High dose pancreatic enzymes in cystic fibrosis

P J Robinson, P D Sly

Abstract

Seven patients with cystic fibrosis taking high
doses of pancreatic supplements were
assessed to determine whether this dose was
necessary to achieve adequate fat absorption.
Patients reduced their intake from a group
mean of 45 to 21 capsules a day. Five patients
did not have any significant alteration in fat
malabsorption while taking the reduced
enzyme dose.

While 90% of patients with cystic fibrosis
require pancreatic enzyme (pancreatin) supple-
ments, wide interpatient variation in the
individual dosage requirement exists. Most
clinicians rely on symptoms such as failure to
gain weight or the passage of offensive bulky
bowel actions to regulate the enzyme dose. By
increasing enzyme dose in the face of such
symptoms the clinician is making two assump-
tions. Firstly, that the symptoms are due to
insufficient pancreatic enzyme function in the
small bowel, and secondly that a further
increase in enzyme administration will improve
fat absorption. However, abdominal symptoms
in patients with cystic fibrosis are not invariably
related to pancreatic enzyme insufficiency.1,2
Increasing enzyme supplementation in the
presence of such abdominal symptoms would not
be expected to relieve the symptoms or to
improve absorption.

The cystic fibrosis clinic at the Royal
Children’s Hospital, Melbourne, cares for
approximately 350 children below the age of 18
years. We were concerned that some of our
patients were taking excessive doses of pan-
creatin supplementation unnecessarily. We
therefore studied a group of patients taking high
doses of enzymes to determine whether a reduc-
tion in the enzyme dose could be achieved
without a deterioration in fat absorption. This
study was performed as a preliminary to an
investigation of patients unable to achieve
normal fat absorption despite taking large quan-
tities of pancreatic enzymes.

Patients and methods

Seven patients with cystic fibrosis (mean age
10-7 years, range 9–14 years) who were taking
large doses of pancreatin were studied. Patients
were included if they had persistent abdominal
symptoms, such as offensive bulky stools or
abdominal pain, failure to gain weight, or
because of concern that they may not require
their high enzyme input (table 1). Two patients
(cases 5 and 6) presented at birth with meconium ileus, which required limited bowel
resection. All patients had a daily fat intake
exceeding 2 g/kg and documented fat mal-
absorption, which improved with the addition
of enzyme supplements. All were currently
taking pancreatin supplements in the form of
enteric coated microspheres (Pancreasel, Cilag,
5000 units lipase/capsule).

Two outpatient three day faecal fat balance
studies were performed, separated by a mini-
um of three weeks and a maximum of six
weeks. Before the second study patients were
counseled how to reduce their enzyme dose,
following an individual regimen, to approxi-
mately 30 capsules per day. The selection of 30
capsules as the modified dosage was arbitrary
but is a figure frequently suggested at cystic
fibrosis meetings as a maximal dose. The
modified enzyme regimen was used for five days
before the faecal collection commenced. Faecal
fat analysis was performed using the acid titra-
tion method of van de Kramer et al3 and oral
input of fat was determined using the Microdiet
programme (Department of Statistics and
Mathematics, University of Salford), modified
for local food values.

Informed consent was obtained from each
patient and at least one parent before enroll-
ment. The study protocol was approved by the
hospital ethics committee.

Results

All parents and the older patients enrolled in
this study expressed concern at the start of the
study as to the likely occurrence of offensive
stools and abdominal pain with the reduction of
the enzyme input. Patients reduced their intake
of pancreatin from a group mean of 45 capsules
per day to a group mean of 21 (table 2).

Five patients had normal fat absorption on
their usual pancreatin dose while two had con-
siderable malabsorption. Five patients did not
have any appreciable alteration in fat mal-
absorption while taking the modified enzyme
schedule. These included four with normal
absorption and one with 16% malabsorption on
the usual enzyme dosage. The two remaining
patients experienced large increases in fat
malabsorption with the reduction in enzyme
dosage. Fat intake was not appreciably different
in the two study periods.

The two patients who had previous bowel
resection for meconium ileus both achieved

Table 1 Anthropomorphic data

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<th>Age (years)</th>
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<td>2</td>
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<td>M</td>
<td>Failure to gain weight</td>
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<td>3</td>
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<td>M</td>
<td>High enzyme intake</td>
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<td>M</td>
<td>Abdominal pain, offensive stools</td>
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<td>Offensive stools, high enzyme intake</td>
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<td>Poor weight gain, high enzyme intake</td>
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<tr>
<td>7</td>
<td>10</td>
<td>M</td>
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</table>

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reductions in their enzyme intake without appreciable alteration in their absorption. Both these patients achieved normal fat absorption with the reduced enzyme dose.

Discussion
This study has shown that some patients with cystic fibrosis take inappropriately high doses of pancreatic enzymes and that reduction of this high input may be achieved without deterioration in fat absorption. However, two of the patients did have an increase in fat malabsorption when their enzyme dose was decreased. This argues against a policy of setting an arbitrary limit to the enzyme dose, as is frequently suggested at cystic fibrosis clinical meetings. All patients in this study had reached their current dose of enzymes in response to symptoms perceived as due to residual malabsorption. This study highlights the risks of assuming that abdominal symptoms in patients with cystic fibrosis are invariably due to pancreatic enzyme insufficiency and therefore will respond to an increase in enzyme treatment; five of the seven subjects had normal absorption despite persisting symptoms.

The major implication of the results of the present study is that objective assessment of nutrient absorption should be routine in patients with cystic fibrosis, particularly those with abdominal symptoms. The best of the currently available tests is the three day faecal fat balance. This procedure is time consuming, prone to large errors if not performed correctly, and rarely welcomed by patients. The results of the present study, however, illustrate the importance of assessing changes in enzyme treatment by direct measurements of nutrient absorption.

In conclusion the present study has shown that some children with cystic fibrosis may be taking inappropriately high doses of pancreatic enzymes because of abdominal symptoms not directly related to exocrine pancreatic insufficiency. It is important to determine whether symptoms are due to fat malabsorption and that increases in enzyme replacement result in improved absorption. Recognition of other potential causes of abdominal symptoms in cystic fibrosis should lead to a more logical approach to the patient with residual symptoms on standard enzyme treatment.

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Dexamethasone treatment for congenital adrenal hyperplasia

M C Young, I A Hughes

Abstract
Ten patients with congenital adrenal hyperplasia (three males, seven females; aged 12–29 years) had their usual glucocorticoid treatment changed to dexamethasone in three crossover dosage regimens. A starting dose of 5 μg/kg/day is suggested but as no one dose regimen resulted in adequate control the timing of the dose must be decided for each patient.

The optimum glucocorticoid preparation, total daily dose, and dose schedule for the treatment of congenital adrenal hyperplasia remain controversial.1 Hydrocortisone is probably the preparation of choice in infancy and childhood, but in adolescents near completion of growth and adults dexamethasone may be a convenient alternative.1–3 The potency of dexamethasone in relation to both pituitary-adrenal suppression and side effects is much greater.

Patients
Ten patients (three males and seven females) aged 12–29 years with 21-hydroxylase deficiency (classic salt losing type) congenital adrenal hyperplasia took part in the study.