Maintenance of growth in cystic fibrosis despite reduction in pancreatic enzyme supplementation

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Abstract

Twenty one children with cystic fibrosis were advised to decrease their pancreatic enzyme supplement (PES) dose to less than 10 000 units lipase/kg/day. Mean PES dosage was significantly decreased in 15 patients from 18 380 to 8647 units lipase/kg/day. There were no significant changes in energy or fat intake, but there were significant increases in weight SD score, height SD score, and weight/height ratio.

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Case control studies in the UK¹ and the USA² have demonstrated a strong dose related association between pancreatic enzyme supplementation (PES) and the risk of developing fibrosing colonopathy. In 1995 the UK Committee on Safety of Medicines (CSM) recommended that the mean daily dose of PES should not exceed the equivalent of 10 000 units of lipase/kg body weight/day irrespective of formulation.³

We advised children under our care with cystic fibrosis to reduce their dose of PES to within the recommendations, but were concerned that this might harm their nutritional status. Our hypothesis was that decreasing the dosage of PES might result in decreased nutrient intake, increased fat excretion, and resultant growth impairment. Therefore, we monitored prospectively the nutrition and growth of these children.

Subjects and methods

From October 1994 we reviewed the nature and dosage of PES for all patients under the care of the paediatric cystic fibrosis service at University Hospital of Wales. Following the 1995 CSM recommendations, all patients receiving more than 11 000 units of lipase/kg body weight/day were recommended to decrease their PES to less than 10 000 units lipase/kg/day. As most patients have some daily variation in PES intake, we excluded patients receiving between 10 000 and 11 000 units lipase/kg/day.

All patients were known to have fat malabsorption, which had improved with the addition of PES. The PES dose was decreased very slowly at each outpatient appointment under the guidance of the cystic fibrosis dietitian, with a subsequent telephone consultation to monitor progress. At each assessment the patients' height and weight were measured, and expressed as height SD score, weight SD score,

and weight for height ratio. Before and after decreasing PES, three day food diaries using household measures (two week days and one weekend day) were recorded and coded.⁴ Mean energy intake was calculated using a computerised food composition database (Microdiet, University of Salford), and expressed as percentage daily energy derived from fat, fat intake/kg body weight/day, total kJ/kg/day, and energy intake as percentage of requirement.

Once the recommended dosage of PES was achieved, three day faecal fat excretion was recorded. All stools were collected between carmine markers into plastic buckets lined with polythene bags. The lipid content of the wet stool was measured,⁵ and expressed as mean daily fat excretion and coefficient of fat absorption. All patients were receiving greater than 3 g dietary fat/kg body weight/day at the time of collection. The upper limit of normal for faecal fat excretion in our laboratory is 5 g/day.

Results

With the exception of one patient, all received standard strength formulations of PES. Of 65 pancreatic insufficient patients under our care, 26 received PES greater than 10 000 units lipase/kg/day. Five were receiving between 10 000 and 11 000 units lipase/kg/day, and were excluded. Of 21 patients receiving greater than 11 000 units lipase/kg/day, 16 (12 male) decreased their lipase dosage to the required level, although one male subsequently required an ileostomy for an unrelated condition (initial dosage 14 700 units lipase/kg/day). All faecal fat collections were successfully completed (n=15) except in one female who refused (initial dosage 14 286 units lipase/kg/day). Five patients were unable to decrease their dose of PES: three categorically refused, one required high strength PES, and one was awaiting a liver transplant. Although these patients were significantly older than those who reduced their PES (11.7 v 5.1 years, 95% confidence interval (CI) 3.4, 9.7; p=0.001), there was no significant difference in mean daily dose of PES (17 573 v 14 797 units lipase/kg/day).

Table 1 shows PES dosage and anthropometric assessments. Mean follow up was for 1.4 years (range 0.7-2.5 years). Over the same time there was a significant increase in weight SD score, height SD score, and weight/height ratio. Table 2 shows dietary analysis. There were no significant changes in percentage daily energy derived from fat, fat intake, daily energy intake, or energy intake expressed as percentage of requirement.

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Table 1 Mean (SD) lipase dosage and anthropometric assessment before and after reduction of lipase dosage (n=15)

	At reduction in PES dosage	After reduction in PES dosage	Difference after reduction	95% CI diff	p Value
Age (years)	5.1 (4.1)	6.6 (4.1)	1.4 (0.5)		
PES intake unit lipase/kg/day	18380 (6280)	8647 (1187)	-9733		
Weight SD score	-0.82 (0.95)	-0.18 (0.79)	0.64	0.95 to 0.33	<0.001
Height SD score	-0.99 (1.29)	-0.35 (1.07)	0.64	1.00 to 0.28	0.002
Weight/height ratio	92 (7.9)	97 (11.1)	5	8.5 to 0.7	0.023

Table 2 Mean (SD) dietary analysis before and after reduction of lipase dosage (n=15)

	At reduction in PES dosage	After reduction in PES dosage	95% CI diff	p value
% Daily energy derived from fat	38 (3.5)	39 (6.4)	-4.8 to 3.5	0.6
Range	32-44	23-46		
Fat intake (g/kg body weight/day)	5.8 (1.9)	4.9 (1.2)	-0.3 to 2.0	0.2
Range	3.0-8.7	3.0-7.4		
Daily energy intake (kJ/kg/day)	573 (179)	489 (123)	-17 to 184	0.1
Range	276-865	326-752		
Energy intake as % of requirement	137 (29.1)	145 (32.1)	-20.5 to 35.4	0.7
Range	103-184	96-209		
Faecal fat excretion (g fat/day) (n=14)	NA*	7.5 (3.2)		
Range		4.1-15.4		
Coefficient of fat absorption (%) (n=14)	NA*	91.9 (2.0)		
Range		89.0-95.0		

*NA = not available.

Discussion

We have shown, in 15 children with cystic fibrosis, that it is possible to decrease the dose of PES to less than 10 000 units lipase/kg/day with acceptable fat absorption while maintaining nutritional intake.

We are unclear why the decrease in PES was associated with improved growth. Follow up was for at least a year in the majority of cases, and during that period patients were neither offered nor received increased nutrition. All had been diagnosed with cystic fibrosis at least one year before the reduction in PES, and only one child was pubertal. There were no significant changes in their management except that they received increased dietetic input. It is possible that very tight supervision of PES intake might have resulted in more appropriate usage.

The appropriate dose of PES is a balance between sufficient to prevent malabsorption and the increased risk of fibrosing colonopathy with some preparations when given at higher

doses. More studies are required to define the maximal safe dosage for PES. Our findings suggest that the dose of PES can be reduced to those recommended in current guidelines in most patients without detriment to growth, and might even improve growth in the long term.

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