Does pancreatic enzyme supplementation reduce pain in patients with chronic pancreatitis: a meta-analysis

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Authors' objectives
To determine whether pancreatic enzyme supplements significantly decrease abdominal pain in patients with chronic pancreatitis.

Searching
MEDLINE was searched for English language studies using the keywords 'pancreatic enzyme supplements', 'pain', and a combination of these terms.

Study selection
Study designs of evaluations included in the review
Prospective, randomised double-blind placebo-controlled trials (RCTs), which evaluated the usage of pancreatic enzymes for the relief of pain in patients with chronic pancreatitis, were included. The duration of the studies ranged from 2 weeks to 8 months.

Specific interventions included in the review
Pancreatic enzyme supplements including the following: Ilozyme, Pankreon, Pancrex-Duo, Pancrease, Panzytrat and Creon. These preparations included both enteric-coated and non-enteric-coated formulations, and included tablets, granules, microspheres and microtablets.

Participants included in the review
Chronic pancreatitis. The participants were patients with chronic pancreatitis who were being treated for pain. The following criteria were used for diagnosing chronic pancreatitis: secretin test, endoscopic retrograde pancreatography, operating room, Lundh test meal, ultrasound, computed tomography, and plain X-ray film of the abdomen. Of the participants, 48% were male and steatorrhoea was documented in 35% of the cases.

Outcomes assessed in the review
The outcome assessed was the percentage of patients expressing a preference for enzyme treatment over placebo. The individual studies used the following criteria to determine the outcome: pain score (1 to 4), pain scale (1 to 5), analgesic use, 10 cm visual analogue pain scale, and pain score (slight, moderate, severe).

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
A pooled estimate of the log odds for the preference of enzymes over placebo was calculated using the method of DerSimonian and Laird (see Other Publications of Related Interest). This estimate was then transformed back to give a pooled estimate of the percentage of patients preferring enzyme treatment.

How were differences between studies investigated?
The homogeneity of the log odds for the preference of enzymes over placebo was assessed using the method of DerSimonian and Laird (see Other Publications of Related Interest).

Results of the review
Six RCTs (189 patients) were included.

The studies used different criteria for diagnosing chronic pancreatitis, and different criteria to assess response to therapy.

The pooled estimate of the percentage of patient preferring enzyme treatment was not statistically significant. There was heterogeneity among the studies (P=0.14).

Authors' conclusions
There was no significant benefit of supplemental pancreatic enzyme therapy to relieve pain associated with chronic pancreatitis. Further research is required.

CRD commentary
This clearly written and presented review includes a discussion of the following limitations of the review: the heterogeneous population in the case-mix; the different lengths of study; the lack of validated pain scores; and the use of different criteria for evaluating response to therapy.

By limiting the literature search to one database and English language studies, some relevant studies may have been omitted. No details were given of the methods used to select the studies for inclusion or to extract the data. In addition, the validity of the included studies was not assessed. More comprehensive details of the patients studied and the drop-out rates would have been welcome. It may have been possible to obtain more information from the original authors. It was unclear whether the analysis was conducted on an intention to treat basis.

In view of the limitations of the primary studies discussed by the author and the factors mentioned here, it is not possible to comment on the place of pancreatic enzyme supplementation in the management of abdominal pain in chronic pancreatitis.

Implications of the review for practice and research
The authors recommend that a larger clinical trial be conducted, which minimises the degree of heterogeneity of the patient population and uses a single pancreatic enzyme preparation that has been shown to be released in the duodenum. Such a study should include more detailed information on the following: aetiology; alcohol consumption; criteria of diagnosis; the presence and severity of diabetes mellitus and steatorrhoea; the use of narcotics; and the use of validated pain scores.

Bibliographic details

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Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.