Treatments for iron-deficiency anaemia in pregnancy

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RHL Commentary by Candio F, Hofmeyr GJ

1. EVIDENCE SUMMARY

This Cochrane review (1) examines the effects of different treatments in women diagnosed with iron-deficiency anaemia in pregnancy, assessing neonatal and maternal morbidity and mortality, haematological parameters, and adverse effects of treatment. A total of 101 studies evaluating treatments for anaemia were identified. Seventeen randomized controlled trials (RCTs), involving 2578 women, met the reviewers’ inclusion criteria. Most of these trials focused on laboratory results. Only six trials assessed clinical outcomes, but they were too small to provide reliable evidence. Thirty-eight studies were excluded after the first review because they did not meet the inclusion criteria.

The RCTs included in this review were too small to estimate significant clinical effects and had low methodological quality. The trials had evaluated different iron preparations, routes of administration and dosages. Comparison of trial data was further complicated by the heterogeneity of the tests used in the trials to diagnose anaemia, and by the different the cut-off points used for the diagnosis of iron-deficiency in pregnancy, especially in the presence of other causes of anaemia and a co-existing infection.

The review found that oral iron reduced the risk of being anaemic during the second trimester of pregnancy and that haemoglobin and serum ferritin levels were higher when compared with placebo (2). One RCT suggested that, at four weeks, daily oral iron treatment increased haemoglobin level more than oral iron twice a week (3). Yet another RCT suggested that, at 16 weeks, a twice weekly dose of iron increased the haemoglobin level more than oral iron given once a week (4). Higher doses of oral iron did not increase haematocrit values (5), but the haemoglobin level was higher and anaemia was less frequent when vitamin A was added to regular iron (2). Unfortunately, the latter trial had evaluated the outcome at the end of treatment during the second trimester of pregnancy, and not at term (or at least the third trimester), which would have been more appropriate.

Maternal haemoglobin at four weeks was higher (6, 7), and haemoglobin level > 11g/dl at birth was more...
frequent, with intravenous iron, as compared with oral iron. Compared with oral iron, haematological parameters were better with intramuscular iron (8), and compared with intramuscular iron, the parameters were better with intravenous iron (9).

The gastrointestinal side-effects (nausea and constipation) were more frequent with oral iron (6, 10, 11) and these side-effects did not decrease with controlled-release iron (11). Intramuscular iron produced pain at the injection site. Skin discolouration at the injection site was more frequent with intramuscular iron than with intravenous iron. This side-effect was more frequently observed in women receiving intramuscular iron-dextran compared with intramuscular iron-sorbitol. Venous thrombosis occurred in four out of 26 women receiving intravenous iron dextran, while there was no occurrence of venous thrombosis in those receiving intramuscular iron. Another trial reported five cases of venous thrombosis among 15 women receiving intravenous iron dextran; however, when hydrocortisone was added to iron dextran, there was no case of venous thrombosis (12). These numbers were too small to arrive at a meaningful conclusion, but the possibility of an association between intravenous iron supplementation and this serious side-effect cannot be ruled out.

As stated above, the RCTs included in the review reported that iron supplementation increases maternal haematological parameters. However, the available data were insufficient to determine the effects of these treatments in terms of clinical endpoints. Therefore, on the basis of this review, no recommendation can be made regarding how to treat iron-deficiency anaemia in pregnancy.

The search strategy and data extraction and analyses performed in this review were done correctly by the authors. The data are presented appropriately in tables, showing relative risks and confidence intervals; however, the scale used in the graphics made the interpretation difficult.

The review does not provide information on the magnitude of the problem of childhood iron poisoning in communities where women receive routine iron supplementation.

2. RELEVANCE TO UNDER-RESOURCED SETTINGS

2.1. Magnitude of the problem

Anaemia (defined by the World Health Organization as haemoglobin levels of ≤ 11 g/dl) is one of the world's leading causes of disability (13), and thus one of the most serious global public health problems. The prevalence of anaemia in pregnancy varies considerably because of differences in socioeconomic conditions, lifestyles and health-seeking behaviours across different cultures. Anaemia affects nearly half of all pregnant women in the world: 52% in developing countries compared with 23% in the developed world (13). The most common causes of anaemia are poor nutrition, deficiencies of iron and other micronutrients, malaria, hookworm disease, and schistosomiasis; HIV infection and haemoglobinopathies are additional factors (14).

Anaemia is one of the most prevalent nutritional deficiency problems affecting pregnant women (15). The high prevalence of iron and other micronutrient efficiencies among women during pregnancy in developing countries is of concern and maternal anaemia is still a cause of considerable perinatal morbidity and mortality (16).

2.2. Applicability of the results

As many of the trials reviewed were conducted in developing countries, the results are applicable to practice in under-resourced settings. Even though the limited number of trials included in the review found oral, intramuscular and intravenous iron to increase maternal haemoglobin values, the data were not sufficient to ascertain the clinical significance of these findings. Hence, this Cochrane review does not recommend any treatment for iron-deficiency anaemia in pregnant women.
2.3. Implementation of the intervention

Severely anaemic pregnant women may require blood transfusion, which is not always feasible in under-resourced settings, and it may even carry some risks for the woman. To avoid this, health services should implement a strategy for the control anaemia in pregnant women, including early detection and appropriate management of the condition. This review suggests that treatment of iron-deficiency anaemia in pregnancy increases haematological parameters, so in pregnant women with mild-to-moderate anaemia this intervention could prevent the need for interventions at a later stage that could prove more dangerous for the mother and her baby. On the other hand, in developing countries, where it is not possible to use different methods to diagnose anaemia, it is advisable to give iron and folate routinely to all pregnant women.

3. RESEARCH

The causes of anaemia vary from region to region. In general, these causes are more or less documented. There is, however, a need for consensus on the cut-off points for mild, moderate, and severe iron-deficiency anaemia. To support the implementation of iron therapy, RTCs comparing iron with placebo need to be conducted in pregnant women with anaemia (using well-defined laboratory values). These trials should be sufficiently powered to address clinical endpoints such as maternal and neonatal morbidity and mortality.

Sources of support: Centro Rosarino de Estudios Perinatales.

References

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