

## Early sodium intake and later blood pressure in preterm infants

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**SUMMARY** The relation between early salt intake and later hypertension is debated. As part of a larger feeding study, 347 preterm infants were randomly assigned to receive early diets differing grossly in sodium content. Feeding a high sodium preterm formula in the neonatal period did not influence arterial blood pressure at 18 months (corrected) age.

Whether the level of salt intake in early life influences later blood pressure is uncertain, yet numerous authorities recommend avoidance of high sodium intake in infancy.<sup>1-4</sup> Most information in this area is epidemiological and inconclusive. Controlled, prospective data are scanty and conflicting.<sup>2-3</sup> In this study, we recorded blood pressure at 18 months post-term in 347 preterm infants who had been assigned randomly, for the early postpartum weeks, to diets differing significantly in sodium content.

### Subjects and methods

In a larger five centre study,<sup>5</sup> infants were assigned randomly to the following diets: in centres 1-3, banked donor breast milk v a preterm formula ('Osterprem,' Farley Health Products Ltd) as sole diets (trial 1) or as supplements to expressed maternal breast milk (trial 2); and in centres 4 and 5, standard 'term' formula ('Osterfeed,' Farley Health Products Ltd) v the preterm formula as sole diets (trial 3) or supplements to expressed maternal breast milk (trial 4). In trials 2 and 4, mothers provided a median of 46% of their infants' feed volume as expressed maternal breast milk. Mean (SE) sodium contents of the diets were: banked milk, 7.2 (0.1) mmol/l (averaged over hospital stay); standard formula, 8.3 mmol/l; and preterm formula, 19.6 mmol/l. The variable contribution to sodium intake from expressed maternal breast milk for infants in trials 2 and 4 was measured in 1776, 24 hour milk collections (overall mean (SE) sodium content, 11.0 (0.15) mmol/l). Additional sodium received enterally was recorded daily. There was no difference between feed groups in sodium intake

administered intravenously to sick infants before attaining full enteral feeds.

Infants remained on the assigned diets until they reached 2000 g or were discharged. Postdischarge feeding regimes (standard formula or breast feeding) did not differ between randomised feed groups. At 18 months of age, corrected for prematurity, systolic and diastolic blood pressures were recorded with a conventional sphygonomanometer by a cuff with integrated bladder and size appropriate to the infant's weight and age.

### Results

As there was no difference in blood pressure between infants fed donor breast milk or standard formula, data were combined to compare randomly: infants fed 'low sodium' donor milk or standard formula v 'high sodium' preterm formula, as sole diets (study 1; trials 1 and 3 above, combined) or in conjunction with expressed maternal breast milk (study 2; trials 2 plus 4).

In study 1, the low sodium group achieved, on full feeds, a mean (SE) sodium intake of 1.8 (0.06) mmol/kg/day compared with 3.6 (0.07) mmol/kg/day in the high sodium group ( $p < 0.0001$ , see table). In study 2, corresponding intakes were 1.8 (0.08) and 2.8 (0.07) mmol/kg/day ( $p < 0.0001$ ). Infants on the preterm formula took longer to attain full enteral feeds, but spent less time in hospital and therefore on the assigned diet (see table).

No group differences were found in systolic or diastolic blood pressure at 18 months in either study (see table). This was confirmed in a subgroup of 87 infants under 1200 g birth weight, despite the longer period (mean 60 days) on the diet allocated.

A small trend to higher blood pressure in boys than in girls—systolic; 97.9 (0.7) v 96.2 (0.7) mm Hg and diastolic 66.4 (0.6) v 64.9 (0.6) mm Hg—was not significant.

### Discussion

Sodium content in available preterm infant formulas varies greatly, though in most products it is substantially higher than in standard formulas or breast milk. While these special feeds have been designed

Table Effect of early diet on blood pressure at 18 months (corrected) age in two randomised studies. Also shown are the sodium intakes on full enteral feeds and details of the study population in each feed group

	Study 1*		Study 2 <sup>‡</sup>	
	Banked breast milk/term formula (n=56)	'High sodium' preterm formula (n=54)	Banked breast milk/term formula + expressed maternal breast milk (n=116)	'High sodium' preterm formula + expressed maternal breast milk (n=121)
Mean (SE) sodium intake mmol/kg/day	1.8 (0.06)	3.6 (0.04)	1.8 (0.08)	2.8 (0.07)
Mean (SE) gestation (weeks)	31 (0.4)	31 (0.3)	31 (0.3)	31 (0.2)
Mean (SE) birth weight (g)	1373 (40)	1408 (36)	1400 (28)	1405 (25)
Sex M:F	26/30	24/30	61/55	67/54
Median days (quartiles)				
To full enteral feeds	7 (6, 11)	9 (7, 13)	7 (5, 10)	8 (6, 10)
On assigned diet	37 (22, 50)	27 (18, 38)	30 (21, 50)	27 (18, 39)
Mean (SE) blood pressure at 18 months (mm Hg)				
Systolic	97.1 (1.3)	96.6 (1.3)	97.8 (0.9)	96.6 (0.9)
Diastolic	65.4 (1.1)	66.1 (0.8)	65.8 (0.7)	65.5 (0.7)

\*Study 1 compares 'low sodium' diets (banked breast milk or standard 'term' formula) with a 'high sodium' preterm formula. †Study 2 compares banked breast milk or standard term formula with 'high sodium' preterm formula as supplements to expressed maternal breast milk.

to meet high sodium requirements of preterm neonates, this requirement falls postnatally. Thus sodium provided in preterm formulas represents a compromise, and many babies may receive unnecessarily high intakes during their later weeks in hospital. Our analysis was prompted by the increasing use of preterm formulas and concern that high intakes of salt may 'imprint' or 'programme' future blood pressure. Furthermore, we considered that preterm infants might prove more sensitive than term infants to early dietary 'programming'.

We found, however, no effect of early diet on blood pressure at 18 months (corrected) age. The intakes of sodium compared were less extreme than in the randomised study on full term infants of Whitten and Stewart, who also found no effect of early salt on later blood pressure,<sup>2</sup> though the intake in those fed exclusively on preterm formula in our study was higher than recommended for early infancy.<sup>4</sup> The diets we used differed in other respects than their sodium content<sup>5</sup>; these differences would have enhanced further the difference in renal solute loading. While we recognise that 18 months post-term is still early to examine a dietary effect on blood pressure, 'tracking' for blood pressure has been observed in the first postnatal year.<sup>6</sup>

In the short term we have not seen an increase in clinical oedema or hypernatraemia in infants fed on a preterm formula providing 3.6 mmol of sodium per kg each day (unpublished data). In this study

our follow up data, obtained thus far only to 18 months, do not support the view that high sodium preterm formulas cause a later rise of blood pressure, or the more general thesis that a high salt intake in early infancy has an adverse imprinting effect on arterial pressure. Nevertheless, our continued follow up of this cohort into adulthood will be important in the further exploration of this area.

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