ORIGINAL ARTICLE

An observational study to evaluate micronutrient status during enteral feeding

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Background: There are few data on the optimal micronutrient composition of paediatric enteral feeds. The recent European Directive on Foods for Special Medical Purposes (1999/21/EC) did not distinguish between the composition of adult and paediatric feeds.
Aims: To evaluate, in an open, observational study, the long term nutritional biochemistry of 12 children aged 1–6 years and/or 8–20 kg.
Methods: The children were receiving at least 50% of their estimated average requirement (EAR) for energy from paediatric enteral formulae: 1.0 kcal/ml (Nutrison Paediatric Standard) or 1.5 kcal/ml (Nutrison Paediatric Energy Plus). Venous blood samples for trace elements, vitamins, and minerals were taken at study entry and six months later. Parents kept three day food and feed records every month.
Results: Despite a median energy intake of only 75% EAR (range 52–158%), 67% (n = 8) achieved their reference nutrient intake (RNI) for all micronutrients. No significant micronutrient deficiencies were seen on blood analysis after six months. Eighty three per cent (n = 10) had vitamin B_{12} and 92% (n = 11) had copper intake >150% RNI. Fifty eight per cent (n = 7) had high plasma B_{12} (>733 µmol/l) and 75% (n = 9) had high serum copper (>22 µmol/l) concentrations.
Conclusions: Children without excess losses maintain adequate micronutrient status on long term enteral feeding. Subjects had high blood concentrations of vitamin B_{12} and copper, and had high dietary intakes of these micronutrients. We suggest that the maximum nutrient guidelines for paediatric enteral feeds should be more clearly defined.

Increasingly, home enteral nutritional support is used for children with chronic illness.[1] As a consequence, the number of specialised paediatric formulae has rapidly expanded. Unfortunately there are no data on the optimal micronutrient composition of enteral feeds designed for young children. Neither are there comprehensive data available on the vitamin and trace element status of children on long term enteral feeding.

Historically, the micronutrient composition of paediatric enteral feeds has been based on the 1991 Dietary Reference Value report,[2] and the recommendations of the 1988 joint working party of the Paediatric Group and the Parenteral and Enteral Nutrition Group of the BDA.[3] More recently feed composition has been stipulated by the EU Commission Directive on Dietary Foods for Special Medical Purposes.[4] These directives provide recommendations for minimum and maximum values for vitamins, minerals, and trace elements in any nutritionally complete feed other than infant formulae. However, with the exception of calcium and vitamin D, they do not distinguish between adult and paediatric feeds.

In practice, it is important that paediatric enteral feeds are formulated so that full micronutrient requirements are met when the volume of feed supplies an appropriate energy intake. However, for many children enteral feeding is not intended to meet their entire energy requirements, but is provided as a supplementary overnight feed only. Although these children eat in the daytime, the quality and quantity of their diet is usually poor, so they are often reliant on their enteral feed to supply a major percentage of their micronutrient requirements.

There is little information available on the bioavailability of vitamins, minerals, and trace elements in paediatric feeds, and there is substantial variation in the efficiency with which micronutrients are absorbed and utilised within the body.[2 5] Furthermore, it is recognised that there is deterioration in the vitamin content of feeds throughout their shelf life. For these reasons it may be considered advantageous for enteral feeds to provide generous quantities of micronutrients that remain within the recommended guidelines, but more than adequately meet estimated nutritional requirements when they are used as a sole source of nutrition.

With so little available information on the optimum nutrient profile of feeds, it is possible that existing formulae may contain inappropriate amounts of micronutrients. It is therefore important to establish the biochemical micronutrient status of young children receiving existing enteral feeds. In an open, observational study we evaluated the micronutrient status of young children aged 1–6 years (or weighing 8–20 kg), receiving standard paediatric feeds to establish whether the micronutrient content of the feeds is appropriate.

SUBJECTS

Inclusion criteria

Subjects were aged 1–6 years or weighed 8–20 kg, and they were expected to need nutritional support for a minimum of six months. They were all receiving at least 50% of their estimated average requirement for energy (DOH, 1991) from either Nutrison Paediatric Standard (Nutricia) or Nutrison Paediatric Energy Plus (Nutricia). Nutrison Paediatric Standard (NPS) and Nutrison Paediatric Energy Plus (NPEP) are ready to use, sterile enteral feeding products aimed specifically at children aged 1–6 years or weighing 8–20 kg. They provide 1.0 kcal/ml and 1.5 kcal/ml respectively but are formulated to have the same micronutrient composition per 100 kcal.

Abbreviations: EAR, estimated average requirement; NPEP, Nutrison Paediatric Energy Plus; NPS, Nutrison Paediatric Standard; RNI, reference nutrient intake

Table 1 Nutrient intakes

Nutrient	Median daily intake from enteral feed (% RNI)	Median daily intake from oral food and drink (% RNI)	Median total daily intake (% RNI)	Range (% RNI)
Energy	62	18	75	52–158
Protein	118	47	166	70–261
Vitamin A	112	21	137	82–264
Vitamin B_1	96	22	117	83–215
Vitamin B_2	108	33	142	76–245
Vitamin C	127	23	152	101–300
Vitamin B_6	97	26	117	76–218
Vitamin B_{12}	219	61	280	146–470
Folic acid	108	22	133	62–240
Iron	110	15	126	74–271
Calcium	112	33	143	78–281
Phosphorus	112	48	161	80–251
Magnesium	92	26	117	47–201
Zinc	92	17	109	75–208
Selenium	117	8	127	68–259
Copper	146	20	171	108–326

Exclusion criteria

Children who were not expected to require enteral feeding for six months or who were receiving additional vitamin, mineral, or trace element supplements were excluded from the study.

METHODS

Dietary assessments

A three day prospective food diary was kept by the parents or carers of each child at recruitment and at monthly intervals. Details of both enteral feed volume received (ml/day) and oral food and drink intake were recorded. Each month dietary intake was recorded over three different days to allow for any variations in dietary intake that may have occurred as a result of differing weekday and weekend patterns. Data were analysed using the Microdiet Software based on McCance and Widdowson's "The composition of foods", version 5, with supplementary data from food manufacturers. Each three day food record was analysed individually for energy, protein, and micronutrient intake and mean nutrient intake data was calculated for each child. Total nutrient intakes were calculated as well as the individual contributions from the enteral feed and oral food and drink.

Anthropometry

At study entry and after six months of enteral feeding, weight, height, and mid upper arm circumference were measured. Weights were recorded to the nearest 0.01 kg on digital scales. Standing height measurements were recorded to the nearest 0.1 cm using a stadiometer. The mean of three mid upper arm circumference measurements was recorded to the nearest 0.1 cm.

Venous blood samples

Venous blood specimens were collected at entry to the study and after six months of feeding. These were analysed for thiamin, riboflavin, folic acid, vitamin D, vitamin C, vitamin E, vitamin B_6, vitamin B_{12}, vitamin A, calcium, phosphorus, magnesium, zinc, selenium, copper, iron, ferritin, and albumin. The analyses were undertaken using the same or similar methods as those used in the National Dietary and Nutrition Survey.[6]

RESULTS

Subjects

Twenty four children were recruited (14 girls, 10 boys; mean age 5.2 years, range 1.0–11.75) to the study. Seven children were given NPS and 17 were given NPEP.

Twelve of the subjects recruited to the study were withdrawn. Five children were receiving less than 50% EAR for energy from their enteral feed, two were changed to a different feed, four refused the final blood sample, and one died following cardiac surgery.

Analysis of the results is therefore based on the remaining 12 subjects (five girls, seven boys; mean age 4.9 years, range 2.4–10) who completed the study. The diagnoses were as follows: developmental delay (n = 5), organ transplant (n = 3), intestinal dysmotility (n = 1), chronic food refusal and failure to thrive (n = 1), tracheo-oesophageal fistula with oesophageal atresia (n = 1), and Schwachman syndrome (n = 1). Three children were receiving NPS and nine were receiving NPEP. Although the subjects were studied for six months, 93% (n = 11) had been receiving enteral feeding with NPS or NPEP before the study. The median length of feeding before the study was 22.5 months (range 0–81).

Dietary intakes

The energy intake from oral food and drink was poor, with a median energy intake of only 18% (range 0–32%) of the EAR

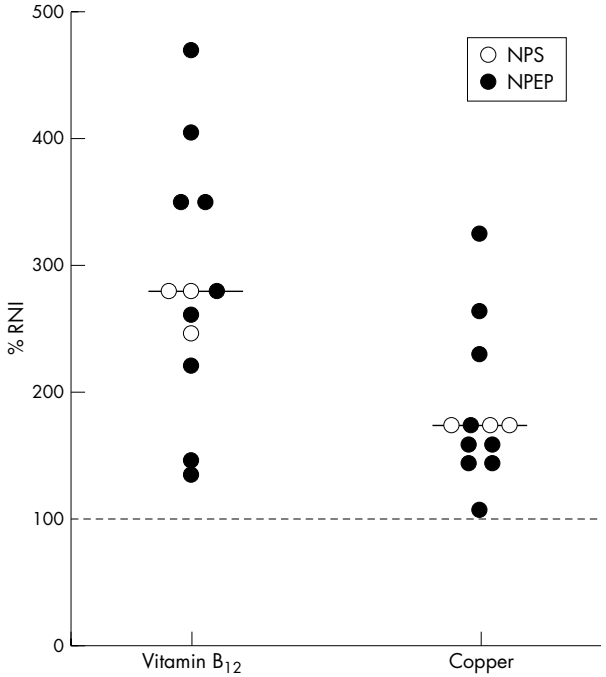

Figure 1 Vitamin B_{12} and copper intake as a percentage of RNI.[2]

Table 2 Plasma biochemistry

Nutrient	Start		6 months		Reference range
	Median plasma concentration for subjects	Range of plasma concentrations for subjects	Median plasma concentration for subjects	Range of plasma concentrations for subjects	
Vitamin B_1 (transketolase activation)	1.06 (n=10)	1–1.17	1.08 (n=7)	1.02–1.3	<1.25
Vitamin B_2 (glutathione reductase activation)	1.27 (n=10)	1.15–1.46	1.26 (n=10)	1.15–1.31	<1.3
Folate (nmol/l)	22.35	10.9–247	22.5	12.3–197	8–27
Red cell folate (nmol/l)	433	276–3905	485	157–2354	345–2030
Vitamin D (nmol/l)	85.5	77.5–120.6	90.3	45–139	25–90
Vitamin C (µmol/l)	51.6	24–78	52	22–78	11–80
Vitamin E (µmol/l)	20.5	14.8–32.4	20.5	14.6–33.6	10–21
Vitamin A (µmol/l)	1.13	0.5–3.2	1.15	0.54–3.2	0.7–2.0
Vitamin B_6 (AST stimulation)	1.75 (n=10)	1.3–2.03	1.61 (n=10)	1.35–2.0	<1.8
Vitamin B_{12} (pmol/l)	710	124–1915	782	136–1478	118–733
Calcium (mmol/l)	2.48	2.03–2.61	2.38	2.16–2.51	2.15–2.65
Phosphorus (mmol/l)	1.52	0.9–2.01	1.62	1.34–1.74	1.30–1.8
Magnesium (mmol/l)	0.86	0.6–0.95	0.83	0.62–0.92	0.6–1.0
Zinc (µmol/l)	14.5	12.7–23.6	15.2	12.7–19.7	10.7–23
Copper (µmol/l)	26	13.4–36.4	24.8	14.2–39.7	11–22
Glutathione peroxidase activity (selenium)	37	28.3–56.8	36 (n=11)	24.2–57.5	12–50
Iron (µmol/l)	12 (n=10)	7–23.1	13.6 (n=10)	6.7–22.3	8–31
TIBC (µmol/l)	59.8	32.1–72.8	56.4	20.0–76.7	45–81
Ferritin (µg/l)	19.5	10.3–256	35	10.4–97	12–200
Albumin (g/dl)	39.1	28.7–49.8	38	25.1–50.6	30–50

(DOH, 1991). The median energy intake from enteral feed was 62% of the EAR. All subjects therefore received the highest percentage of their dietary micronutrients from their enteral feed. One subject received additional supplements of folic acid, but the other subjects did not receive additional vitamin, mineral, or trace element supplements before or during the study period. None of the subjects were taking medications likely to interfere with micronutrient absorption or metabolism.

Table 1 summarises the results of the dietary assessments. Despite a total median energy intake of only 75% EAR (range 52–158%), the median total intake of all micronutrients exceeded the reference nutrient intake (RNI, range 109–280%). Sixty seven per cent of subjects (n = 8) achieved their RNI for all micronutrients; 100% of subjects (n = 12) met the RNI for vitamin C, vitamin B_{12} and copper. Intakes of iron, selenium, zinc, calcium, phosphorus, magnesium, folic acid, thiamin, riboflavin, and vitamin B_6 were below the RNI between 8% (n = 1) and 33% of subjects (n = 4). Intakes of micronutrients below the RNI were seen in the four children with the lowest daily energy intakes (range 52–69% of the EAR), but all intakes were above the lower reference nutrient intake.[1]

The intakes of some micronutrients were particularly high (fig 1). The total median daily intake of copper was 171% of the RNI (range 108–326%), with a median daily copper intake from oral food and drink of only 20% of the RNI (range 0–69%). The total median daily intake of vitamin B_{12} was 280% of the RNI (range 146–470%), with a median daily vitamin B_{12} intake from oral food and drink of 61% of the RNI (range 0–150%).

Anthropometry

The median weight z score at recruitment was −1.7 (range −2.4 to 0.8). Ninety three per cent subjects (n = 11) gained weight after six months of enteral feeds with one child maintaining weight. The median weight z score after six months of enteral feeding was −1.1 (range −2.1 to 2.0), with a median change in weight z score of +0.3 (range 0 to 1.3).

Height was measured in 75% subjects (n = 9). Three subjects could not be measured because of severe contractures and scoliosis. The median height z score at recruitment was −1.3 (range −3.2 to 1.2). Eighty nine per cent (n = 8) showed an increase in height, with a median z score after six months of feeding of −0.8 (range −2.9 to 1.2). The median change in height z score was + 0.4 (range 0 to 0.9). The median weight for height z score change (n = 8) was +0.35 (range −0.33 to 1.93). The median change in z score (n = 11) after six months of feeding was +0.44 (range −0.87 to 1.28).

Plasma biochemistry

The median plasma or serum concentrations of micronutrients analysed were within the normal range, both at recruitment to the study and after six months of enteral feeding. The analyses did not suggest deficiencies in selenium, copper, magnesium, calcium, phosphorus, and vitamins D, E, and C in any of the children studied (table 2). The venous samples taken after six months of feeding suggested deficiencies in some of the subjects: riboflavin (n = 2), folate (n = 3),

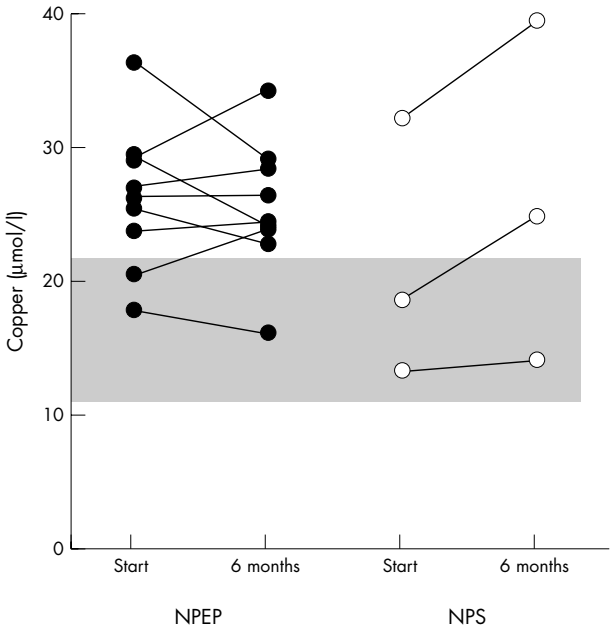

Figure 2 Serum copper concentrations.

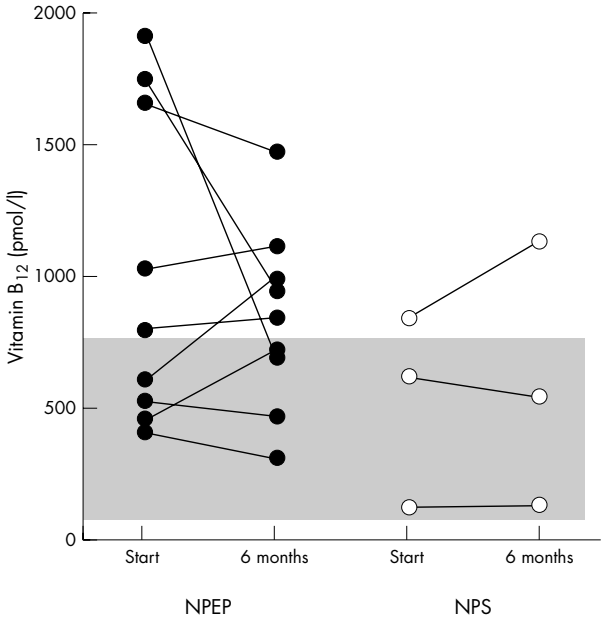

Figure 3 Plasma vitamin B_{12} concentrations.

iron (n = 1), vitamin B_6 (n = 1), and vitamin A (n = 2). Full sets of results were available for most assays; where results were not obtained for all subjects, the numbers are indicated in the table.

One hundred per cent of subjects (n = 12) had raised plasma or serum concentrations of one or more micronutrients. Raised copper and vitamin B_{12} concentrations were most frequently seen (figs 2 and 3). Fifty per cent subjects (n = 6) had raised plasma vitamin B_{12} concentrations after six months of feeding (>733 pmol/l) and 87% of subjects (n = 10) had raised serum copper concentrations (>22 μmol/l). There was no relation between length of feeding prior to recruitment and plasma copper and vitamin B_{12} concentrations.

DISCUSSION

Despite low feed volumes and low energy intakes, children receiving enteral feeds over a six month period achieved an adequate micronutrient intake and an acceptable blood profile. However, the intakes of copper and vitamin B_{12} were high with corresponding high plasma concentrations. In the absence of other suitable guidelines, nutrient intake was compared with the DOH 1991 dietary reference values, although this may be inappropriate, particularly in chronically sick children.[7] There is little scientific evidence supporting the recommendations given for micronutrient requirements in young children. Many values have no supporting evidence or are interpolated from infant or adult recommendations.[2]

The children studied had varying nutritional requirements. Almost half (n = 5) of the subjects had cerebral palsy. These children may have energy requirements lower or higher than the EAR,[8] but overall the group had a satisfactory improvement in anthropometric measurements. A small number of the children may have had high micronutrient requirements because of malabsorption or catabolism. In addition, the oral

Table 3 Composition of Nutrison Paediatric Standard and Nutrison Paediatric Energy Plus compared to the EU Commission Directive Guidelines for Foods for Special Medical Purposes 1999

Nutrient	Nutrison Paediatric Standard and Nutrison Paediatric Energy Plus per 100 kcal	EU Commission Directive Guidelines per 100 kcal	
		Minimum	Maximum
Energy		–	–
kcal	100		
KJ	420		
Protein (g)	2.75	–	–
Carbohydrate (g)	12.2	–	–
Fat (g)	4.5	–	–
Sodium (mg)	53	30	175
Potassium (mg)	93	80	295
Calcium (mg)	50	35/50*	175/250*
Phosphorus (mg)	39	30	80
Magnesium (mg)	11	7.5	25
Iron (mg)	0.73	0.5	2.0
Zinc (mg)	0.6	0.5	1.5
Copper (μg)	87	60	500
Manganese (μg)	130	50	500
Fluoride (mg)	0.12	–	0.2
Molybdenum (μg)	3.33	3.5	18
Selenium (μg)	2.33	2.5	10
Chromium (μg)	1.9	1.25	15
Iodine (μg)	8.7	6.5	35
Vitamin A (μg)	46.7	35	180
Vitamin D (μg)	0.83	0.5	2.5/3*
Vitamin E (mg)	0.6	0.5	3.0
Vitamin K (μg)	1.3	3.5	20
Thiamin (mg)	0.07	0.06	0.5
Riboflavin (mg)	0.09	0.08	0.5
Niacin (mg)	0.43	0.9	3.0
Pantothenic acid (mg)	0.33	0.15	1.5
Vitamin B_6 (mg)	0.09	0.08	0.5
Folate (μg)	10.7	10	50
Vitamin B_{12} (μg)	0.17	0.07	0.7
Biotin (μg)	4.2	0.75	7.5
Vitamin C (mg)	4	2.25	22

*For products intended for children 1–10 years.

intake of many of the children may have been poor for a long period prior to commencement of enteral feeding, and this may have increased nutritional requirements.

Paediatric feeds should meet the RNI (DOH, 1991) for micronutrients when fluid and energy requirements are met by the feed. Our subjects would be considered at risk of developing deficiencies as they were receiving low feed volumes. However, despite these low feed volumes the median daily intake of all micronutrients was above the RNI, and 67% of subjects (n = 8) met the RNI for all micronutrients. The median plasma concentration of all micronutrients was also within the normal range, suggesting that children on long term standard paediatric enteral feeds maintain adequate biochemical nutrient status.

With many children on low feed volumes, high intakes of micronutrients were unexpected. Vitamin B_{12} intakes were particularly high. The National Diet and Nutrition Survey of 1995 for children aged 1½–4½ shows a similarly high intake of vitamin B_{12}, with the children studied having a median dietary intake of 471% of the RNI. The median plasma concentration from the National Survey was 578 pmol/l; in our study group the median plasma concentration after six months of feeding was 782 pmol/l. There is no scientific evidence supporting the RNI for vitamin B_{12} for young children. Figures are interpolated from those derived for infants and adults.

Subjects had high dietary intakes of copper with a median intake of 171% RNI (range 108–326%). This was significantly higher than the intake reported by the National Diet and Nutrition Survey, where the median intake of copper was 109% RNI. There is little data on human copper requirements and the RNI for young children has been interpolated from infant data.

Table 3 summarises the EU Commission Directive Guidelines for the composition of enteral feeds. Both study feeds had a micronutrient composition at the lower end of the recommended range. Feeds provided 87 µg copper per 100 kcal (recommended range 60–500 µg per 100 kcal). Our data show that 87% of subjects had a raised serum copper concentration at the end of the study. If a manufacturer produced a feed with a micronutrient composition at the maximum limit specified by the EU Commission Directive Guidelines, children would receive excessive intakes of micronutrients. The risk of toxicity, particularly to children on long term enteral feeding, must be considered.

With the exception of vitamin A, vitamin D, and fluoride, there are no specific guidelines on toxicity of micronutrients in children. Vitamin B_{12} has very low toxicity, with no toxic effects reported in man,[2] and consequently the high intakes and blood concentrations of vitamin B_{12} seen in our study are likely to be insignificant. Copper intoxication has not been reported in the UK, but high intakes of copper are known to be toxic. Interpretation of circulating copper concentrations can be difficult. An increased concentration may indicate increased circulating concentration of the carrier protein caeruloplasmin rather than an increased free copper. Caeruloplasmin may be increased in cancer, trauma, and other inflammatory conditions when there is an acute phase response. Caeruloplasmin was not measured directly in our subjects. However, there was no acute phase response with normal albumin and normal C reactive protein (CRP) in all subjects, except for one subject with a marginally raised CRP (9.65 mg/l).

In conclusion, the micronutrient composition of standard paediatric enteral feeds appears to meet the long term micronutrient requirements of young children with chronic illness. However, they may be consuming excessive quantities of some micronutrients, and the maximum nutrient guidelines for paediatric enteral feeds need to be defined more clearly.

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