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THE SAFETY OF MCT BASED FORMULA IN THE DIETARY TREATMENT OF LONG CHAIN FATTY ACID DISORDERS

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In long chain fatty acid ß-oxidation (LCFAOD) disorders there is an abnormal response to fasting adaptation (1), with consequential accumulation of fatty acids and a decrease in cell energy metabolism. Traditionally, children with LCFAOD disorders presenting with clinical symptoms are treated with a specialist infant formula, with medium chain triglyceride (MCT) mainly replacing long chain triglyceride (LCT) as its fat source.

In part one of this series, the ideal composition of special formulae for LCFAOD disorders was discussed. There are few reports in the literature reporting the safety or efficacy of any special formula for any of these conditions. The optimal amount of MCT remains undefined, and practice has been to adapt formula designed for other 'conditions' (e.g. malabsorption, liver disease and chylothorax).

Defining the ideal nutritional composition of a formula to treat all LCFAOD disorders is challenging, but it is important they contain MCT, carbohydrate equivalent to at least standard normal infant formula, essential fatty acids and ideally, a source of long chain polyunsaturated fatty acids (LCPs) [docosahexaenoic acid (DHA) and arachidonic acid (AA)].

It is essential the safety and efficacy of any new specialist formula designed for LCFAOD disorder is tested in infants and children. In an open, observational, 21 day, phase 2 trial, we studied the safety of a new MCT based formula designed for LCFAOD disorders in a group of children aged over five years.

One of the UK's top paediatric dietitians, Anita's specialism lies with inherited metabolic disorders. She spends 50 percent of her professional time in clinical work with children and 50 percent researching and teaching.

METHODS

Subjects

Six subjects (3 boys; 3 girls) with well controlled LCFAOD disorders from one treatment centre, aged 7-13 years, who normally received a high MCT/low LCT formula (≥ 500 ml/day) as their milk replacement, either orally or via a gastrostomy/nasogastric tube, were recruited. Their conditions were: very long chain acyl CoA dehydrogenase deficiency (VLCADD), n=2; Long chain 3 hydroxyacyl CoA dehydrogenase deficiency (LCHADD), n=2; and Carnitine Acyl Carnitine Translocase Deficiency (CACTD), n=2. Their ethnic origin was: Pakistani, n=4; white Caucasian, n=2.

They all followed a low fat diet, aiming to consume less than 10 percent of their energy intake as LCT. All required daily MCT oil/formula. Their usual median daily volume of MCT formula (containing 2% fat; 90% in the form of MCT) was 720 ml (range 500-1900 ml/day). Four of the children used MCT oil on bread or in cooking daily. All children required overnight tube feeds; five via a continuous gastrostomy tube and one child drank his feed overnight. All had oral diet during the day with the exception of one boy with CACTD, who had an unsafe swallow. All the diets were supplemented with walnut oil, and four children had a separate source of DHA/AA. Four of the six children had a fasting tolerance of only four hours (at the last assessment); and two boys with CACTD had a fasting tolerance of six hours.

Study Formula

Lipistart (study formula) (Vitaflo International) is a nutritionally complete powdered formula suitable from birth. It contains whole protein, carbohydrate, fat (78.3% MCT, 20.3% LCT), vitamins, minerals, trace elements, essential fatty acids, and long chain polyunsaturated fatty acids (AA and DHA). Thirty percent of the total calories are from MCT, 7.7% from LCT and three percent from linoleic acid, with an n6:n3 ratio of 7:1.

Table 1: Example of nutrient intakes from 2 different MCT infant formula

Nutrient intake from study feed										
	Volume ml/daily	Kcal/d from formula	LCT g/day	% LCT/ kcal from formula	MCT g/d	%MCT/ kcal from formula	Linoleic acid mg/ day	Alphalinoleic acid mg/day	Arachidonic acid mg/day	DHA mg/ day
Subject 1	500 ml	340	2.9	7.7	12.5	29.4	1295	180	150	75
Subject 5	500 ml	340	2.9	7.7	12.5	29.4	1295	180	150	75
Subject 3	1200 ml	816	6.84	7.7	30	29.4	3108	432	360	180
Subject 2	1800 ml	1224	10.3	7.7	45	29.4	4662	648	540	270
Subject 4	1900 ml	1292	10.84	7.7	47.5	29.4	4921	684	570	285

3% kcal from linoleic acid/0.48% kcal from alpha-linolenic acid

Nutrient intake from usual feed										
	Volume ml/daily	Kcal/d from formula	LCT g/day	% LCT/ kcal from formula	MCT g/d	%MCT/ kcal from formula	Linoleic acid mg/ day	Alphalinoleic acid mg/day	Arachidonic acid mg/day	DHA mg/ day
Subject 1	500 ml	368	1.9	4.7	7.7	16.7	450	70	0	0
Subject 5	500 ml	368	1.9	4.7	7.7	16.7	450	70	0	0
Subject 3	1200 ml	882	4.6	4.7	18.5	16.7	1075	183	0	0
Subject 2	1800 ml	1323	6.9	4.7	27.7	16.7	1620	250	0	0
Subject 4	1900 ml	1397	7.3	4.7	29.2	16.7	1720	270	0	0

1.1% kcal from linoleic acid/0.17% kcal from alpha-linolenic acid

Study Design

This was a 21 day, open, observational phase 2 trial. Participants consumed their usual feed (Monogen, SHS Nutricia) for seven days (days -7 to 0) followed by seven days on the study formula (days 1 to7) and then resumed their usual feed on days 8-14. The amount of usual and study feed was tailored according to individual requirements, but the volume of each was the same and remained unchanged throughout the study. All the diets were routinely supplemented with walnut oil, and four children had a separate source of DHA/AA but it was only taken routinely in two of the children.

Study procedures/investigations

The children were reviewed on day -7, 0, 2, 7 and 14 including a medical examination and measurement of vital signs (blood pressure, heart rate, respiratory rate, and temperature) and an electrocardiogram (ECG) on days 0 and 7. Capillary blood tests (liver function tests, total lipids, full blood count, glucose, creatine kinase, glucose, U and Es, creatinine, acyl carnitines, free fatty acids and 3 hydroxy butyrates) were collected on day -7, 0, 2, 7. A further blood sample was collected on day 14 only if any clinical symptoms had been reported during the study. All blood test times were standardised for each subject, and were always performed three hours after the last feed was administered.

RESULTS

Subject withdrawals

One girl with LCHADD withdrew on day -7. She was unable to tolerate the capillary blood samples.

Nutrient intake and administration of formula (Table 1)

Either formula provided anything from 20 to 100 percent of total energy intake. However, two older children dependent on formula as a major source of their total nutritional intake had the same amount of supplementary carbohydrate added to both usual and study formulae. Three children took both formula solely via their gastrostomy (either as their overnight feed or their entire source of nutrition); one via his gastrostomy overnight but also orally during the day; and one child took his entire requirement orally. The children did not appear to notice any taste difference between the two types of formula.

Both feeds were well tolerated, but the study formula provided a significant amount of essential fatty

acid requirement in an appropriate ratio of linoleic to alpha-linolenic acid. In subjects taking over 700 ml of study formula, there appeared no need for additional long chain polyunsaturated fatty acids. The intake of study formula also provided a higher intake of MCT, with each 200 ml providing 5g MCT instead of 3.1g from the usual formula.

Feed tolerance

Few symptoms were reported throughout the trial. One boy with CACTD reported constipation (on both feeds), and then an ear infection and infected gastrostomy in the last 14 days of the trial. Another girl with VLCADD complained of loose stools on the study feed.

Investigations

ECG

No child had an abnormal ECG reported on day 0 or day 7 (after 7 days of taking study feed).

Biochemistry

There were few differences between the 2 feeds for any biochemical measure.

DISCUSSION

This is the first safety trial reported of a special MCT formula with a nutrient composition specifically designed for infants and children with LCFAOD disorders. It was associated with minimal changes in tolerance or biochemistry. No child complained of muscle pain on the study feed. The children taking over 700 ml/daily of study feed did not require further supplementation with long chain polyunsaturated fatty acids. The study feed appeared safe, efficacious and was well tolerated in this challenging group of children with LCFAOD disorders.

Table 2: Biochemical results for subjects

Electrolytes and glucose	Sodium, potassium, urea, creatinine and glucose all stayed within normal reference ranges throughout the trial for all the children.
Haemoglobin	This remained unchanged.
Liver function tests	Alanine transferase was high in one boy with CACTD throughout the trial who had a heavy growth of Staphylococcus aureus on an ear swab. Another boy with LCHADD had a marginal rise of alanine transferase on the study feed. Two girls with VLCADD had high levels of alanine transferase on their usual feed and low alkaline phosphatase throughout the entire study. One boy with CACTD had high alkaline phosphatase throughout the study.
Creatinine kinase	This was high in one girl with VLCADD throughout the trial but improved on the study feed. In another girl it increased on day 7 after taking study feed. In one boy with CACTD it decreased on day 14 after returning to his usual feed.
Lipids	Triglycerides were high in all children throughout the trial on either formula.
3-hydroxybutyrates and free fatty acids	These remained unchanged on either formula.

References
1 Bennett MJ, Rinaldo P, Strauss AW. Inborn errors of mitochondrial fatty acid oxidation. Crit Rev Clin Lab Sci. 2000. 37: 1-4

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Questions relating to: *The safety of MCT based formula in the dietary treatment of long chain fatty acid disorders.* Type your answers below and then **print for your records.** Alternatively print and complete answers by hand.

Q.1	What are the main symptoms of long chain fatty acid ß-oxidation disorders?
A	
Q.2	Ideally, what should the nutritional composition of infant formula be in treating LCFAOD?
A	
Q.3	Briefly summarise the MCT formula study trial 'design' as reported in this article.
A	
Q.4	What were the trial results in children taking over 700ml of study formula?
A	
Q.5	What symptoms were reported throughout the trial?
A	
Q.6	Please summarise the outcome of the trial giving an example of the biochemical results.
A	

Please type extra notes here . . .