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ORIGINAL ARTICLE

Intravenous Iron-Sucrose Complex for Treatment of Iron Deficiency Anaemia in Pregnancy - Experience in an Obstetric Day Care Clinic in a Tertiary Hospital

Tan AE[1], Siti SA[2]

Department of [1]Obstetrics & Gynecology, [2]Family Medicine, Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Kuala Lumpur

ABSTRAK

Satu kajian keratin rentas telah dilakukan untuk menilai kesesuaian rawatan anemia kekurangan besi semasa dan selepas kehamilan dengan menggunakan suntikan vena *iron sucrose complex* (Venofer) secara pesakit luar. Seramai 120 pesakit dari Klinik Rawatan Harian Obstetrik, Hospital Universiti Kebangsaan Malaysia telah dikaji selama 18 bulan, diantara March 2003 hingga Ogos 2004. Hasil ukuran utama ialah kenaikan aras hemoglobin, pematuhan pesakit, kesan sampingan dan kejimatan dari yuran masuk wad. Sebelum menerima rawatan, aras hemoglobin ibu mengandung ialah 8.5±0.85g/dl dan 7.6±0.80 g/dl bagi ibu selepas bersalin. Min kenaikan aras hemoglobin selepas 14 hari merima rawatan ialah 3.52g/dl (2.9- 4.6g/dl). Hasil kajian menunjukkan seorang pesakit mengalami ruam kulit, dan seorang lagi mengalami demam panas ringan. Tujuh orang pesakit mengalami rasa metalik. Tiada kesan buruk yang serius atau reaksi anafilaktik berlaku. Sepuluh pesakit (8.3%) tidak meyempurnakan terapi – lapan orang ibu bersalin sebelum pelengkapan rawatan, dan dua orang ibu gagal menghadiri diri selepas bersalin. Secara purata, setiap orang pesakit menggunakan tujuh ampul Venofer iaitu 700mg, dan menjalani tempoh rawatan selama tiga hari. Rawatan sebagai pesakit luar mengelakkan dari tinggal di wad selama tiga hari dan dapat menjimatkan RM135 untuk rawatan wad kadar RM45 sehari. Dengan itu, sejumlah RM16,200 untuk bayaran masuk hospital dapat dielakkan oleh 120 orang pesakit ini. Sebagai kesimpulan, penggunaan Venofer untuk merawati anemia semasa dan selepas kehamilan sebagai pesakit luar adalah selamat, munasabah, menjimatkan dan mendapat pematuhan pesakit yang tinggi.

Kata kunci: anaemia kekurangan besi, kehamilan, *Iron sucrose complex*, pesakit luar

ABSTRACT

A cross-sectional study was undertaken to evaluate if outpatient administration of intravenous iron sucrose complex (Venofer) was a sensible option in treating iron deficiency anaemia during pregnancy and puerperium. A total of 120 patients with iron deficiency anaemia were recruited from the Obstetric Day Care Clinic at the Universiti Kebangsaan Malaysia Medical Centre (UKMMC) over 18 months from March 2003 to August 2004. The main outcome measures were haemoglobin increment, patients'

Address for correspondence and reprint requests Assoc. Prof Dr Tan Ay Eeng, Department of Obstetrics & Gynecology, UKM Medical Centre, Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur. Email: ae_tan2002@yahoo.com.au

compliance, adverse effects and saving from hospitalization fees. The pre-treatment haemoglobin (Hb) level was 8.5±0.85g/dl for the antenatal patient and 7.6±0.80 g/dl in the post-partum group. The mean post-treatment haemoglobin increment at day fourteenth was 3.52±0.75g/dl. One patient developed skin rash while another had low-grade pyrexia. Seven patients experienced mild metallic taste. There were no serious side effects or anaphylactic reactions. Ten patients (8.3%) did not complete their therapy - eight delivered before completion of treatment; another two defaulted following delivery. The average number of Venofer used was seven ampoules i.e. 700mg per person, most of them required three sessions to complete the course. Outpatient treatment allows each patient to save hospitalization fees of RM45 per day, which totalled up to RM135 for a 3-days ward stay. An estimation of RM16,200 hospitalization fees for the 120 patients was avoided during the study period. In conclusion, outpatient treatment of anaemia in pregnancy and post-partum period using Venofer was safe and feasible, with high patient compliant and cost-savings from hospitalization fees.

Key words: iron deficiency anaemia; pregnancy; iron sucrose complex; outpatient.

INTRODUCTION

Pregnancy anaemia is defined by haemoglobin (Hb) of less than 110g/l in the first or third trimester or less than 105g/l in the second trimester. Iron deficiency with or without anaemia has many adverse effects on the nervous system, intellectual capacity, physical performance, immune response and pregnancy outcome (Fairbanks & Beutler 1995, Baynes 1994). The mother may be overwhelmed by easy fatigability, dyspnoea, headache, reduced exercise tolerance and weakness. On the other hand, the fetus may encounter an increased risk of low birth weight and preterm delivery.

Up to 30% of women in the post-partum period are affected by anaemia of under 10g/dL and about 10% by severe anaemia of less than 8%. By far the main cause for this is the deficiency of iron supplied during pregnancy and blood loss during and after birth (Lebrecht et al. 1995). Under normal circumstances, oral iron is the treatment of choice since it is simple, effective, safe and cheap. However, oral iron is better absorbed in an empty stomach but patient may experience side effects such as nausea, vomiting, gastritis, diarrhea and constipation. These side effects can be minimized by co-administration with food, although this may substantially decrease absorption, particularly of ferrous preparation (Perewusnyk et al. 2002). Even a patient who responds well to oral iron therapy would require a long time, usually months to reach the target haemoglobin level. This means that they have to suffer from iron deficiency for extended periods unnecessarily (Al-Momen et al. 1996).

A pregnant woman without anaemia may require at least 1000mg of elemental iron to be delivered to the haemopoietic organs while the anaemic patient may need more than 2600mg. This requirement cannot be met by the oral route in the majority of patients because of limited absorption, bio-availability and compliance (Bynum et al. 1977, Lee & Feldman 1993, Kahrilas & Hogan 1993).

Parenteral iron therapy with intravenous iron-sucrose complex (Venofer) was first introduced to UKMMC in 2002. It has been used to correct anaemia in pregnant women in whom the elemental iron requirement cannot be met by oral route.

Previous studies have shown that intravenous Venofer is safe and effective in pregnant and post-partum women with iron deficiency anaemia (Breymann et al. 2000, Al-Momen et al. 1996).

OBJECTIVE

The aim of this study was to assess if administration of intravenous iron sucrose complex (Venofer) was a sensible option in treating iron deficiency anaemia in pregnancy and puerperium using day-care clinic in an urban hospital. A favorable outcome would imply its safe usage as an outpatient for treating anaemia in pregnancy.

METHODOLOGY

This was a cross-sectional observational study, recruiting all patients with iron deficiency anaemia who were referred to the Obstetrics Day Care Unit, UKMMC for intravenous Venofer. The study was completed in 18 months from March 2003 to August 2004. Baseline haemoglobin (Hb) level was determined and reassessed in 14 days after treatment. Patients' demography, number of visits to the Day Care Unit, total dosage, increment of haemoglobin level, adverse effect and their compliance to complete the full therapy were recorded. Patients with other causes of anaemia such as thalassemia trait, haemolytic anaemia, liver or renal disease were excluded.

Calculation of Venofer dosage

Total iron deficit (mg) = [Body weight (kg) x (target Hb–actual Hb)g/l x 0.24*] + depot iron (mg)

For body weight of above 35 kg, the target Hb is 120 g/l and depot iron is 500mg.

*Factor = 0.0034 x 0.07 x 1000 (iron content of Hb ~0.34%; Blood volume ~7% of body weight; factor 1000 is conversion from g to mg)

Administration of Venofer

The first 25mg of iron (i.e. 25mls of solution) was infused as a test dose over a period of 15 minutes. If there were no adverse events the remaining portion of the infusion was given. Infusion of 200mg iron sucrose in 200ml normal saline over 1 hour 30 minutes was administered at an interval of 1 to 3 days to complete the total dose required.

RESULTS

A total of 120 patients were recruited. There were 70% Malay, 16% Chinese, 10% Indian and 4% from other ethnic background. About half the patients (48%) were working mothers, 45% were housewives and 7% were students.

The mean gestational age of those who were referred for anaemia in pregnancy was at 34.5 weeks. The pre-treatment Hb level was 8.5$\pm$0.85g/dl (7.2-8.9g/dl). In the post-partum group, the pre-treatment Hb was 7.6$\pm$0.80g/dl (7.2-8.8g/dl). Majority of these patients (92%) had a history of either non-compliance or intolerable to oral iron supplement, hence were offered intravenous Venofer. The other 8% required rapid restoration due to recent blood lost from post-partum haemorrhage.

Of those who completed treatment, the mean increment of Hb within 14 days was 3.52g/dl (2.9-4.6g/dl). Each patient received an average of seven ampoules i.e. 700mg of Venofer.

Majority of the patients tolerated the treatment well with no discomfort or any significant complaint (Table 1). One patient developed skin rashes while on infusion. She responded to intravenous Chlorpheniramine Maleate (Piriton) and the Venofer was completed at a slower

Table 1: Adverse effects of intravenous Venofer

ADVERSE EFFECTS	NUMBER
Skin rash/Itching	1
Fever < 38°C	1
Metallic taste	7
Nausea	15
Anaphylactic reaction	0

infusion rate. Another patient had low-grade pyrexia of 38^{o}C after receiving her second dose and the fever settled with Paracetamol. Seven patients complained of having a mild metallic taste and 15 patients had nausea. There were no other undesirable effects such as headache, dizziness, palpitations, dyspnoea, vomiting, abdominal pain, diarrhoea, muscle cramps, myalgia, shivering, chest pain, injection site pain, anaphylactic reaction or hospitalization for further treatment.

Of the 120 patients who were recruited for the study, 10 patients (8.3%) did not complete their therapy - eight of them were antenatal mothers who delivered before completion of treatment; another two post-partum patients defaulted their follow-up.

Venofer was approved as a formulary item and patients received free supply be it as an in or outpatient. However, the ward charge for an in-patient in UKMMC was RM45 per day. As most patients required at least a three-day infusion, it was estimated that each patient might save up to RM135. Our estimation was that during the study period on the 120 outpatients, a total of RM 16,200 hospitalization fee was avoided.

DISCUSSION

Anaemia is a common deficit in pregnancy. Though traditionally it is treated by oral haematinics, some may require parenteral iron due to poor compliance to oral supplement, poor absorption or intolerable gastro-intestinal side effects. Prior to year 2002, intra-muscular preparation iron dextran (Imferon) was the available parenteral preparation in UKMMC However, iron dextran is to be discouraged because of its adverse effects including pain at injection site, irregular absorption, staining of buttock and rarely, malignancy (Martini et al. 1994, Roberson 1973).

Parenteral iron using iron-sucrose complex (Venofer) has largely replaced iron dextran. Numerous reports from European countries have proven its effectiveness and patient tolerability (Al-Momen et al. 1996, Perewusnyk et al. 2002). The results of our observational study have shown that iron-sucrose complex is safe, is well tolerated and effective in treating anaemic pregnant and postpartum patients in a day care setting. There were 120 patients in this study, twenty-four sustained minor adverse effects such as skin rash, low-grade pyrexia, metallic taste and nausea. There was no serious side effects or anaphylactic reactions reported.

Iron-sucrose complex releases iron to the iron-binding proteins with a half-life of about 6 hours. This relatively short half-life grants it effective and carries minimal risk of allergic reaction (Danielson 1998, Kraft et al. 2000, Rohling et al. 2000). Skin rash and fever can be prevented by giving a slow infusion over one to four hours or dividing the total dose into smaller portions (100-200mg/day). The side effects are mostly self-limited and resolve with symptomatic treatment.

Unlike other parenteral iron preparations, iron-sucrose complex is taken up mainly by the reticuloendothelial system and not by the parenchymal cells of the liver, kidney, adrenal gland or other organs. Therefore, organic toxicity such as pancreatic, myorcardial or hepatic hemosiderosis is less likely even with iron-sucrose complex over-load (Macdougall et al. 1989).

Majority of the patients (92.8%) in this study completed the treatment course. The local urban population around UKMMC has proven themselves to be highly compliant to outpatient treatment, regardless of their background as housewives, working mothers or students. Outpatient treatment allows less interruption to family or working life, is more convenient and cost saving. The avoidance of hospitalization could itself encourage patients' compliance.

Although iron-sucrose complex is expensive and the treatment requires intravenous infusion and is time consuming as compared to oral iron supplement, it is highly tolerated and rapidly effective. This study showed that the mean increment of Hb within 14 days was 3.52g/dl (2.9-4.6g/dl). On the contrary, oral iron takes a longer time to achieve the target haemoglobin level and the increment rate is significantly slower (Al-Momen et al. 1996). It is very important to correct an anaemic pregnant patient before delivery, as the maternal iron status will influence the newborn iron status as well. Infants of anaemic mothers are more likely to become anaemic at 12 months of age, even when possible confounders such as socio-economic status, feeding practices and morbidity were taken into account (Colomer et al. 1990). In conclusion, outpatient treatment of anaemia in pregnancy and post-partum period using Venofer is safe, feasible, with high patient compliance and saves cost from hospitalization fees.

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