Systematic review of total pancreatectomy and islet autotransplantation for chronic pancreatitis

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CRD summary
The review concluded that removal of the entire pancreas (organ producing insulin hormone - total pancreatectomy) and islet autotransplantation (transplantation of the patient’s own pancreas cells) reduced pain in people with chronic pancreas disease (pancreatitis) and allowed most patients to remain independent of insulin hormone supplements. Given a very limited and poor quality evidence base, the authors’ conclusions should be treated with caution.

Authors’ objectives
To assess the role of total pancreatectomy and islet autotransplantation in the management of chronic intractable pain in patients with chronic pancreatitis and to determine the optimal timing of treatment in the disease course.

Searching
MEDLINE (from 1950), EMBASE (from 1980) and The Cochrane Library were searched; search terms were reported. The final date of the search was not reported.

Study selection
Studies that reported the outcome of patients with chronic pancreatitis treated with total, subtotal or completion pancreatectomy followed by islet transplantation were eligible for inclusion the review. Case series were included only if they reported outcomes for consecutive patients and reported on more than five participants. Studies with follow-up of less than one year, paediatric studies, and studies that included patients with pancreatic malignancy were excluded. The outcomes of interest were difference in preoperative and postoperative analgesia use (morphine equivalents), and insulin dependence rate at two years. Secondary outcomes were postoperative quality of life and islet yield (islet equivalents per kilogram of pancreatic tissue).

In the included studies, the mean age of participants ranged from 38 to 43 years; over half were women (where reported). Mean weight ranged from 59 to 74kg, where reported. Chronic pancreatitis was either idiopathic or as a result of alcohol consumption. Only three patients were diabetic prior to surgery. Computed tomography, magnetic resonance cholangiopancreatography and endoscopic retrograde cholangiopancreatography were used in the preoperative assessment of severity and grading in most studies (measurement were not reported in the paper). The most common technique for islet cell isolation was the modified Ricordi method; the Lee method and pancreatic fragments were also used. The most common site for islet transplantation was the liver via the portal vein or one of its tributaries. The pancreatectomy technique included duodenum-preserving total pancreatectomy, spleen preserving technique, pylorus preserving technique, routine splenectomy pylorus preserving duodenal resection, and spleen preservation if normal appearance after hilar ligation. Most patients were from centres in the USA.

Two reviewers independently selected studies, with discrepancies resolved by a third reviewer.

Assessment of study quality
It appeared that studies were not assessed for quality.

Data extraction
Data were extracted on insulin use, requirement for morphine and islet yield, according to how they were described in the included studies by two reviewers and checked by a third reviewer. Any discrepancy was resolved by discussion with a fourth reviewer and reanalysis of the publication.

Methods of synthesis
The results of the included studies were described narratively.

Results of the review
Five studies (296 patients, sample sizes ranged from 6 to 173) were included in the review. Four studies were case series and one study was a retrospective cohort. Mean follow-up ranged from 1.5 to eight years (where reported).

**Morphine use:** Two studies reported that mean morphine use had decreased postoperatively (by 116mg and 55mg) compared with baseline. The three other studies did not measure morphine use.

**Insulin independence:** Insulin independence varied according to follow-up. One trial reported a rate of 33% insulin independence at follow up to 25 months. One trial reported a rate of 18% at mean follow-up of 1.5 years. In two studies, insulin independence ranged from 46% to 64% at a mean follow-up of five years. In two studies, insulin independence was 10% at a mean follow-up of eight years and 28% at a mean follow-up of 10 years.

**Islet yield:** One study found that mean islet yield equivalent per kilogram of pancreatic tissue was 297,889 in insulin-dependent patients and 413,542 in insulin-independent patients. One study reported that mean islet yield ranged from 23 to 17,035. Three other studies did not measure this outcome.

The review had insufficient data to measure quality of life or answer the second review question on optimal timing of treatment.

**Authors’ conclusions**
Total pancreatectomy and islet autotransplantation reduced pain and concurrent islet autotransplantation use allowed a significant proportion of patients to remain independent of insulin supplementation.

**CRD commentary**
The review addressed two clear research questions, supported by broad inclusion criteria. Relevant sources were searched but no specific attempts were made to find unpublished studies, so publication bias could not be excluded. Appropriate methods were used to select studies and extract data, which minimised the chance of reviewer error or bias.

It appeared that included studies were not assessed for quality; the studies were observational and had small sample sizes, so bias could not be ruled out. One of the primary outcomes in the review was measured by only two of the five studies; the other primary outcome had variable follow-up, which made it difficult to determine the relevance of the findings. Synthesis of studies in narrative format was appropriate, given the variation in the included studies.

Given a very limited and poor quality evidence base, the authors’ conclusions should be treated with caution.

**Implications of the review for practice and research**
**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that the formation of a national or international registry would provide a larger data set that would enable analysis of outcomes. They also stated that research should use more standardised inclusion criteria and analyse effects on chronic pain, quality of life and timing of surgical intervention. Centres running total pancreatectomy and islet autotransplantation treatment programs should publish their results.

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