To the rescue: the role of intravenous iron in the management of severe anaemia in the peri-partum setting

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Introduction

Maternal death from obstetric haemorrhage remains a common cause of maternal mortality worldwide¹. Iron deficiency and iron-deficiency anaemia (IDA) in pregnancy is a global health problem affecting around 20% of women in the western world and increasing to 56% in developing countries². It is associated with adverse physiological and psychological outcomes in both mother³,⁴ and child⁵,⁶ (Table I). Iron-deficient women are also at increased risk of requiring an allogeneic red blood cell (RBC) transfusion during the peri-partum period, which is an expensive and often scarce resource with well-described risks⁷,⁸. Additional complexity arises in the management of women refusing blood products¹.

Meticulous antenatal care and careful planning of the delivery is crucial for all pregnant women. Optimisation of iron stores with oral iron supplementation plays an important role in treating IDA and improving haemoglobin (Hb) but up to 59% of those to whom oral iron is prescribed report significant gastrointestinal side effects⁹. However, intravenous (IV) iron can be an effective, rapid and safe alternative for non-responding or non-compliant patients and for those presenting too late for successful oral supplementation¹⁰,¹¹.

We report two cases of severe peri-partum anaemia in which the administration of IV iron was utilised to support erythropoiesis in order to boost Hb and compensate for iron loss.

| Table I - Effects of iron deficiency in pregnancy. |
| Maternal | Infant |
| Preterm delivery | Preterm birth |
| Increased transfusion risk | Risk of low birth weight |
| Post-partum iron deficiency | Neonatal iron deficiency |
| Impaired physical performance | Changes in brain biochemistry |
| Depression | Deficits in neurocognitive development |
| Lower cognitive performance | Poor locomotive development |
| Reduced immune function | Poor cognitive performance |
| Shorter lactation periods | Impaired socio-emotional behaviour |

Case 1

A 29-year old woman (gravida 5, parity 3), with a past medical history of depression, presented for delivery at 39+2 weeks, following spontaneous onset of labour. Her antenatal history revealed vitamin D and iron deficiency, for which supplements had been prescribed at 30 weeks of gestation.

The labour lasted 6 hours 15 minutes. Analgesia was provided with nitrous oxide and a 4.7 kg healthy female infant was delivered at 18:05 hours via a normal vaginal birth. Both a third degree tear and an atonic uterus were observed and an associated blood loss of 800 mL was recorded in the labour ward. The immediate management included IV crystalloid, bimanual uterine compression, insertion of a urinary catheter, an intravenous infusion of syntocinon (40 IU in 1,000 mL normal saline) and the administration of 1,000 µg misoprostol per rectum. Following transfer to the operating theatre, surgery commenced under spinal anaesthesia at 19:17 hours. After repair of the tear further uterine blood loss was noted and clots were manually evacuated from the lower uterine segment. No retained products were found but the uterus remained atonic, vaginal blood loss continued requiring 500 µg of IV ergometrine and 3 mg of intramyometrial prostaglandin (PG) F-2 alpha. A Bakri balloon was inserted and its position confirmed via ultrasound. The vaginal loss settled and the total blood loss was estimated at 2,500 mL. The Hb was measured and found to be 65 g/L (Table II).

A RBC transfusion was discussed and it was at this stage that the patient disclosed to the anaesthetist, for the first time, that she was a Jehovah’s Witness and would not accept blood products.

Post-operative admission to the Intensive Care Unit was arranged. The treatment plan included an iron infusion with 1,000 mg ferric carboxymaltose, (Ferinject®, Vifor Pharma Ltd., Glattbrugg, Switzerland), administered immediately after surgery, ongoing haemodynamic monitoring and the removal of the Bakri balloon the following day.

On day 1 after delivery the Hb decreased to 46 g/L. There was no further blood loss and haemodynamics remained stable. The Bakri balloon was deflated...
in stages and removed after 24 hours without any complications.

After transfer to the Women’s Health Ward on day 2, discharge home followed on day 5. A further 1,000 mg of ferric carboxymaltose were electively administered on day 10 post-partum, by which time the Hb had risen to 88 g/L (Table II). The post-partum period was uneventful apart from a short stay in hospital for mastitis 5 weeks later. On admission laboratory testing revealed normalisation of haematological indices and iron status.

Case 2
A 27-year old aboriginal woman (gravida 6, parity 3), was admitted for a scheduled lower segment Caesarean section at 38+6 weeks of gestation. Pre-operative blood samples were taken prior to admission and a Hb of 76 g/L was noted (Table III). A repeat blood test after admission confirmed the result. No iron studies were available but a very low mean corpuscular haemoglobin of 19.6 pg (Table III) and a past history of iron deficiency supported the diagnosis of severe IDA.

A team approach by obstetricians and the anaesthetist resulted in a detailed conversation with the patient. It was reiterated that severe anaemia carries a high risk of a peri-partum RBC transfusion and that it would be beneficial to manage the condition with an iron infusion and to delay surgery. After agreeing to the plan, an iron infusion with 1,000 mg of ferric carboxymaltose was administered and surgery was scheduled 5 days later.

By the time the woman was readmitted, her Hb had increased to 90 g/L (Table III). An uneventful repeat lower segment Caesarean section was carried out under spinal anaesthesia and an infant weighing 3,880 grams was delivered. Estimated blood loss was 650 mL resulting in a post-operative Hb of 77 g/L (Table III). Discharge from hospital followed on day 3 after delivery. Oral iron supplements to take home were refused. Again, an opportunity arose for an unscheduled follow up. Antenatal screening for a further pregnancy 9 months later revealed normalisation of her Hb and red cell indices (Table III).

Discussion
The 2 cases illustrate some of the potential complexities and challenges in the peri-partum period. Oral iron is considered the mainstay of antenatal iron delivery but this approach is far from universal, frequently not tolerated or adhered to and often ineffective. Obstetric haemorrhage remains one of the leading causes of maternal mortality, is unpredictable and on the increase. Despite its enormous clinical utility, RBC transfusion is a treatment with well-described adverse events and risks, and should ideally be avoided. Transfusion was not a treatment option in the first patient and not the preferred option of clinicians in the second patient. Iron deficiency resulting in anaemia increases the risk of peri-partum transfusion. IV iron offers a promising treatment modality if iron deficiency with or without anaemia only becomes apparent in late pregnancy or if the peri-partum blood loss is significant. Use of IV iron resulted in a satisfactory outcome without allogeneic transfusion in both these cases.

An increasing number of studies report the safe and successful administration of IV iron in a wide range of clinical settings. Inexperience with IV iron, logistical difficulties in arranging administration, a misconception regarding the rapidity of the response and anecdotal fear of serious adverse reactions appear to be preventing

| Table II - Case 1: peri-partum haematological indices and iron status. |
|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|
| Prior to delivery   | Time (days)         |                      |                      |                      |                      |
|                     |                     | Day 1*              | Day 2               | Day 3               | Day 4               | Day 11              | Day 40              |
| Hb g/L              | 105                 | 65                  | 46                  | 49                  | 53                  | 88                  | 120                 |
| MCH                 | 27.4                | 26.6                | 26.7                | 26.6                | 27.5                | 28.9                | 28.6                |
| Ferritin µg/L       | NA                  | NA                  | NA                  | NA                  | NA                  | 241                 |                      |
| Transferrin saturation % | NA              | NA                  | NA                  | NA                  | 22                  |                      |                      |

**Post-operative: IV iron given, *2nd dose of IV iron given. Hb: haemoglobin; MCH: mean corpuscular haemoglobin; NA: not available.**

| Table III - Case 2: haematological indices before and after IV iron treatment. |
|---------------------|---------------------|---------------------|---------------------|---------------------|
| Time (days/months)  |                      |                      |                      |                      |
| Haemoglobin g/L     | 76                  | 90                  | 77                  | 138                 |
| MCH pg              | 19.6                | 20.4                | 22.3                | 27.8                |

**MCH: mean corpuscular haemoglobin.**

widespread use of the therapy\cite{15} despite current evidence-based recommendations\cite{16,17}. The need for a paradigm shift was recently addressed in an editorial by Muñoz\cite{18}.

Appropriate and timely management of iron deficiency or IDA with the right choice of treatment modality may mean the difference for many pregnant women between requiring an allogeneic RBC transfusion or not. In addition, this rapid and safe intervention has the potential to offer protection from serious functional and mental deficits to mothers and their newborn, by preventing iron depletion.

**Authorship contribution**

BF collected the data and wrote the manuscript. GM helped draft and revised the paper. GD revised the draft paper.

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