SHORT REPORT

Feeding difficulties in long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency

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Abstract

Feeding difficulties are common in long chain 3-hydroxyacyl-CoA dehydrogenase deficiency in early childhood and are not associated with developmental disability, metabolic abnormalities, or the overnight feeding regimen. They are an inherent part of the phenotype and it is important to recognise them because of the distress and disruption they cause.

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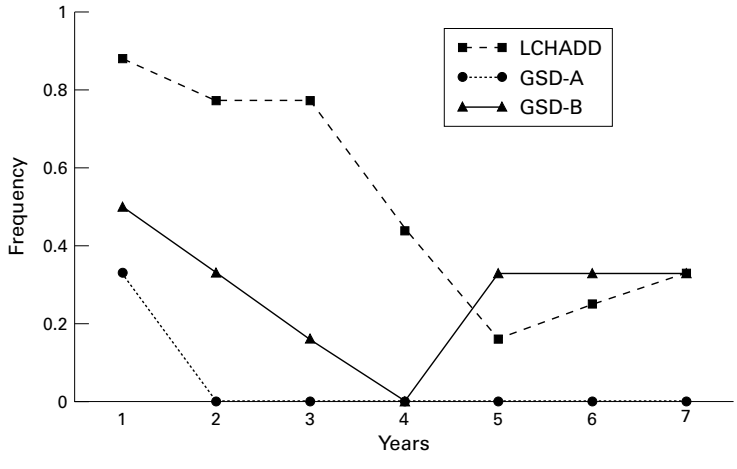
Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHADD) is a defect of fatty acid β oxidation. Most patients present before age 1 year with acute illness characterised by hypoketotic hypoglycaemic encephalopathy combined with hepatopathy and cardiomyopathy.[1 2] Further episodes of metabolic decompensation may be precipitated by fasting or intercurrent illness, but between episodes some children with LCHADD are well; others have persistent sequelae of metabolic decompensation, including neurodevelopmental abnormalities, or symptoms caused by the disease per se, such as pigmentary retinopathy. Treatment includes a diet very low in long chain fats, high in carbohydrates, and in some cases a supplement of medium chain triglycerides (MCT). It is essential to avoid fasting, so the children have frequent feeds by day and either continous feeding or bolus feeds similar to the daytime feeds during the night.

Feeding difficulties are common in many inborn errors of metabolism, but they are generally not prominent in disorders of fatty acid oxidation. However several families of children with LCHADD commented on feeding difficulties, which prompted us to study the problem.



LCHADD	8/9	7/9	7/9	4/9	1/6	1/4	1/3
GSD-A	2/6	0/6	0/6	0/6	0/6	0/6	0/6
GSD-B	3/6	2/6	1/6	0/6	2/6	2/6	2/6

Figure 1 Feeding difficulties in LCHADD and GSD-1 (excluding problems related to breakfast, GSD-A; including problems related to breakfast, GSD-B). For each year the number of patients with feeding problems in relation to the total number of patients is shown below the graph.

Methods

We studied nine patients with LCHADD (six boys, three girls). The diagnosis was based on characteristic blood spot acylcarnitines, tritium release assys in cultured fibroblasts, and molecular genetic studies. Four were homozygotes for the common G1528C mutation and five were heterozygotes (the second mutation has not been defined). Additional clinical data has been published previously.[3 4] We compared their feeding difficulty with that of six patients with glycogen storage disease type 1 (GSD1), all of whom had frequent feeds by day and continuous nasogastric feeding at night. The GSD1 patients (four boys, two girls) were generally slightly older than the LCHADD patients; five had GSD1a and one GSD1b. Diagnosis was confirmed by enzymology on liver biopsy.

We obtained information about the eating habits of each child by questioning the family and reviewing the notes. Only the notes were reviewed in the GSD1 patients. The duration and presence of swallowing difficulties, nausea, poor appetite, and the duration of meals were recorded, as well as whether the symptom was present all day or only during part of the day. Feeding was considered a problem when: (1) one or more of the above symptoms were present daily for months; and (2) there was a consistent refusal each day to complete feeds within approximately 30 minutes.

Results

Feeding difficulties were common in the first year of life (experienced in eight of nine patients) and only decreased slowly, so that 50% of patients still had feeding difficulties at 4 years of age (fig 1).

Despite their feeding difficulties, they grew well; eight of nine were above the 25th centile for weight (range 9–98), and seven of nine above the 25th centile for height (range 0.4–90). Neurodevelopment status did not seem to be important. Five were intellectually normal, one had motor delay only, and three children had developmental delay, but the feeding habits of those with developmental delay did not differ from those of intellectually normal children. The one child with no feeding problems from the first year of life was developmentally delayed, had attention deficit disorder and had one of the most stormy presenting episodes. There was no difference between the four children who were homozygous for the common G1528C mutation and the five who were compound heterozygotes and who clinically had a milder spectrum of disease. The patients were metabolically well controlled.[3] At the time of questioning four had abnormal bloodspot acylcarnitines. Creatine kinase and alanine aminotransferases were raised slightly in three and four, respectively. Three patients have had episodes of rhabdomyolysis, associated with metabolic decompensation and encephalopathy in two. None of the above biochemical features correlated with the frequency of feeding difficulties.

Discussion

We speculated that the high frequency of feeding problems could be caused by frequent/continous overnight feeding. At the time of the study, energy in the overnight feeds provided 13–33% of the total energy intake, mostly around 20%. One of the two who had more than 30% of total energy intake overnight had severe feeding problems (8 years old), but generally there was no correlation between overnight intake and feeding problems. If overnight feeding had been a problem, it seems likely that feeding problems would be more pronounced in the mornings than during the rest of the day. However, children with LCHADD had feeding problems throughout the day.

To assess the possible influence of overnight feeding in more detail, we reviewed six patients with GSD1 as controls. All had continuous overnight feeding of carbohydrate. In their first year of life two had feeding problems similar to those seen in LCHADD, but none had such difficulties after the first year of life. However, they did have problems with breakfast (fig 1). Thus, despite a comparable feeding regimen, feeding difficulties in GSD1 were much less frequent and they were different. Severe problems were seen only during the first year of life, and thereafter only breakfast caused difficulties.

Our findings suggest that feeding problems are an inherent part of the LCHADD phenotype in early childhood. Feeding difficulties are frequent despite good metabolic and clinical condition. They were not associated with developmental disability, metabolic abnormalities, or the overnight feeding regimen. During the day some food may be taken orally, but it is important to recognise that daytime tube feeding (either nasogastric or via gastrostomy) may be necessary. The feeding difficulties cause a lot of distress and disruption at home and it is important to recognise these as early as possible.

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