Cows' milk and anaemia in preterm infants

H L HALLIDAY, T R J LAPPIN AND G McCLURE

Departments of Child Health and Haematology, Queen's University of Belfast and Royal Maternity Hospital, Belfast

SUMMARY Introduction of pasteurised cows' milk to the diet of preterm infants before 36 weeks' post-natal age caused iron deficiency without anaemia. Cows' milk before 24 weeks was associated with iron deficiency and anaemia. The cause was either inadequate absorption or increased loss rather than reduced intake of iron.

Introduction of cows' milk to the diet of term infants after 2 months of age is associated with microcytic anaemia and low serum iron.¹ Term infants given cows' milk from 16 to 28 weeks, however, had more positive occult blood tests in their stools but no differences in haemoglobin, serum iron, total iron binding capacity, or transferrin saturation when compared with controls fed a formula milk.² Less information is available about the preterm infant or the timing of cows' milk feeding in relation to the development of anaemia. As part of a study of iron status of preterm infants during the first year of life³ we looked at the effect of cows' milk on concentrations of haemoglobin, transferrin saturation, and ferritin.

Patients and methods

Forty three preterm infants who were enrolled in a study of anaemia and iron status³ were retrospectively divided into three groups based on postnatal age at introduction of pasteurised cows' milk into the diet. Group I received cows' milk after 40 weeks (n=14), group II after 24 to 36 weeks (n=17), and group III before 24 weeks (n=12).

Haemoglobin concentration, transferrin saturation, and serum ferritin were measured as in a previous report.³ Iron and protein intake were calculated from dietary history. Iron deficiency was taken as a serum ferritin value of less than 12 ng/ml and anaemia as a haemoglobin concentration of less than 11 g/dl.⁴ Comparisons between the groups were made using the independent *t* test, Fisher's exact test, or Kruskal-Wallis test where appropriate. Serum ferritin, transferrin saturation, and iron intake were not normally distributed and differences between groups were analysed using the Kruskal-Wallis test.

Results

Babies in the three groups were very similar with regard to gestational age, sex distribution, social class of mother, and haematological status at birth (Table 1). Group I babies were lighter (mean birthweight 1740 g) than those in groups II (2070 g) and III (2080 g) ($P<0.05$).

Table 2 shows the haematological status at 36 and 54 weeks of age. At 36 weeks transferrin saturation was significantly lower in groups II and III compared with group I ($P<0.01$). Haemoglobin concentration was also lower at this age, but the differences were not significant. Group II babies had lower iron intake than groups I and III but the differences were not significant. Groups II and III had higher protein intake than group I ($P<0.05$).

At 54 weeks of age haemoglobin concentration was lower in groups II and III than group I, the difference being significant in group III ($P<0.05$). Serum ferritin was also significantly lower in group III than group I ($P<0.05$). There was a trend towards lower serum ferritin with earlier introduction of cows' milk (Table 2). Fifty eight per cent of babies in group III were iron deficient compared

Table 1 *Clinical characteristics and haematological status at birth*

	Group I (cows' milk >40 wks)	Group II (cows' milk 24-36 wks)	Group III (cows' milk <24 wks)
Number	14	17	12
Gestation (wks)			
Mean (SD)	32.1(2.8)	33.1(2.6)	33.8(2.0)
Birthweight (g)			
Mean (SD)	1740 [*] (420)	2070(450)	2080(530)
Boy:girl	6:8	10:7	6:6
Social class of mother			
No (%)			
I + II	2(14)	4(23)	3(25)
III	6(43)	8(47)	4(33)
IV + V	6(43)	5(29)	5(42)
Haematological status at birth			
Haemoglobin (g/dl)			
Mean (SD)	18.0(2.5)	18.2(2.2)	18.7(2.5)
Transferrin saturation (%) Median (range)	20(11-99)	40.5(12-80)	25(9-89)
Serum ferritin (ng/ml) Median (range)	267(65-410)	250(50-837)	262(132-492)

^{*} $P<0.05$.

Table 2 *Haematological status at 36 and 54 weeks of age*

	Group I (n=14)	Group II (n=17)	Group III (n=12)
36 weeks			
Haemoglobin (g/dl)			
Mean (SD)	12.6(0.9)	12.0(1.3)	11.9(1.5)
Sat. transferrin (%)			
Median (range)	27.5(14-38)	17(9-30)**	14(5-29)**
Serum ferritin (ng/ml)			
Median (range)	18(11-74)	19(4-88)	17(4-36)
Iron deficiency†			
No (%)	3(21)	4(23)	4(33)
Anaemia‡ No (%)	1(7)	2(12)	1(8)
Iron intake (mg/kg/day)			
Median (range)	2.45(1.3-4.7)	1.6(0.4-3.8)	2.25(0.4-8.7)
Protein intake (g/kg/day)			
Mean (SD)	3.5(1.1)	4.5** (0.9)	4.7* (1.8)
54 weeks			
Haemoglobin (g/dl)			
Mean (SD)	12.8(1.1)	11.8(1.7)	11.7* (1.4)
Transferrin saturation (%)			
Median (range)	23(9-45)	20(8-33)	14.5(8-38)
Serum ferritin (ng/ml)			
Median (range)	30.5(11-63)	21(2-63)	11(4-40)*
Iron deficiency† No (%)	1(7)	3(18)	7(58)***
Anaemia‡ No (%)	0	2(12)	3(25)
Iron intake (mg/kg/day)			
Median (range)	2.15(1.1-4.0)	1.5(0.6-3.5)	2.0(0.9-6.7)
Protein intake (mg/kg/day)			
Mean (SD)	4.8(1.2)	4.7(0.9)	4.3(1.0)

* P<0.05, ** P<0.01, *** P=0.015.

† Iron deficiency=serum ferritin <12 ng/ml⁴.‡ Anaemia=haemoglobin concentration <11g/dl⁴.

with 7% in group I (P=0.015, Fisher's exact test). Twenty five per cent of group III babies had anaemia. There were no significant differences in iron or protein intake at this time.

Discussion

Iron deficiency in term infants has been associated with early cows' milk feeding.^{1,4} The cause is uncertain but inadequate iron intake, reduced iron absorption, and increased iron loss in stools have all been proposed.

Wilson *et al.*⁵ by a radioisotope technique, have shown abnormal occult blood loss in 50% of babies fed cows' milk. Gross *et al.*⁶ have found that a low haemoglobin concentration is associated with higher protein intake, and protein sensitivity has been suggested to cause enteropathy with blood loss in the stools.^{1,5}

Our babies showed reduced transferrin saturation at 36 weeks of age if they had been given cows' milk either before 24 weeks or between 24 and 36 weeks. During this time these babies had higher protein intakes than babies receiving cows' milk after 40 weeks. Reduced iron intake did not seem to be important as the group receiving cows' milk earlier had similar intake to those fed cows' milk later. At 54 weeks, haemoglobin concentration and ferritin values were lower in the babies fed cows' milk before 24 weeks. That is, these babies showed iron deficiency and anaemia.⁴ Furthermore, the earlier the introduction of the cows' milk the greater the changes in iron status.

Our study did not determine the cause of this iron deficiency anaemia but we feel that it may be due to either inadequate absorption or increased losses of iron from the gastrointestinal tract. Mothers should be advised to delay introduction of cows' milk to the diet of the preterm infant until after 36 to 40 weeks of age. This is in line with current recommendations for the term infant.⁷

We thank Mrs Lynda Thompson for typing the manuscript, and Mr Chris Patterson for assistance with the statistical analyses.

References

- Woodruff CW, Wright SW, Wright RP. The role of fresh cow's milk in iron deficiency. II. Comparison of fresh cow's milk with a prepared formula. *Am J Dis Child* 1972;124:26-30.
- Fomon SJ, Zeigler EE, Nelson SE, Edmonds BB. Cow milk feeding in infancy: gastrointestinal blood loss and iron nutritional status. *J Pediatr* 1981;98:540-5.
- Halliday HL, Lappin TRJ, McClure G. Iron status of the preterm infant during the first year of life. *Biol Neonate* 1984;45:228-35.
- Sadowitz RD, Oski FA. Iron status and infant feeding practices in an urban ambulatory centre. *Pediatrics* 1983;72:33-6.
- Wilson JF, Lahey ME, Heiner DC. Studies on iron metabolism. V. Further observations on cow's milk-induced gastrointestinal bleeding in infants with iron-deficiency anemia. *J Pediatr* 1974;84:335-44.
- Gross S. The relationship between milk protein and iron content on hematologic values in infancy. *J Pediatr* 1968;73:521-30.
- Department of Health and Social Security. *Present day practice in infant feeding*. London: HMSO, 1974.

Correspondence to Dr H Halliday, Nuffield Department of Child Health, Queens University of Belfast, Belfast BT12 6BJ.

Received 6 July 1984