Iron status of preterm low birthweight infants and their response to oral iron

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Brozović, B., Burland, W. L., Simpson, K., and Lord, J. (1974). Archives of Disease in Childhood, 49, 386. Iron status of preterm low birthweight infants and their response to oral iron. The iron status of a group of preterm low birthweight infants, treated with oral iron, has been studied by measuring haemoglobin concentration, serum iron concentration, and total iron binding capacity (TIBC) at intervals from birth to 9 months. 47 infants born at an average gestational age of 34 weeks, with a mean birthweight of 1517 g, were investigated. They received 180 mg ferrous sulphate (= 36.3 mg Fe) daily from the fifth week and throughout the study. At 3 months of age most of the infants had low serum iron concentration and increased TIBC indicative of iron deficiency, and over half of them had iron deficiency anaemia (Hb <11 g/100 ml). At 6 and 9 months of age the mean Hb increased slightly, but mean serum iron concentrations remained low, and mean TIBC increased to over 500 μg/100 ml. It is not clear why the amount of iron, administered orally, was insufficient to prevent iron deficiency in almost all the infants, and iron deficiency anaemia in nearly half of the infants studied.

It has been well established that the ‘late’ anaemia, almost invariably found in a preterm low birthweight infant, is due to iron deficiency (Mackay, 1928). We have investigated the iron status of preterm low birthweight infants before and during treatment with oral iron, by measuring their Hb concentration, serum iron concentration, and total iron binding capacity. Together these parameters provide essentially the same information regarding iron deficiency as does its evaluation by means of iron staining of bone marrow aspirates (Bainton and Finch, 1964).

Material and methods

Forty-seven preterm low birthweight infants (28 males and 19 females) admitted at birth to the Special Care Baby Unit, Leicester General Hospital, were investigated. The average age was 34 weeks (range 29 to 37 weeks) and their mean birthweight was 1517 g (range 920 to 1870 g). The infants were not suffering from any disease and were born to mothers who were not anaemic during pregnancy. All were fed with the same brand of evaporated milk throughout the period of inpatient care. All received 1 mg vitamin K at birth and were prescribed paediatric mixture of ferrous sulphate BP, 180 mg/day, from the age of 5 weeks. Iron fortified cereals were introduced in the infants’ diet according to common practice. In addition, during the first month of life 17 randomly selected infants of those to be discussed in this paper received a total of 14 mg vitamin B₁₂ coenzyme and another 10 a total of 1.4 mg pteroylmonoglutamic acid. The administration schedules for pteroylmonoglutamic acid and vitamin B₁₂ coenzyme have been described in detail elsewhere (Burland, Simpson, and Lord, 1971; Lord, Simpson, and Burland, 1971).

The infants were bled on at least three occasions and most of them on six occasions: for the first time within 3 days of birth, then between the 17th and 21st day, during the fifth week of life, and at 3, 6, and 9 months. Venous blood samples were used for all the haematological determinations. The measurements of Hb concentration (cyanmethaemoglobin) was carried out as described by Dacie and Lewis (1968). In the absence of an

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established normal range of Hb concentration for preterm low birthweight infants, a concentration of 11 g/100 ml was taken to represent the lower limit of normal as for term infants (Committee on Nutrition of the American Academy of Pediatrics, 1969).

Serum iron concentration was measured by the automated micromethod (Garry and Owen, 1967), and unsaturated iron binding capacity of serum by a semi-automated method (Brozović and Copestake, 1969). From these two measurements total iron binding capacity of serum (TIBC) was calculated. Transferrin saturation represents the ratio between serum iron and TIBC expressed in per cent. As there is no generally accepted normal range for serum iron concentration and TIBC for infants, the normal range for serum iron (65 to 160 µg/100 ml), TIBC (290 to 410 µg/100 ml), and transferrin saturation (20 to 50%) for adults of both sexes was used for comparison. In this study a distinction between iron deficiency and iron deficiency anaemia has been made with respect to Hb concentration, which is normal in the former and reduced in the latter condition (Finch et al., 1968). It has been assumed that a low serum iron concentration, high TIBC, and low transferrin saturation indicate reduced or absent storage iron.

Results

All the infants were included into a single group because there was no significant difference in Hb concentration, serum iron concentration, and TIBC of serum between the infants treated with pteroylmonoglutamic acid or vitamin B₁₂ coenzyme and those who were untreated.

**Hb concentration.** There was a rapid fall of total Hb concentration from the mean of 16·8 g/100 ml at birth to the lowest mean of 9·7 g/100 ml at the age of one month (Fig. 1). Thereafter Hb increased to mean values of 10·1, 11·4, 11·5 g/100 ml at 3, 6, and 9 months, respectively.

**Serum iron concentration and iron binding capacity of serum.** The mean serum iron concentration increased from 78 µg/100 ml at birth to 105 µg/100 ml after 2 weeks of life. Thereafter, the mean serum iron concentration fell gradually to its lowest value (44 µg/100 ml) at 6 months, and increased only slightly (51 µg/100 ml) by 9 months of age.

The mean TIBC was 252 µg/100 ml at birth and increased only slightly during the first 5 weeks of life. The mean TIBC increased considerably to 492 µg/100 ml at 3 months and reached 537 and 539 µg/100 ml at 6 and 9 months of age, respectively.

The relation between serum iron and TIBC in individual infants is presented in Fig. 2. The area representing the 'normal range' is drawn from adult values and helps only in comparing changes in these two parameters observed at different times. In the majority of infants during the first 5 weeks of life the distribution of serum iron concentration and TIBC did not change. Serum iron concentration was in the range from 50 to 180 µg/100 ml, TIBC from 200 to 300 µg/100 ml, and transferrin saturation was between 20 and 50%. In sharp contrast, when they reached an age between 3 and 9 months, most of the infants had serum iron concentrations below 65 µg/100 ml and TIBC higher than 400 µg/100 ml, with transferrin saturation less than 20%.

Discussion

Hb concentration, serum iron, and TIBC can be considered for two distinct periods in the group of preterm low birthweight infants described above. These correspond to the periods of early and late anaemia of prematurity. During the first period of a month there was a marked and progressive fall in Hb without any significant change in serum iron and TIBC. The second period had become established by 3 months of age. During this second period almost all the preterm low birthweight infants had the haematological pattern of iron deficiency, and approximately half of them had iron deficiency anaemia. This was in spite of regular oral iron supplementation providing 36·3 mg elemental iron
daily. The described changes in preterm low birthweight infants treated with iron are essentially the same as those found in nontreated infants presented in a classical review of the anaemia of prematurity by Schulman (1959). The pattern of changes of serum iron concentration and TIBC in preterm low birthweight infants treated with iron is reported for the first time and it is similar to that found in term infants receiving iron-fortified diets (Smith and Hunter, 1970).

The results presented here suggest that iron absorption in preterm low birthweight infants receiving supplementation is not sufficient to provide the amount of iron required for erythropoiesis. At present the reason is unknown, but the following two observations from published reports provide a basis for speculation.

It has been reported that in adult patients with iron deficiency anaemia there is a two- to fourfold decrease in iron absorption one month after the initiation of treatment with iron, and even before Hb rises to the normal range (Norrby and Sölvell, 1970). It is possible that a similar reduction in iron absorption occurs in infants receiving iron supplements. Secondly, Halvorsen and Halvorsen (1973) found that in young rabbits the rate of iron release from plenteous iron stores was too slow to prevent the development of anaemia by the time they were 3 weeks old. If the mechanism of iron release from the tissues which store iron is at fault, then perhaps the release of iron from the intestinal mucosal cell may also be impaired. One or both of these two mechanisms may be responsible, at least in part, for an inadequate uptake of iron by the mucosal intestinal cell and/or its subsequent release to the circulation in preterm low birthweight infants treated with oral iron.

In conclusion, the provision of therapeutic doses of oral iron in preterm low birthweight infants does not prevent the development of iron deficiency and even iron deficiency anaemia. Further investigation into the absorption of iron by preterm low birthweight infants on oral iron supplements seems to be desirable.
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References


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