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Refining low protein modular feeds for children on low protein tube feeds with organic acidaemias☆,☆☆,☆☆☆

A. Daly*, S. Evans, C. Ashmore, S. Chahal, S. Santra, A. MacDonald

Birmingham Children's Hospital, Steelhouse Lane, Birmingham B4 6NH, United Kingdom

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ABSTRACT

Children with inherited metabolic disorders (IMD) who are dependent on tube feeding and require a protein restriction are commonly fed by 'modular tube feeds' consisting of several ingredients. A longitudinal, prospective two-phase study, conducted over 18 months assessed the long-term efficacy of a pre-measured protein-free composite feed. This was specifically designed to meet the non-protein nutritional requirements of children (aged over 1 year) with organic acidaemias on low protein enteral feeds and to be used as a supplement with an enteral feeding protein source.

Methodology: All non-protein individual feed ingredients were replaced with one protein-free composite feed supplying fat, carbohydrate, and micronutrients. Thirteen subjects, median age 7.4y (3–15.5y), all nutritionally tube dependent (supplying nutritional intake: ≥ 90%, n = 12; 75%, n = 1), and diagnosed with organic acidaemias (Propionic acidaemia, n = 6; Vitamin B_{12} non-responsive methyl malonic acidaemia, n = 4; Isovaleric acidaemia, n = 2; Glutaric aciduria type1, n = 1); were studied. Nutritional intake, biochemistry and anthropometry were monitored at week − 8, 0, 12, 26 and 79.

Results: Energy intake remained unchanged, providing 76% of estimated energy requirements. Dietary intakes of vitamins, minerals and essential fatty acids significantly increased from week 0 to week 79, but sodium, potassium, magnesium, decosahexanoic acid and fibre did not meet suggested requirements. Plasma zinc, selenium, haemoglobin and MCV significantly improved, and growth remained satisfactory. Natural protein intake met WHO/FAO/UNU 2007 recommendations.

Conclusions: A protein-free composite feed formulated to meet the non-protein nutritional requirements of children aged over 1 year improved nutritional intake, biochemical nutritional status, and simplified enteral tube feeding regimens in children with organic acidaemias.

1. Introduction

Enteral feeds for children with severe organic acidaemias, (propionic acidaemia, [PA]; vitamin B_{12} non-responsive methyl malonic acidaemia, [MMA B_{12}nr]; isovaleric acidaemia, [IVA]; glutaric aciduria type 1, [GA1]); dependent on tube feeding are complex. Protein-free composite feeds supplying adequate macro and micronutrients are unavailable for children over 12 months of age, necessitating feeding regimens to consist of multiple ingredients to meet the non-protein nutritional requirements. Adaptation of enteral formulations designed for other clinical conditions may lead to nutritional imbalance, suboptimal growth and body composition in children who are at risk of metabolic decompensation. It is essential to provide an age appropriate, protein-free composite feed to supplement sources of natural and precursor-free L-amino acid supplements for enteral feeds in this vulnerable group.

Our hypothesis was that an age appropriate protein-free composite feed (supplemented with fat, carbohydrate, vitamins, minerals and essential fatty acids) formulated for children over the age of 1 year with IMD would improve nutritional status and simplify enteral tube feeding regimens for children requiring low protein diets with organic acidaemias. The protein-free composite feed was designed to accompany a protein containing feed, which supplied the protein source.

We have previously reported the short-term efficacy and tolerance

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* Corresponding author.
E-mail address: a.daly3@nhs.net (A. Daly).

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of a powdered pre-measured protein-free composite feed [Basecal 200 Vitaflo Ltd. Liverpool UK], containing fat, carbohydrate and micronutrients designed for children with organic acidaemias, over 1 year of age. The children required a protein restriction, and were tube feeding dependent. In this open, extension study, we report the nutritional efficacy and caregiver feed preparation data after the protein-free composite feed formulated for children aged over 1 year of age had been used for 18 months when patients were fully transitioned onto the protein-free composite feed. This protein- free feed provided energy and an important source of carbohydrate, fat, essential fatty acids, vitamins and minerals. The protein requirements were provided by a separate feed and we were not aiming to study the impact on protein nutrition.

2. Methods

2.1. Study design

An 18-month, longitudinal prospective open-label, intervention, extension study using a protein-free composite feed (study feed) developed for children over 1 year of age. The introduction of the study feed in the first 6 months (phase 1) has been reported [1]. In phase 2, patients with organic acidaemias on tube feeds were studied for a further 12 months, when all individual modular energy sources were replaced with only one ingredient, the study feed

2.2. Study formulation (Table 1)

The pre-measured study feed has a nutritional profile that meets the nutritional requirements of children over 1 year of age when reconstituted at 1 kcal/ml. It contains carbohydrate, fat (including long chain polyunsaturated fatty acids), vitamins, minerals, and trace elements. It does not contain fibre. Each sachet (43 g) mixed with 200 ml water, provides 200 kcals (1 kcal/ml).

2.3. Inclusion criteria

Children were recruited if they had a proven organic acidaemia, aged over 1 years of age or weighed between 8 and 31 kg, and were taking a modular feed providing ≥75% of enteral feed intake. All children had taken part in study phase 1 [1].

2.4. Phased introduction of study feed (Table 2)

At the start of the study, when analysis is based on the follow-up subjects (n = 13), enteral feeds consisted of a median of 4 ingredients comprising of: a natural protein source, precursor-free L-amino acids (disorder specific) and energy modules (either an infant energy module [± additional energy modules] or individual energy modules).

2.4.1. Phase 1 (week 0–26)

In this phase, the aim was to ensure children tolerated the study feed. This feed replaced the infant protein-free composite feed (Energivit [Nutricia Ltd]). However, to maintain a constant energy intake supporting metabolic stability, other energy sources [glucose polymer (n = 8) and 50% fat emulsion (n = 1)] remained in the feed recipes. All precursor-free L-amino acids were changed to pre-measured sachets. (Vitaflo International Ltd)

2.4.2. Phase 2 (week 27–79)

The study protein-free composite feed completely replaced the remaining energy sources (glucose polymer and 50% fat emulsion).

2.5. Protein prescription

Changes were made to protein (intake/sources) as children increased in age (e.g. natural protein source changed from infant formula to standard enteral feed). Natural protein was prescribed according to WHO/FAO/UNU (2007) [2] safe levels of protein intake for MMA/PA and IVA and in GA1 according to European guidelines [3]. In MMA/PA, an additional 15 to 20% of total protein intake was prescribed from MMA/PA precursor-free L-amino acids (AA); in GA1, lysine-free, low tryptophan AA supplements were prescribed according to GA1 European guidelines [3]. No precursor-free AA supplements were prescribed for patients with IVA.

Table 1
A comparison of the nutritional composition (per 100 ml and per 100 Kcal) of study protein-free module ingredient (Basecal) with a protein-free infant feed (Energivit).

	Basecal 200 (Vitaflo Ltd) per 100 Kcal equivalent to 100 ml	Energivit (Nutricia) per 100 ml (15% dilution as recommended by manufacturer)	Energivit (Nutricia) per 100 Kcal equivalent to 20% dilution. NB. This is in excess of manufacturers recommendation
Energy Kcal/kJ	100/420	74/309	100/420
Protein g	0	0	0
Carbohydrate g	15	10	13.3
Fat g	4.5	3.8	5.1
Vitamin A μg	65	58.8	78.4
Vitamin D μg	1.7	1.3	1.7
Vitamin E mg	2	1	1.3
Vitamin C mg	15	7.4	10
Vitamin K μg	5.7	5.6	7.5
Thiamin mg	0.11	0.08	0.1
Riboflavin mg	0.16	0.08	0.1
Niacin mg	1.1	1.1	1.5
Vitamin B6 mg	0.13	0.08	0.1
Folic acid μg	18.5	8.3	11.1
Vitamin B 12 μg	0.28	0.2	0.27
Iron mg	1	1.2	1.6
Zinc mg	1	0.9	1.2
Copper mg	0.07	0.07	0.09
Selenium μg	3	2.3	3
Magnesium mg	10.2	8.7	11.6
Manganese mg	0.1	0.06	0.08
Biotin μg	3.5	2.7	3.6
Pantothenic acid mg	0.55	0.4	0.5
Sodium mmol	1.8	1.2	1.6
Potassium mmol	2.5	1.9	2.5
Chloride mmol	1.6	1.5	2
Phosphorous mg	1.3	1.5	2
Iodine μg	17	12.5	17
Molybdenum μg	4.8	1.8	2.4
Choline mg	20.6	13.7	18.3
Inositol mg	11	14.7	19.6
DHA mg	16	0	0
AAmg	16	0	0

2.6. Dietary analysis

For 3 days during week 79, caregivers recorded the volume of modular feed consumed and any oral food and drink intake (n = 1) by weighing dietary intake. Dietary analysis was calculated using the software program *Electronic Dietetic Manager* (EDM 2000™ Microman 2000 PO box 3721 Newport Pagnell UK) and McCance and Widdowson's 'The Composition of Foods.' [4]. The intake of energy, total protein (natural protein and protein equivalent from precursor-free L-amino acids), fibre, calcium, magnesium, iron, zinc, selenium, sodium, potassium, vitamin B_{12}, vitamin D, essential fatty acids (DHA and AA) and fluid was assessed. Each nutrient (except protein, essential fatty acids (DHA and AA), fluids and fibre) was compared as a percentage of the DH 1991 reference nutrient intakes (RNI) or estimated average requirement (EAR) for energy [5] Protein intake was compared