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REVIEW ARTICLE

Treatment options in painful chronic pancreatitis: a systematic review

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Abstract

Background: Longlasting and unbearable pain is the most common and striking symptom of chronic pancreatitis. Accordingly, pain relief and improvement in patients' quality of life are the primary goals in the treatment of this disease. This systematic review aims to summarize the available data on treatment options.

Methods: A systematic search of MEDLINE/PubMed and the Cochrane Library was performed according to the PRISMA statement for reporting systematic reviews and meta-analysis. The search was limited to randomized controlled trials and meta-analyses. Reference lists were then hand-searched for additional relevant titles. The results obtained were examined individually by two independent investigators for further selection and data extraction.

Results: A total of 416 abstracts were reviewed, of which 367 were excluded because they were obviously irrelevant or represented overlapping studies. Consequently, 49 full-text articles were systematically reviewed.

Conclusions: First-line medical options include the provision of pain medication, adjunctive agents and pancreatic enzymes, and abstinence from alcohol and tobacco. If medical treatment fails, endoscopic treatment offers pain relief in the majority of patients in the short term. However, current data suggest that surgical treatment seems to be superior to endoscopic intervention because it is significantly more effective and, especially, lasts longer.

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Introduction

Chronic pancreatitis (CP) is a painful inflammatory disease that leads to progressive and irreversible destruction of the pancreatic parenchyma.[1,2] Recurrent episodes of acute pancreatitis may result in tissue fibrosis and the loss of exocrine and endocrine function, along with steatorrhea, malabsorption, diabetes and unbearable pain.[3] The majority of patients with CP demonstrate constant or recurrent severe and often opioid-refractory abdominal pain. Pancreatic pain characteristically presents as deeply penetrating and dull epigastric pain, which radiates to the back and is often worsened by ingestion. This classical pattern of pain is not universal, and the character, location and quality of pain can be quite inconsistent.[4]

A pathophysiological mechanism for pain in CP that has been repeatedly discussed is the increase in intrapancreatic pressure either within the pancreatic duct or in the pancreatic parenchyma, which leads to ischaemia and the inflammation of pancreatic tissue.[5,6] It is noteworthy in this context, however, that there seems to be no direct relationship between the presence of duct dilatation and pain.[7] Furthermore, it has long been recognized that the severity of abdominal pain sensations correlates with the extent of intrapancreatic neural damage and alterations.[8,9] However, the underlying molecular pathways are incompletely understood and probably multifactorial. A hypothesis that is increasingly discussed proposes that neural inflammatory cell infiltration leads to pancreatic neuritis and neural plasticity with enlarged nerves and the formation of a dense intrapancreatic neural network. All these

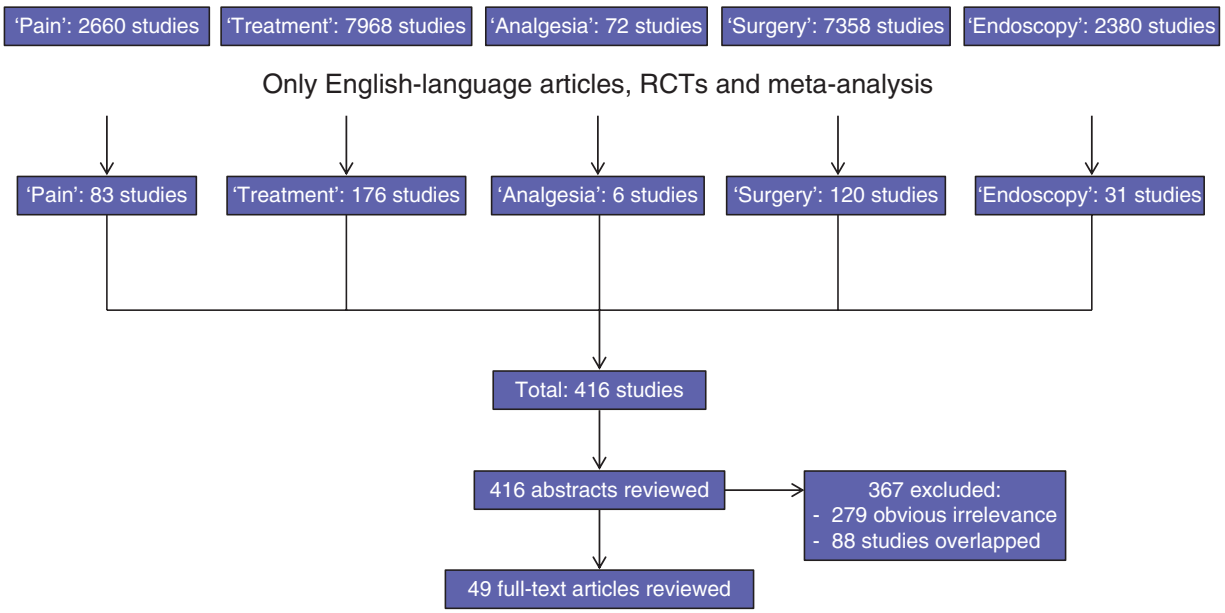

Figure 1 Flow diagram showing the present literature review, determination of eligibility and inclusion of studies in the systematic review. RCT, randomized controlled trial

neural alterations are responsible for causing the characteristic pancreatic neuropathy and consequent neuropathic pain.[8–12] Because the underlying pain mechanisms are just beginning to be understood, the treatment of pain in CP is often empirical and insufficient. The objective of this article was to review, summarize and assess the level of evidence on the effectiveness of different treatment options in painful CP.

Materials and methods

Searches of the MEDLINE, PubMed and Cochrane Library databases were performed using the search terms 'pain', 'treatment', 'analgesia', 'surgery' and 'endoscopy' and, alternatively, these terms matched with 'chronic pancreatitis' for papers published from the inception of the database in question to 31 March 2013. Searches were limited to English-language articles describing randomized controlled trials (RCTs) and meta-analyses as these are considered to represent the highest level of evidence.

The results obtained were examined individually by two independent investigators (JGD'H, GOC). Firstly, titles and abstracts were read; if the article was considered relevant by at least one of the investigators, full-text articles were retrieved and studied. Articles for inclusion were required to report on studies that had systematically investigated any form of treatment in patients with painful CP and used pain reduction as one of their outcome measures. Articles reporting on studies outwith the scope of the review and those that overlapped across the searches were excluded. Reference lists extracted from the 49 full-text articles published between 1983 and 2012 and selected for systematic review were hand-searched for additional relevant titles.

The following study characteristics were extracted from the articles: authors; publication year; publishing journal; study design and size; study duration; type of intervention, and outcome measures related to pain. Studies were categorized according to the primarily investigated treatment strategy for painful CP based on whether they referred to medical treatment, interventional treatment (including endoscopic and radiological interventions), surgical treatment, and any comparisons between any of these types of treatment.

Results

The initial search identified 416 articles. Duplicate studies were excluded ($n = 88$). Screening of titles and abstracts resulted in the exclusion of a further 279 articles, the content of which fell outwith the scope of this review and was obviously irrelevant (Fig. 1). Finally, 49 studies were included for full-text review.

Medical treatment

The initial challenge in CP concerns making the correct diagnosis. Early-stage CP has been recognized in the context of endoscopic ultrasound (EUS) when patients present with typical pancreatic-type pain. However, whether these EUS findings represent true early-stage CP that will progress or whether they are false positive findings remains unclear.[13] Diagnosis can be especially challenging in small duct disease because patients often lack characteristic structural changes. Accordingly, patients with small duct CP are generally poorly represented in all of the published studies on treatment of painful CP. Once the diagnosis of CP is confirmed, patients are advised to maintain a strict abstinence from tobacco