranged from 19 to 32 years. The mean age was 24 years. Most of the patients were multigravida. The average gestational age was 28 weeks. Among antenatal subjects the mean pre-treatment Hb was 7.01 gm%. In present study, dose of ISC required ranged between 600-1200 mg with mean of 744.44 mg. Among antenatal subjects, mean 1 month post treatment day Hb was 10.34 gm% with rise 3.33 gm% on 1 month post treatment day (p-value <0.001). Hb rise was independent of gestational age at administration of ISC.

After the test dose of ISC infusion, none of the patients developed allergic reaction. The duration to achieve the target Hb level of 10 gm/dl was five weeks. Before ISC infusion, the mean Hb level was 7.5 gm/dl and mean MCV was 65 fl. After ISC infusion, the mean Hb level rose to 10 gm/dl and mean MCV became 75 fl. The differences in values were statistically significant ($p<0.05$).

Discussion

Worldwide, anemia affects over two billion people and the World Health Organization (WHO) has estimated that half of these are due to iron deficiency[10, 11]. There are two known factors which contribute to the development of iron deficiency anaemia (IDA) in pregnancy; the first is the woman's iron stores at the time of conception and the second is the amount of iron absorbed during gestation. The fact that anaemia frequently does occur in pregnancy among women in developing countries is an indication that preexisting iron stores are often inadequate and physiological adaptations to pregnancy are insufficient to meet the increased requirements[12]. Hence, iron supplementation in pregnancy has become a standard and routine practice as a preventive treatment for iron deficiency anaemia in pregnancy in developing countries. Intravenous iron sucrose in particular has been used in several recent studies and might be highly beneficial in refractory patients or those intolerant of oral iron formulations[12]. Though, because of its immediate bioavailability, it may result in a more rapid rise in Hb level in anaemic patients compared with oral iron; but it probably does not confer an advantage in preventing anaemia in pregnancy[13,14].

The WHO technical working group on the prevention and the treatment of severe anaemia has documented that parenteral iron therapy produces a rapid and complete correction of iron deficiency, including replacement of iron stores; thereby producing a more rapid erythropoietic response than oral iron replacement[15]. It is also indicated in pregnant women whose hemoglobin level is required to be restored rapidly such as those who present too close to term and those who have severe anemia[16].

Study shows that intramuscular or intravenous iron

is thought to be associated with allergic reactions and anaphylactic shock; furthermore, parenteral iron is thought to predispose to venous thrombosis and occasionally cardiac arrest and death[17]. However, parenteral iron sucrose complex is known to have several advantages because of its low- allergenic properties and consequently, an extremely low incidence of severe side effects such as anaphylactic reactions[18,19]; however, its use requires caution as it may not be completely devoid of side effects.

Other disadvantage of intravenous iron supplementation includes cost and invasiveness of the procedure. However, it is argued that cost benefit of intravenous iron prophylaxis may be large taking into consideration the opportunity costs of erythropoiesis-stimulating agents, blood transfusions, and hospitalization[13].

In this study, the efficacy, safety and tolerability of intravenous iron sucrose and its acceptance by patients in rural areas in treating pregnancy iron deficiency anaemia was observed. Iron sucrose complex is safe in pregnancy. It corrects anemia at short duration and replenishes iron stores. This has been the observation in other studies too[14,10].

Al Momen *et al*., observed that the intravenous iron sucrose group achieved significantly higher hemoglobin level (*P* value ≤ 0.001) in a shorter period (*P* value ≤0.001)[20]. In a study done by Al *et al*., hemoglobin was different for patients in the oral iron and intravenous iron sucrose groups across time in each individual group as well as at any given point of time. The hemoglobin level was significantly higher in the intravenous iron sucrose group[21].

In the present study, hemoglobin within the group was significantly higher across time. After treatment, the group maintained hemoglobin with routine supplementation of oral iron in the present study, unlike in Bayoumeu *et al*.'s study, where no additional oral supplementation was given. Because of the high prevalence of anemia (57.9%) in pregnant women as per the National Family Health Survey-3[22], oral supplementation even with normal iron stores is essential in India. Unlike in the parenteral iron-treated group, once the anemia is corrected with oral iron, absorption slows down. This is responsible for the iron stores not being replenished with oral iron, unlike intravenous iron.

Many Indian studies have used the intramuscular route for parenteral iron and reported side-effects such as pain, staining at injection site and arthralgia[23,24]. Intravenous iron sucrose cannot be given intramuscularly and does not have these side-effects. Anemia was corrected satisfactorily in this study with the use of weight-dependent formula for calculation of iron dose as by Bayoumeu, who also used a weight dependent formula[14]. Parenteral iron uses calculated dose depending on the degree of deficiency, unlike oral iron, which has a static dose. Gastrointestinal side-effects with the oral iron reported incidence varied from negligible to 31% in varies studies[14,20,21]. No adverse events noted in the present study. Other studies reported unpleasant taste and fever, which were not observed in the present study[14,20]. Because there were no serious adverse drug reactions and no episodes of anaphylaxis, we feel that it is safe for anemia in pregnancy. Iron sucrose is costlier than oral iron and requires a hospital setting for administration.

We conclude that Intravenous Iron Sucrose increases hemoglobin and replenishes iron stores. This is significant in our country where women may become anemic again during lactation, especially when their iron stores have not been corrected. However, oral iron is cheaper and is easy to take. As no major adverse effects were noted with iron sucrose, it is a safe option with good efficacy for the treatment of IDA with a narrow side-effect profile.

Conclusion

Iron sucrose complex is safe and effective in the treatment of iron deficiency anemia during pregnancy. It is well tolerated and acceptable by patients. It can be used safely in peripheral health centers in rural areas as adverse reactions were absolutely nil in the present study.

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