How much iron does a healthy pregnant woman require?

Susan Fairweather-Tait

Norwich Medical School, University of East Anglia, Norwich NR4 7TJ, Norfolk, UK

Telephone: +44 1603 591304

Email: s.fairweather-tait@uea.ac.uk

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Dietary reference values for iron in pregnancy vary widely. For example, the US Estimated Average Requirement (EAR) for pregnant women (aged 18y and above) is 22 mg/d, based on factorial modelling with the assumption that 18% of dietary iron is absorbed during the first trimester and 25% in the second and third trimesters (1). This compares with an EAR in non-pregnant women of 8.1 mg/day. In contrast, the UK Department of Health (2, 3) and the European Food Safety Authority (EFSA) (4) both concluded that there is no need for additional dietary iron during pregnancy provided there are adequate iron stores at conception. According to the UK DRVs, the Estimated Average Requirement for pregnant women is 11.4 mg/d, whereas EFSA gives an Average Requirement for pregnant women of 7 mg/day (4). EFSA used factorial modelling to calculate the quantity of absorbed iron required to meet maternal and fetal needs and reached broadly similar values to the IOM, but they used different values for iron absorption; heme iron absorption was assumed to be 25% and values for non-heme iron absorption were assumed to be 7.2% in the first trimester, 36.3% in the second trimester and 66.1% in the third trimester, as reported by Barrett et al (5). These values were selected on the basis that the test meals administered by Barrett et al. were more reflective of dietary iron intakes than some of the other studies in which higher levels of iron were given as iron salts. The limited data for dietary iron absorption during pregnancy is the main reason for the substantial difference in reference values between these two authorities, but there are many other unanswered questions relating to iron metabolism in pregnancy.

Two articles are published in this edition of the AJCN that provide data on iron absorption during pregnancy using stable isotope techniques. Stoffel et al (6) measured fractional iron absorption (FIA) in normal weight and overweight pregnant women during the second and

third trimester. Women were given a bread roll test meal, labelled with 12 mg stable isotopically enriched iron, and absorption was calculated from RBC isotope enrichment 14 days post-ingestion. In normal weight women median FIA was 13.6% and 23.9% in the second and third trimester respectively. FIA in overweight pregnant women was 13.5% in the third trimester, significantly lower than normal weight women. The authors conclude that impaired upregulation of iron absorption in overweight women during the third trimester is associated with inflammation, but it was independent of serum hepcidin. This is an important finding as it concurs with data from animal models demonstrating that fetal signals drive maternal iron absorption (7). The study by Delaney et al (8) gave 20 mg iron as ferrous sulphate and reported 9 and 20% iron absorption in the second and third trimester respectively, which is a similar two-fold increase to the findings of Stoffel et al (6) for normal weight women. They found that total body iron, calculated from serum ferritin and soluble transferrin receptor, explained well over half the variance in iron absorption but, again, there was no association with hepcidin concentration.

Iron absorption data from these two studies will be a useful addition to the literature, the results of which are summarised in Delaney et al (8) and can be used for future updates of dietary reference values for iron. However, a seemingly intractable question remains unresolved, namely how much additional iron is required to support a pregnancy? Pregnancy is a normal physiological state and the high prevalence of iron deficiency in pregnant women and widespread need for iron supplements is puzzling. The most likely explanation is an inadequate dietary supply of iron in women of child-bearing age which results in low body iron stores, combined with insufficient absorbable dietary iron during pregnancy. Over the course of evolution, physiological adaptations that favoured a positive

outcome for pregnancy were conserved, but diets were very different at that time, and iron absorption from pre-agricultural diets has been estimated to be much higher than from present day diets (9). On the other hand, it could be argued that depletion, even exhaustion, of maternal iron stores during pregnancy is a normal physiological mechanism, and that repletion should take place in the months and years after delivery, facilitated, for example by the amenorrhea of lactation.

The study by Delaney et al (8) sheds light on how iron is delivered to the fetus and the importance of red blood cells, particularly in women with low iron stores. The study by Stoffel et al (6) shows the inability of overweight pregnant women to upregulate iron absorption and transfer sufficient iron to the fetus. Thus, in addition to modern diets containing iron of low bioavailability, inflammation induced by overweight is another phenomenon that may have an adverse impact on the iron status of both mothers and infants. The fetus is able to accumulate iron normally in the presence of maternal iron deficiency, most likely through compensatory up-regulation of placental iron transport, but with severe anemia fetal iron status becomes compromised with undesirable consequences (7). It is a widely accepted that the fetus acts as a parasite on the mother, but we still do not know whether maternal iron depletion during pregnancy represents a normal physiological state and to what extent efforts should be made to prevent it. The study by Delaney et al (8) demonstrates that red blood cell iron turnover is faster in women with diminished iron stores and that red blood cell iron is a significant source for fetal iron. This pool of iron will be smaller with anemia, illustrating how important it is to avoid anemia in pregnancy, and also to enter pregnancy with sizeable body iron stores. However, we still do not know whether depletion of iron stores has any adverse effects on the mother or fetus and

whether preventative actions are desirable, such as taking iron supplements. Further to the Cochrane review on iron supplementation in pregnancy (10), in which intermittent regimens and daily supplementation produced similar maternal and infant outcomes, an analysis of the risks and benefits of iron supplements in pregnancy is needed. Consensus on iron requirements in pregnancy is urgently required. The two papers published in this volume of the AJCN contain data that will help to update dietary reference values for iron, which will, in turn, inform future public health policies and worldwide strategies focused on the important goal of reducing iron deficiency in women and infants.

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