

Preoperative Pharmacological Correction of Severe Anaemia Due to Uterine Fibroids

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Abstract

Context: Severe anaemia from menorrhagia is a common complication of uterine fibroids. If all patients with such a problem were to accept blood transfusion and if blood transfusion were risk free, then it is the ideal treatment for correcting severe anaemia preoperatively. However, this is not the case and so alternatives have to be sought for those who reject blood transfusion. Treatment with haematinics is one alternative. But views have been expressed that they may not be able to adequately correct severe anaemia in such cases.

Objective: To study the effect of total dose iron-dextran infusion and folic acid with or without a progestogen in the preoperative correction of severe anaemia due to fibroid induced menorrhagia.

Materials and Methods: A prospective interventional study of severely anaemic patients with uterine fibroids who refused pre-operative blood transfusion over a 31-month period. Eligible subjects were given total dose iron-dextran infusions followed by oral folic acid with or without norethisterone. The outcome measures were serial haemoglobin concentrations, rate of rise of haemoglobin concentration, and number of days required to raise the haemoglobin concentration to 10 grams/dl. Data analysis was by means of simple percentages and descriptive statistics.

Results: Eight patients were treated. The initial haemoglobin concentrations in the eight patients ranged from 5.7 to 6.9 g/dl while final ones prior to surgery ranged from 9.0 to 11.0g/dl. The eight patients reported subjective improvement (felt stronger) within 24 hours of receiving iron-dextran infusion. It was possible to operate on all of the patients within 3 weeks of administering iron-dextran infusion and folic acid. One patient had maculopapular skin rashes on the third day after the total dose iron-dextran infusion. No intraoperative or postoperative problems were encountered.

Conclusions: Iron-dextran as a total dose infusion followed by oral folic acid and a progestogen (if necessary) is a useful alternative to multiple blood transfusions in the pre-operative correction of severe anaemia due to uterine fibroids.

Key Words: Preoperative Correction, Anaemia, Menorrhagia, Uterine Fibroids

Introduction

Multiple large uterine fibroids presenting with menorrhagia and severe anaemia are common gynaecological problems in the tropics and developing countries¹. Characteristically, before the anaemia becomes severe, the patient usually gets to know that she has fibroids but for one reason or the other attempts to avoid an operative treatment. At a point, ill health from the menorrhagia and anaemia makes the operation inevitable. At that point, the degree of anaemia is such that urgent blood transfusion may be required to correct it preoperatively.

For religious reasons, Jehovah's Witnesses do not accept blood transfusion². Because of the current HIV/AIDS pandemic in sub-Saharan Africa, even some non-Jehovah's Witnesses in these countries now reject blood transfusion. Yet non-correction of anaemia preoperatively is associated with poor surgical outcome^{1,3}. Thus haematinics may have to be used to correct anaemia preoperatively in patients with severe anaemia but who refuse blood transfusion. However, views have been expressed that haematinics may not be able to correct severe anaemia in such cases¹. This is because the patient may be in heart failure. Additionally, the gains in haemoglobin concentration with haematinics are usually reversed following bleeding during subsequent menses. This paper is an interim

report of an on-going study on the effect of total dose iron-dextran infusion and folic acid with or without a progestogen in the preoperative correction of severe anaemia due to fibroid induced menorrhagia.

Subjects and Methods

The study took place at Mbanefo Hospital, Ogui Enugu from 25th November 2001 to 30th June 2004. The inclusion criteria for the study included the following: menorrhagia attributable to uterine fibroids, severe anaemia (defined as a haemoglobin concentration of less than 7g/100 mls), patient must have refused blood transfusion and requested for an alternative. She must also not have had any previous history of allergy to iron therapy and must have accepted to undergo surgery as soon as the anaemia was corrected. In addition to other tests peculiar to the individual patient, all patients fulfilling the above conditions had a full blood count, blood film examination, reticulocyte count, and pelvic ultrasound examination.

For those who were recruited into the study, the total iron requirements (in milligrams) to raise their

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Table 1
Summary results of preoperative correction of severe anaemia due to uterine fibroids with total dose iron-dextran infusion

| S/O | Patients Initials | Hospital No | Age (years) | Parity | Date of first attendance | Initial Hb (g/100mls) | Date of total dose imferon | No of days before final HB check | Final Hb conc (g/100mls) | Reaction | Date of Operation | Operation | Preop blood transfusion | Op blood loss(mls) | Postop Hbg /100 mls |
|-----|-------------------|-------------|-------------|--------|--------------------------|-----------------------|----------------------------|----------------------------------|--------------------------|-------------|-------------------|-------------|-------------------------|--------------------|---------------------|
| 1. | O.O. | 2001/11/786 | 34 | 0+0 | 25/11/01 | 6.5 | 26/11/02 | 21 | 11.0 | Nil | 11/12/02 | Myo* | Nil | 400 | 10.2 |
| 2. | C.O. | 2002/8/3010 | 49 | 5+0 | 8/8/02 | 5.7 | 9/8/02 | 35 | 12.0 | Skin rashes | 25/9/02 | TAH + BSO** | Nil | 400 | 11.0 |
| 3. | N.A. | 2002/8/3020 | 41 | 0+0 | 19/8/02 | 6.5 | 22/8/02 | 8 | 10.5 | Nil | 4/9/02 | Myo* | Nil | 500 | 9.6 |
| 4. | C.O. | 2003/06/26 | 30 | 0+0 | 6/9/03 | 6.7 | 6/9/03 | 20 | 9.7 | Nil | 26/9/03 | Myo | Nil | 600 | 8.8 |
| 5. | A.E. | 1999/10/14 | 55 | 7+0 | 9/10/02 | 6.4 | 9/10/02 | 13 | 9.5 | Nil | 23/10/02 | TAH* | Nil | 550 | 8.9 |
| 6. | H.O. | 2003/05/61 | 29 | 0+0 | 31/5/03 | 6.0 | 31/5/03 | 7 | 9.0 | Nil | 9/6/03 | Myo | Nil | 300 | 8.5 |
| 7. | A.A. | 2004/02/05 | 39 | 0+6 | 4/1/04 | 6.7 | 10/2/04 | 13 | 9.7 | Nil | 25/2/04 | Myo | Nil | 350 | 8.6 |
| 8. | C.E. | 2004/5/11 | 48 | 4+0 | 8/5/04 | 6.8 | 11/5/04 | 7 | 9.3 | Nil | 23/5/04 | TAH | Nil | 450 | 9.1 |

*Myo = myomectomy

**TAH = Total Abdominal hysterectomy

**BSO = Bilateral salpingo-oophorectomy

haemoglobin concentrations to 14.8g/dl were calculated using the formula that 250mg of iron raises the haemoglobin concentration by 1 gram per decilitre⁴. The calculated dose was multiplied by one and a half in order to take care of the iron stores. For each patient, the calculated required dose was put into 1 litre of Normal saline and thoroughly mixed. An intravenous line was established and intravenous hydrocortisone 200mg statim given as a premedication. The iron-dextran infusion was then commenced at 10 drops per minute while the patient was observed for anaphylaxis and other side effects. If, after 30 minutes, no adverse reaction was observed, then the drip rate was increased to 60 drops per minute until it finished. The patient's vital signs were recorded every 15 minutes and urticaria and other untoward side effects looked out for.

Following the iron-dextran infusion, the patients were placed on folic acid tablets 5 mg daily. The patient's haemoglobin concentration and reticulocyte count were rechecked weekly. Where the next menses was imminent, the patient was commenced on norethisterone tablets (Primolut NTM) 5mg tds to withhold the menses. When the haemoglobin concentration was at least 9 grams/dl and the patient considered fit for surgery, the patient then underwent either a myomectomy or a total abdominal hysterectomy as appropriate and agreed upon between the doctor and the patient. Pre-operatively, the patients gave a written consent to the effect that provided adequate precautions were taken, the doctor would not be held liable for any problem that might arise from not transfusing them. Intra-operatively, several units of HaemaccelTM (a plasma expander) were kept handy. In all cases, diathermy was used to minimise intra-operative blood loss. During the myomectomies, uterine tourniquet was applied intra-operatively in the conventional way to occlude the uterine and ovarian vessels prior to enucleating the fibroids.

Results

The results are summarised in Table 1. Eight patients have so far been treated with iron-dextran and folic acid with or without norethisterone. The initial blood film in all the patients showed anisocytosis and hypochromia consistent with iron deficiency anaemia. Their initial reticulocyte counts were above 2.5% consistent with active bone marrow. The initial haemoglobin concentrations in the eight patients ranged from 5.7 to 6.9 g/dl while final ones prior to surgery ranged from 9.0 to 11.0g/dl. The mean rate of haemoglobin rise was 29.1 grams/dl over 128 days (mean of 0.23g/dl/day). The eight patients reported subjective improvement (e.g. feeling stronger and/or less breathless) within 24 hours of receiving iron-dextran infusion. In six out of the 8 patients treated, the haemoglobin concentration

increased to approximately 10 grams/litre within 2 weeks of treatment. It was possible to operate on all of the patients within 3 weeks of administering iron-dextran infusion and folic acid. Case No 2 (Mrs. C.O.) had maculopapular skin rashes on the third day after the total dose iron-dextran infusion. Two weeks after she had received the total dose iron-dextran infusion, her haemoglobin concentration was 10.2g/dl. Because of financial reasons, there was a delay in operating on her (Table 1). Within this period, she continued on norethisterone tablets.

Norethisterone tablets were necessary to postpone the menses in five (62.5%) of the patients while the remaining three (37.8%) did not need this. Three (37.5%) of the eight patients had total abdominal hysterectomy with or without bilateral salpingo-oophorectomy while the remaining five (62.5%) underwent myomectomy. No intraoperative or postoperative problems were encountered. Their post operative haemoglobin concentrations ranged from 8.5 to 11 grams/dl. Postoperatively all the patients received ferrous sulphate, folic acid and multivitamin tablets. Case No 6 (Mrs. HO) became pregnant subsequently and at the time of this report had had a caesarean delivery of a live female baby due to placenta praevia.

Discussion

The negative correlation between anaemia and operative outcome is not in doubt^{1,3}. For this reason efforts are usually made to correct anaemia prior to surgery. Preoperative correction of anaemia can be carried out in various ways, depending on the severity of the anaemia and the urgency of the operation. In elective cases with mild anaemia, giving haematinics for several weeks may be all that is required¹. Such preoperative correction of anaemia using haematinics usually minimises the need for blood transfusion intra- and postoperatively⁶. Some authorities¹ believe that haematinics may not correct severe anaemia from fibroid induced menorrhagia fast enough especially as subsequent menses tend to deplete the patient's blood again. According to this view, preoperative transfusion with packed cells should be preferred in such severe cases of anaemia (especially if the patient is in incipient or frank heart failure) since it corrects the anaemia instantly¹.

With the current HIV/AIDS pandemic in sub-Saharan African countries, each unit of blood transfused increases the risk of a patient being infected with the virus. This is because the current method of screening blood donors for HIV detects antibodies to the virus and not the viral particles and so does not detect those who are in the window period of the HIV infection⁷. Clinicians are likely to increasingly encounter severely

anaemic patients who will reject blood transfusion either because of religious reasons or fear of being infected with HIV as in the cases treated in this study. Faced with such a patient, the clinician has one of three options to follow: operate on the patient without correcting the anaemia; correct the anaemia with haematinics instead of blood transfusion or else refuse to treat her and so refer her to another service that will accede to her request. For reasons stated earlier on, most clinicians will not want to operate on a severely anaemic patient.

This study has shown that severe anaemia from fibroid induced menorrhagia can be corrected preoperatively without blood transfusion by using iron-dextran infusions and folic acid to promote haematopoiesis and restore the haemoglobin concentration while preventing further blood loss by the pharmacological use of progestins to delay menstruation until surgery can be carried out. What is impressive is that subjective improvement is noticeable in the patients shortly after the iron therapy while almost normal haemoglobin concentration is restored in at least 50% of them within two weeks of administering iron-dextran.

The route of administering iron is debatable. It has been shown that the rate of rise of haemoglobin concentration after oral or parenteral iron is the same (approximately 0.2 g/100mls/day)⁵. Therefore, where compliance to oral iron can be guaranteed on the part of the woman and there are no other factors that impede intestinal iron absorption, oral iron therapy can theoretically restore haemoglobin concentration as fast as parenteral iron in cases of iron deficiency anaemia. We, however, know

that such situations rarely obtain in practice⁸. Because of this, parenteral iron as used in these cases may be preferable to oral iron. The rate of rise of haemoglobin concentration obtained in this study (0.23g/dl/day) is almost same with the 0.2g/100mls/day documented previously in Caucasians⁵. Furthermore, it is established that parenteral iron restores the iron stores faster than oral iron⁵ and this may be a further reason for preferring it to oral iron. However, anaphylactic reaction is a major though rare side effect of parenteral iron⁵. Apart from one case of mild skin rashes, no serious side effect was recorded in the eight cases treated.

If the time course of normalising haemoglobin concentration with parenteral iron is about three weeks, then using progestins to postpone menstruation may not be necessary in all cases especially if the woman presents when she is menstruating and receives iron-dextran during this period. Where the iron-dextran is given towards the end of the menstrual cycle, then progestins are indicated to delay menses until the anaemia has been corrected and surgery carried out. Gonadotrophin releasing hormone analogues can also be used not only to postpone menstruation but also to shrink the fibroids preoperatively⁹. However, side effects, high cost, lack of availability in the tropics and the high recurrence rates of the fibroids after myomectomy are their drawbacks.

We conclude that iron-dextran as a total dose infusion followed by oral folic acid and a progestogen (if necessary) is a useful alternative to multiple blood transfusions in the pre-operative correction of severe anaemia due to uterine fibroids.

References

1. Pinkerton JHM, Stewart DB. Uterine fibroids. In: Lawson JB, Stewart DB (eds) *Obstetrics and Gynaecology in the Tropics and Developing Countries*. 1st edition. London: E. Arnold, 1967: 385-397.
2. Izuorah KLA, Okonkwo JEN, Aghaji AE. Surgery in the Jehovah's Witness: blood conservation method. *Orient J Med* 1992; 4:111-114.
3. Howkins J, Hudson CN. *Shaw's Textbook of Operative Gynaecology*. 5th ed. Edinburgh: Churchill Livingstone, 1983:18.
4. Abudu OO. Anaemia in pregnancy. In: Agboola A (Ed) *Textbook of Obstetrics and Gynaecology for Medical Students Vol II*. Lagos, Nigeria: University Services Educational Publishers Limited 1988: 77.
5. Hillman RS, Finch CA. Drugs effective in iron-deficiency anaemia and hypochromic anaemias. In: Gilman AG, Goodman LS, Rall TW, Murad F (eds) *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 7th ed, New York: Macmillan Publishing Company 1985: 1308-1322.
6. Sheth SS, Das SB. Preoperative management of anemia to avoid blood transfusion. *Int J Gynaecol Obstet* 2002; 77:245-247.
7. Gallant JE. The HIV-positive patient: the initial encounter CME. *Medscape Clinical Update* 7th May 2002. Available at http://www.medscape.com/viewprogram/660_pnt
8. Dare FO, Ademowore BA, Chukuneye UC, Amole FA. Compliance of oral iron intake in pregnancy: the Ile-Ife experience. *Orient J Med* 1991; 3:113-115.
9. Vollenhoven BJ, Lawrence AS, Healy DL. Uterine fibroids: a clinical review. *Br J Obstet Gynaecol* 1990; 97:285-290.