Plasma Calcium and Magnesium in Newborn Babies

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Harvey, D. R., Cooper, L. V., and Stevens, J. F. (1970). *Archives of Disease in Childhood*, 45, 506. **Plasma calcium and magnesium in newborn babies.** Normal values for plasma calcium and magnesium levels during the first week of life, in breast- and bottle-fed babies, have been determined. It has been shown on the sixth day that plasma levels of calcium, magnesium, and protein are all significantly lower in bottle-fed babies than in breast-fed babies, while the reverse is true of the plasma inorganic phosphorus.

The normal babies have been compared with 30 babies who had convulsions, beginning towards the end of the first week of life. In only six of the babies was the plasma calcium outside our normal range and only four had abnormally low magnesium levels. As so many of these babies had calcium and magnesium levels within the normal range it must seriously be questioned whether hypocalcaemia or hypomagnesaemia could have been the sole cause of the convulsions.

In order to establish normal values for the first week of life, calcium and magnesium have been measured in samples of plasma for normal infants who were either breast- or bottle-fed.

Convulsions beginning on the 5th to 8th days of life are often attributed to hypocalcaemia (Bakwin, 1937) or hypomagnesaemia (Davis, Harvey, and Yu, 1965). A group of babies with convulsions at the end of the first week has been compared with the normal infants.

Material and Methods

Two maternity units were used for this survey. The first series was conducted at Hammersmith Hospital from June to September 1967; the blood was collected immediately before the 9 a.m. feed from normal babies on the first seven days of life. Samples obtained from 85 babies were not consecutive though most babies were bled more than once. Heel-prick samples were obtained without squeezing and were centrifuged and separated immediately; any grossly haemolysed samples were discarded. Heparin was used as an anticoagulant. The babies' weights ranged from 2300 to 4460 g., and their gestational ages from 38 to 42 weeks. They were either entirely breast fed, apart from an initial feed of glucose and water, or were fed on an evaporated milk formula ('Carnation Milk'). This was diluted 1 part with $2\frac{1}{2}$ parts of water, and given in volumes of 90–160 ml./kg. per 24 hours on the second day, increasing gradually to 140–160 ml./kg. per 24 hours on the sixth day. In this dilution the milk contained: phosphorus 67 mg./100 ml.; calcium 76 mg./100 ml., and vitamin D 28 I.U./100 ml.

The second series was conducted at Hillingdon Hospital from April to September 1968. Normal babies of birthweight 2400 to 4465 g., and gestational age 37 to 42 weeks were bled at 9 a.m. on the sixth day of life. Blood was collected and processed in the same way as in the first series, and in addition arterialized capillary blood was taken into sealed heparinized capillary tubes for blood gas analysis. In this series babies were either breast fed, apart from a supplement of 15–45 ml. of half-cream dried milk formula ('Cow and Gate') on each of the first two nights, or were entirely bottle fed on the same dried milk formula. Half-cream milk was used for the first four days and full-cream thereafter, in amounts increasing from 15–30 ml./feed on the first day of life to 90–105 ml./feed on the sixth day. This milk contained: phosphorus 66 mg./100 ml.; calcium 49 mg./100 ml., and vitamin D 37 I.U./100 ml.

In all cases the mother's permission was obtained before blood was taken.

All the babies at the Hammersmith Hospital, who had convulsions beginning on the 5th to 8th days of life between October 1965 and November 1968, had their plasma calcium, magnesium, and phosphorus levels measured. There were 30 of these babies and they have been compared with the normals. Blood was taken from these babies in the same way as the normals before any treatment was given. In addition, the usual investigations for neonatal convulsions were performed, including a lumbar puncture in all cases. The convulsions were, as usual in the newborn, of the multifocal type described by Harris and Tizard (1960) and seen with hypocalcaemia by Keen (1969).

Plasma calcium and magnesium were estimated on an EEL atomic absorption spectrophotometer. The method used was a modification of that developed by Willis (1960) using EDTA solution as a diluent. This

TABLE I
Series I: Plasma Calcium and Magnesium Levels in Normal Babies

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Calcium (mg./100 ml.)							
Breast-fed	Mean Range No.	7.5 5.2-9.8 9	9.3 7.2-11.2 9	8.6 7.2-10.2 10	8.3 2.4-12.6 8	8.6 6.4-10.2 9	8.9 6.8-11.4 6
Bottle-fed	Mean Range No.	7.2 5.8-8.6 9	8.6 7.4-9.8 9	8.0 5.8-11.4 10	7.4 6.0-8.4 10	7.6 6.4-9.0 11	8.6 6.0-11.4 9
Total	Mean Range No.	9.1 5.8-12.6 16	7.6 5.2-9.8 19	7.6 7.2-11.2 18	8.6 5.8-11.4 20	8.0 2.4-12.6 18	8.4 6.4-10.2 20
Magnesium (mg./100 ml.)							
Breast-fed	Mean Range No.	1.20 0.9-1.8 9	1.40 0.9-1.7 9	1.30 1.1-1.6 10	1.10 0.42-1.86 8	1.60 1.1-1.71 9	1.36 1.1-1.6 6
Bottle-fed	Mean Range No.	1.30 1.1-1.5 9	1.30 0.7-1.6 9	1.20 1.0-1.4 10	1.00 1.0-1.32 10	1.10 0.9-1.4 11	1.15 0.8-1.8 9
Total	Mean Range No.	1.30 0.9-1.6 16	1.20 0.9-1.8 19	1.40 0.7-1.7 18	1.40 1.0-1.6 20	1.06 0.42-1.86 18	1.37 0.8-1.8 15

Calcium 1 mEq/l. = 2 mg./100 ml. Magnesium 1 mEq/l. = 1.2 mg./100 ml. No. = number of samples.

method has been shown in our laboratory to give results comparable to those obtained by flame photometry. Plasma inorganic phosphorus and protein were estimated by ultra-micro-techniques (Stevens, 1965). The blood pH, PCO₂, and standard bicarbonate were measured by the Astrup technique (Siggaard Andersen *et al.*, 1960).

Results

Normal babies. The results from the first series are shown in Table I.

The plasma calcium level is variable; dropping on the second day, rising on the third day, and falling again on the fourth and fifth days. The only daily variations which are statistically significant are those between days 1 and 2, 2 and 3, 3 and 4, and 2

and 7. On all days after breast feeding had been established the breast-fed babies had higher plasma calcium levels than the bottle-fed babies. However, when subdivided according to the type of feeding, the numbers were too small and the range too wide to permit a valid statistical analysis. For this reason we have expressed the results as the mean and range for each day. The magnesium levels were also lower in the bottle-fed babies towards the end of the first week.

The differences between the breast-fed and bottle-fed babies appeared to be maximal on the sixth day, and it was for this reason that we undertook the second series. Table II shows the results obtained; the number of babies in each group varies slightly

TABLE II

Plasma Calcium, Magnesium, Inorganic Phosphate, and Total Protein on 6th Day of Life in Normal Babies.

Type of Feeding		Calcium (mg./100 ml.)	Magnesium (mg./100 ml.)	Inorganic Phosphate (mg./100 ml.)	Total Protein (g./100 ml.)
Bottle-fed	Mean Standard deviation Range No.	8.8 1.9 3.8-11.2 24	1.40 0.25 0.85-1.90 26	8.25 3.35 4.60-21.00 25	5.05 0.55 3.40-5.80 23
Breast-fed	Mean Standard deviation Range No.	10.1 1.2 8.0-12.4 24	1.70 0.20 1.20-2.05 29	6.25 1.20 4.10-9.80 27	5.70 0.90 4.30-8.30 30
p		0.01-0.005	<0.001	0.01-0.005	0.005-0.001

p was calculated using a 2-tailed significance test for difference between the means. No. = number of samples.

because in a few cases there was insufficient blood for all estimations. Each group of figures is normally distributed on an arithmetic scale, and therefore direct statistical analysis is justified. Using a two-tailed significance test, the plasma calcium, magnesium, and protein levels were all significantly lower ($p < 0.05$) in the bottle-fed babies than in the breast-fed babies. The reverse was true for the plasma inorganic phosphorus.

No significant differences were shown between male and female babies. There were also no significant differences in pH, PCO_2 , and standard bicarbonate between the breast- and bottle-fed groups (mean $\pm$ SD, breast-fed babies pH 7.35 ± 0.04 , PCO_2 (mm. Hg) 40.63 ± 4.30 , standard bicarbonate (mEq/l.) 22.07 ± 1.68 ; bottle-fed babies pH 7.34 ± 0.04 , PCO_2 42.25 ± 11.34 , standard bicarbonate 22.58 ± 3.77).

Table III shows the values of the correlation coefficient (r). The probability levels indicate that calcium and magnesium, magnesium and phosphorus, magnesium and protein, calcium and phosphorus are all significantly related. Protein was not significantly related with either calcium or phosphorus.

TABLE III

Series 2: Comparison of Values Obtained on 6th Day of Life in Bottle- and Breast-fed Babies

	No. of Samples	Correlation Coefficient r	p
Calcium-magnesium	47	+0.469	<0.001
Calcium-phosphate	54	-0.335	0.05-0.02
Magnesium-phosphate	52	-0.316	0.05-0.01
Phosphate-protein	52	+0.148	>0.1
Magnesium-protein	54	-0.340	0.05-0.01
Calcium-protein	48	-0.265	0.1-0.05

Babies with convulsions. The values for these babies are compared with the normal range in the Fig. As can be seen, the plasma phosphorus levels are evenly distributed within the range for normal babies. There are only six cases in which the calcium falls outside the normal range ($> 2SD$ below the mean), but the mean plasma calcium level for the convulsing babies is 6.3 mg./100 ml., a significant difference ($p < 0.001$) from the mean of 8.4 mg./100 ml. for normal babies of the same age. Similarly, in only four cases was the magnesium level outside the normal range, though the mean was 1.15 mg./100 ml. compared to 1.31 mg./100 ml. for the normal babies ($p = 0.01$ to 0.02).

No other cause for convulsions was found in any of the 30 babies. One baby who had a plasma calcium of 6 mg./100 ml. and magnesium 1.3 mg./

FIG.—Lowest levels of calcium recorded with accompanying plasma inorganic phosphorus and magnesium levels in babies having fits on the 5th–8th day of life (●), compared with the mean $\pm 2SD$ of normal babies of the same age.

100 ml. when he first had a convulsion, developed meningitis two days later. In all other cases the cerebrospinal fluid was normal.

Discussion

The pattern of the plasma calcium values during the neonatal period—a fall in the first 48 hours, a rise, and then another fall at the end of the first week—has been reported by other authors (Todd, Chuinard, and Wood, 1939; Graham, Barness, and György 1953; Gittleman, Pincus, and Schmertzler, 1964; Acharya and Payne, 1965). Cow's milk is known to produce lower calcium levels (Graham *et al.*, 1953; Oppé and Redstone, 1968), as does vitamin D (Gittleman *et al.*, 1964). However, there has been no real agreement on the actual level of calcium; our figures are lower than most of those reported, though Spivek (1956) had a group of 31 babies with a mean serum calcium of 7.4 mg./100 ml. on the fifth day. The plasma magnesium levels are also lower than other series reported (Anast, 1964; Bajpai *et al.*, 1966; Kobayashi, 1967), though they were using different techniques.

The real importance of these figures lies in the

comparison with the babies who had convulsions. For over three decades 8 mg./100 ml. has generally been accepted as the lower limit of normal for the plasma calcium in the newborn (Bakwin, 1937), but we consider this figure to be unrealistically high. The subject of hypocalcaemia and neonatal fits has been recently reviewed by Keen (1969) who accepted a figure of 7.5 mg./100 ml. as normal. Only 6 of our 30 babies had values outside our normal range. One could doubt the relevance of the low plasma calcium to the convulsions except that the mean calcium for the group was significantly lower than the normal mean for this age. Presumably some other factor must determine whether a baby will have a convulsion at a given plasma calcium or magnesium level. It is possible that the ionized calcium level is more important than the total calcium which we have measured.

The apparent increase in the incidence of convulsions attributed to hypocalcaemia may have been due to the comparatively large volumes of milk which the babies in our wards were receiving at this time (Baum, Cooper, and Davies, 1968). We consider our present regimen of 30 ml./kg. per 24 hours on the first two days of life, gradually increasing to 150 ml./kg. per 24 hours by the end of the first week, of evaporated milk diluted 1 part plus $2\frac{1}{2}$ parts of water, to be more suitable for full-term normal weight-for-dates babies.

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