IRON

Use

The main use of oral iron in the first year of life is to prevent iron deficiency anaemia during growth in babies fed breast milk who weighed less than 5 lb (2·3 kg) at birth. It is also used after birth to correct the iron loss that a few babies suffer as a result of chronic fetal blood loss before birth. Routine supplementation during pregnancy serves no useful purpose for most women, but is of real value in countries where their nutritional status is poor

Nutritional factors

Iron is a major constituent of the haemoglobin molecule and routine supplementation is traditional in pregnancy, although the scientific basis for this is far from convincing and the practice is now actively discouraged except in developing countries where the nutritional status of many women is poor. Here the baby clearly benefits if the mother takes a regular daily supplement (60mg of iron and 400 microgram of folic acid) during pregnancy. The value of adding other micronutrients is, at the moment, much less clear. Iron tablets can, however, pose a very real hazard to young children because they are often mistaken for sweets, and the ingestion of as little as 3 g of ferrous sulphate can kill a small child. We also know that maternal iron deficiency has to be very severe before it causes neonatal anaemia or iron deficiency during infancy. However all babies need to acquire a further 0·4–0·7 micrograms of iron a day to maintain their body stores because the circulating blood volume triples during the first year of life, and this requires a diet containing 1–2 mg/kg of iron a day.

While babies normally have substantial iron stores at birth even when born many weeks before term (and even in the face of severe maternal iron deficiency), these stores start to become depleted unless dietary intake is adequate by the time the child's blood volume has doubled. Microcytosis (MCV < 96 μm^3) at birth is ***never*** a sign of iron deficiency, but can be due to a haemoglobinopathy (usually some form of thalassaemia). The iron in breast milk is extremely well absorbed (as long as the baby is not also being offered solid food), but absorption from artificial feeds is only a fifth as good, and the use of unmodified cow's milk in the first twelve months of life is particularly likely to cause iron-deficiency anaemia. It used to be thought that this might be due to iron loss as a result of occult gastrointestinal bleeding, but recent studies have failed to confirm this. It is possible that the high-phosphate content of whole cows' milk may interfere with iron absorption.

Haemoglobin and haematocrit levels change rapidly during the first 2–4 weeks of as outlined in the monograph on Blood, but these changes are *not* due to iron deficiency and cannot be influenced by iron supplementation. While 'anaemia of prematurity' can be modified using recombinant human erythropoietin (q.v.) as long as the baby is also given at least 3 mg/kg of supplemental iron, it is doubtful whether such treatment is justified given the cost and the evidence that it may increase the risk of retinopathy of prematurity. The commonest cause of iron deficiency in the first year of life is iatrogenic because, if the cord is clamped early before the uterus contracts again after birth, this can deprive the baby of 20% of the elemental iron normally present in the body after an intervention-free delivery. Similarly, the commonest cause of neonatal anaemia is also iatrogenic – from doctors taking blood for laboratory analysis! Such babies should be offered a replacement transfusion: they do not respond to supplemental iron.

The fortification of artificial feeds with 0·6 mg iron/100 ml is enough to prevent iron deficiency in babies of normal birth weight and it is now reasonably clear, despite official advice to the contrary, that this is also enough for the preterm baby. Almost all the commonly used formula milks in current use contain at least as much iron as this (as outlined in the monograph on Milk Formulas) making the widespread practise of further supplementation quite unnecessary. There is rather more uncertainty as to how well the iron in most fortified infant cereal foods is absorbed. Wholegrain cereals and some tannins (as found in tea) bind iron and prevent absorption. The most easily assimilated form of iron is haem iron. Some vegetarian diets, therefore, may increase the risk of iron deficiency. Children on a poor diet often become anaemic during the second year of life, especially if they are given cows milk rather than a fortified formula, but randomised trials have yet to confirm observational studies (and animal studies) suggesting that iron deficiency at a critical time during the brain's growth can cause sustained psychomotor delay. Of equal concern is the finding that routine supplements during the first 3 years of life can actually *increase* mortality in an area where malaria is rife, and that it may be the babies who were not iron deficient who were placed most at risk by routine prophylaxis.

Breast fed babies weighing less than about 5 lb (2·3 kg) at birth are, however, at some risk of developing iron deficiency anaemia 2–3 months after birth, as a result of the rapid expansion of their circulating blood volume with growth, and these babies benefit from supplemental iron started within 4–6 weeks of birth. There is no good reason for starting supplemental iron before this because there is some doubt whether the gut absorbs iron in excess of immediate requirement, and some reason for believing that the iron binding protein, lactoferrin, present in milk (and particularly in breast milk), only inhibits bacterial growth when not saturated with iron. Some think that early supplementation of breast milk with iron might also unmask latent Vitamin E deficiency.

Assessment

A serum ferritin of less than 20 µg/l is considered diagnostic of iron deficiency in a 4 month old child, especially if the transferrin saturation is below 10%. A 10 µg/l 'cut off' can be used after 6 months. Anaemia in young children is very seldom due to iron deficiency, and most babies who are iron deficient are not anaemic. Send 1 ml of blood in a plain tube or EDTA tube to the Department of Haematology. An attempt was made to keep the serum ferritin level above 100 µg/l in some neonatal trials of erythropoietin use.

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Prophylaxis and treatment

Normal babies: Breast fed babies benefit from supplementation if no other source of iron is introduced into the diet by about 6 months. Term babies fed one of the standard, artificially fortified, neonatal milk formulae (q.v.) never require further supplementation.

Preterm babies: Iron deficiency anaemia can be avoided in babies fed ***breast*** milk who weigh less than 5 lb (2·3 kg) at birth by giving them a single daily dose of sodium feredetate (Sytron®). Prophylaxis is most logically started 6–8 weeks after birth (or, more simply, at discharge) and sustained until mixed feeding is established. The precise dose of Sytron necessary to meet the nutritional guideline is 0·4 ml/kg (2·2 mg/kg of elemental iron) once a day, but for most babies over 3 kg it is probably enough to tell the parents to give half a teaspoon (2·5ml) once a day. Although it is traditional to offer all preterm babies further supplemental iron after discharge, this advice is a "hang over" from the days when the powdered artificial milks used for infant feeding were not specially fortified. There is no good evidence that ***formula*** fed babies benefit from further supplementation after discharge (unless they are still on Osterprem®), and excess intake can have disadvantages.

Babies with anaemia at birth (Hb <120 g/l): Babies who have suffered *chronic* blood loss from feto-maternal bleeding or twin-to-twin transfusion benefit from supplemental iron once their initial deficit has been corrected by transfusion. Babies with anaemia due to *acute* blood loss at birth do not usually become iron deficient. Neither do babies with haemolytic anaemia.

Babies on parenteral nutrition: Babies unable to tolerate even partial enteral feeding by 3 months benefit from 100 micrograms/kg of iron a day IV (most conveniently given as iron chloride). Babies on erythropoietin (q.v.) also need IV supplementation if they can not be given oral iron.

Toxicity

Get the stomach emptied and organise prompt lavage if oral ingestion is suspected. Activated charcoal is of no value, but an attempt should be made to identify the amount ingested, and treatment started by giving 15 mg/kg of desferrioxamine mesilate (deferoxamine mesilate [pINNM]) per hour IV for 5 hours if the ingested dose is thought to exceed 30 mg/kg. No universally agreed treatment protocol exists and advice should be sought from the local Poisons Centre. Acute toxicity is likely if the serum iron level exceeds 90 µmol/l 4 hours after ingestion. A leukocytosis of over 15 x 10^9/l, or a blood glucose of over 8·3 mmol/l, also suggests serious toxicity. Early symptoms include diarrhoea and vomiting followed, after 12–48 hours, by lethargy, coma, convulsions, intestinal bleeding and multi-organ failure. Intestinal strictures may develop 2–5 weeks later.

Supply

It is best to choose a sugar-free preparation requiring no further dilution. Sodium feredetate (previously known as sodium ironedetate) is widely used in the UK. Each ml of the commercial elixir (Sytron) contains 5·5 mg of elemental iron (38 mg of sodium feredetate). 500 ml bottles cost £5, but smaller volumes can be dispensed on request. Ferrous fumarate is one alternative for those concerned that Sytron contains 96% ethanol. Each ml of the commercial syrup (Galfer®) contains 9 mg of elemental iron (28 mg of ferrous fumarate). Ferrous sulphate (still widely used in North America) is a second alternative – two widely used commercial formulations (Ironorm® and Fer-Gen-Sol®) come in dropper bottles containing 25 mg/ml of iron (~1 mg per drop). Parents can obtain all these similarly priced products from any community pharmacist without a doctor's prescription.

10 ml ampoules of iron chloride for IV use containing 1 mg (17·9 micromol) of iron are obtainable through the pharmacy from the Queens Medical Centre, Nottingham.

Vials containing 500 mg of desferrioxamine mesylate powder (costing £4·30) suitable for reconstitution with 5 ml of water for injection could be provided by the pharmacy on request.

References

See also the relevant Cochrane reviews ©

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