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ORIGINAL ARTICLE

The Use of Nasojejunal Nutrition in Patients with Chronic Pancreatitis

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ABSTRACT

Context Abdominal pain, malabsorption and diabetes all contribute to a negative impact upon nutritional status in chronic pancreatitis and no validated standard for the nutritional management of patients exists. **Objective** To assess the effect of nasojejunal nutrition in chronic pancreatitis patients. **Design** All consecutive chronic pancreatitis patients fed via the nasojejunal route between January 2004 and December 2007 were included in the study. Patients were assessed via retrospective review of case notes. **Results** Fifty-eight chronic pancreatitis patients (35 males, 23 females; median age 46 years) were included. Patients were discharged after a median of 14 days and nasojejunal nutrition continued for a median of 47 days. Forty-six patients (79.3%) reported resolution of their abdominal pain and cessation of opioid analgesia intake over the study period and median weight gain at 6 weeks following nutritional cessation was +1 kg (range -24 to +27 kg; P=0.454). Twelve (20.7%) patients reported recurrence of their pain during the follow-up period and complications were both minor and infrequent. Significant improvements were noted in most blood parameters measured, including: sodium (from 134.8 to 138.1 mEq/L; P<0.001); urea (from 3.4 to 5.1 mmol/L; P<0.001); creatinine (from 58.3 to 60.3 µmol/L; P<0.001); corrected calcium (from 2.24 to 2.35 mmol/L; P=0.018); albumin (from 34.5 to 38.7 g/L; P=0.002); CRP (from 73.0 to 25.5 mg/L; P=0.006); and haemoglobin (from 11.8 to 12.4 g/dL; P=0.036). **Conclusion** Nasojejunal nutrition, commenced in hospital and continued at home, is safe, efficacious and well tolerated in patients with severe chronic pancreatitis and is effective in helping to relieve pain and diminish analgesic requirements.

INTRODUCTION

Chronic pancreatitis develops following repetitive or sustained injury to the pancreas and occurs secondary to excessive alcohol intake in 60-70% of chronic pancreatitis patients [1]. The UK incidence of chronic pancreatitis is 1 per 100,000 per annum (UK prevalence 3 per 100,000) [2] and it may follow a slow burning pattern or be characterised by acute episodes with quiescent intermittent periods. The complications of chronic pancreatitis are part of a wide spectrum that not only affect the pancreas itself, but also other organ systems and the condition is associated with significant morbidity and mortality.

The management of chronic pancreatitis remains challenging. Patients should be encouraged to stop drinking and smoking, and to partake of a healthy lifestyle; however, analgesia, often in the form of opiates, is almost always required and can lead to dependence [3, 4]. Ultimately, invasive options such as endoscopic and surgical manoeuvres, including Frey's and Beger's procedures, as well as total pancreatectomy with autologous islet cell transplantation, may become necessary [3]. Novel methods such as pain-modifying agents, coeliac plexus and nervous blocks, antioxidants and radiation therapy may have a role to play in the future [3, 5].

Following disease development, a combination of factors lead to nutritional deterioration and significant weight loss, often necessitating long-term programmes of nutrition, prolonged hospital admission and substantial use of health-care resources. Attacks of chronic pancreatitis generate a metabolic response that may be indistinguishable from attacks of acute pancreatitis [6] or sepsis [7, 8], and that may increase with the severity of the disease episode [9]. Experimental studies reveal that hypermetabolic states may subsequently occur with resting energy expenditure of 30-50% above normal [10, 11], effects that can be raised even further by the presence of sepsis [10]. Further, skeletal muscle proteolysis may lead the circulating aminoacid pool to fall to 40% of normal and

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Abbreviations CCK: cholecystokinin; CRP: C-reactive protein

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muscle mass by 15% [12]. Furthermore, pancreatitis patients with a persistently negative nitrogen balance have been shown to have a significantly elevated mortality rate [13].

Therefore, chronic pancreatitis creates a hypermetabolic state that rapidly depletes in-built nutritional stores and is exacerbated by pain, nausea and vomiting, ileus, gastric stasis, dysmotility, outlet obstruction, and continuing alcohol consumption that all contribute to decreased nutritional intake and ongoing pancreatic damage [14, 15]. Pancreatic damage in chronic pancreatitis results in reduced pancreatic enzyme secretion, as well as decreased bicarbonate secretion, thus acting to further affect the functionality of the secreted pancreatic enzymes by providing an inhospitable environment [14].

Pancreatic damage clinically affects fat digestion before that of carbohydrate and protein, resulting in steatorrhoea [15] and deficiencies in vitamins A, D, E and K [16]. As function deteriorates further and lipase and trypsin secretion decrease, azotorrhoea may also develop [16]. Metabolic errors can also occur, as the catabolic stress state leads to increased levels of catecholamines and cortisol, and a subsequent disturbance in the insulin/glucagon ratio, beta cell dysfunction and insulin resistance may follow [6, 17]. Insulin may therefore be required in more than 80% of patients not previously diagnosed as diabetic [6] and new diagnoses of diabetes will follow in 20-30% as beta cell mass decreases [6, 18, 19]. Fat metabolism is further altered as lipolysis and lipid oxidation increase [6, 20]. Despite this, fat clearance can be reduced, leading to hypercholesterolaemia and hypertriglyceridaemia [6, 12, 21]. Specific deficiencies in calcium, magnesium, zinc, thiamine and folic acid have also been reported [1] and thus the trace element and nutritional deficiencies already present in ethanolic patients can be further compounded [18].

Although guidelines now advocate the use of nasogastric or nasojejunal feeding in acute pancreatitis, at present there are no British Society of Gastroenterology or Department of Health guidelines to guide the nutritional management of patients with chronic pancreatitis. Although small bowel can be routinely accessed for enteral feeding, by either percutaneous endoscopic gastrojejunostomy or direct percutaneous endoscopic jejunostomy, there is only minimal data regarding clinical outcome and safety of long-term jejunal feeding in chronic pancreatitis.

Aims

The aim of our study was to assess the effectiveness of a nasojejunal nutrition programme in patients with chronic pancreatitis, and in particular to evaluate weight effects, as well as tolerance and complications associated with nasojejunal nutrition.

METHODS

Patients

All patients admitted to our tertiary pancreatic unit, with a diagnosis of chronic pancreatitis that were fed via the nasojejunal route, between January 2004 and December 2007, were included in the study. Data were retrospectively collected from the patient's medical records.

A diagnosis of chronic pancreatitis was made based upon the Marseille-Rome classification (1988) following assessment of symptom profile (including abdominal pain, weight loss, nausea and vomiting) and imaging characteristics of chronic pancreatitis (including calcification, duct dilatation and stricturing and glandular atrophy).

Abdominal pain, analgesic requirements and gastrointestinal symptoms were evaluated by clinical assessment during the patient's initial admission, during any re-admissions and also during their follow-up consultations.

Insertion of Nasojejunal Catheters

Nasojejunal catheters were inserted for standardised indications including inability to tolerate oral feeding or inability to ingest sufficient calories for body weight (pain or duodenal stenosis); gross weight loss (more than 10% of pre-morbid body weight); or acute complications of chronic pancreatitis contributing to the aforementioned (such as pseudocyst, fistula, pseudoaneurysm, acute inflammation or acute pain).

Nasojejunal catheters were inserted by direct endoscopic placement through the pylorus and over a guidewire. Fine-bore (6-10 French gauge) tubes were inserted and fluoroscopic screening was utilised if necessary to confirm placement.

Feeding

Correct placement of nasojejunal catheters was confirmed radiologically and feeding commenced within 24 hours of insertion. A standard, semi-elemental nasojejunal feeding regime was initiated in all patients at a rate of 30 mL/h. The feeding rate was subsequently increased by 10 mL/h every 12 hours until the patient was reviewed by a dietician; 1,200 mL of the standard feed provided 1,560 kcal (1.3 kcal/mL), 80 g protein, 52 mmol Na^+ and 53 mmol K^+.

All patients were reviewed by a dietician within 48 hours and an individualised feeding regimen established with the goal of reaching full caloric requirement on day 3 (30 mL/kg/day of 1 kcal/mL feed). The regimen was subsequently altered according to the patient's clinical course and physical activity. Patients were allowed to consume oral liquids as their clinical course improved and their tolerance increased; they were also allowed to take oral medications.

All patients were discharged with a nasojejunal tube in situ only once their analgesic provision was adequate or their pain had settled; they were capable of managing their nasojejunal catheter and nutrition; they had no active or acute complications of chronic pancreatitis; and a home care package had been established.

Follow-up

Patients were closely followed up in the out-patient department by surgery, gastroenterology and dietician

teams. Upon review, patients were routinely asked about complications associated with the feeding technique and also to crudely rate their tolerance of the feed as 'excellent', 'good', 'average', or 'poor'.

ETHICS

The study incorporated a retrospective, observational cohort and therefore no formal, written informed consent was taken or institutional ethical approval requested. The study protocol conformed to the Declaration of Helsinki.

STATISTICS

Data are reported as frequencies and median and range or mean±SD values. Statistical analysis was carried out by using the SPSS (Statistical Package for the Social Sciences; version 16) software package. The Fisher's exact and the Pearson chi-square tests were used for comparison of proportions for categorical data, where appropriate. The one-way ANOVA and the paired Student's t test were used for comparisons of continuous data, where appropriate. Two-tailed P values less than 0.05 were considered statistically significant.

RESULTS

Patient Demographics

Fifty-eight (35 males, 23 females) patients with chronic pancreatitis were admitted to our tertiary pancreatic unit and fed via a nasojejunal route, between January 2004 and December 2007.

The median patient age was 46 years (range: 20-67 years) and median age of diagnosis was 43 years (range: 18-62 years). Median time from diagnosis of chronic pancreatitis to nasojejunal feeding was two years (range 0-23 years) and the median follow-up period was 16 months (range: 3-36 months).

Available data identified the aetiological cause as alcohol in 35 patients (60.3%), gallstones in 23 (22.4%), idiopathic in 6 (10.3%), and hyperlipidaemia, post-ERCP, drugs (steroids) and a peri-ampullary mass in one patient (1.7%) each.

Patients were discharged from hospital after a median of 14 days (range: 8-74 days) and nasojejunal feeding continued for a median of 47 (28-139 days) days in total.

Table 1. Comparison between chronic pancreatitis patients with prolonged weight gain and chronic pancreatitis patients with minimal weight gain, no weight gain or weight loss.

	Weight gain (n=22)	No weight gain (n=36)	P value
Sex:			0.054 [b]
- Male	17 (77.3%)	18 (50.0%)	
- Female	5 (22.7%)	18 (50.0%)	
Aetiology:			0.135 [c]
- Alcohol	17 (77.3%)	18 (50.0%)	
- Gallstones	4 (18.2%)	9 (25.0%)	
- Idiopathic	1 (4.5%)	5 (13.9%)	
- Other	-	4 (11.1%)	
Age (years) [a]	45.5 (36-50)	51.0 (37-59)	0.427 [d]
Weight pre-nasojejunal (kg) [a]	59.5 (50-73)	61.0 (54-75)	0.083 [d]
Weight post-nasojejunal (kg) [a]	65.0 (58-74)	60.0 (51-71)	0.753 [d]
Weight difference (kg) [a]	3.5 (2.0-6.0)	0 (-6.0-0.0)	<0.001 [d]
Nausea	5 (22.7%)	4 (11.1%)	0.278 [b]
Diarrhoea	4 (18.2%)	10 (27.8%)	0.533 [b]
Pain improvement	18 (81.8%)	19 (52.8%)	0.047 [b]

[a] Median and (range) values
[b] Fisher's exact test
[c] Pearson chi-square test
[d] One-way ANOVA

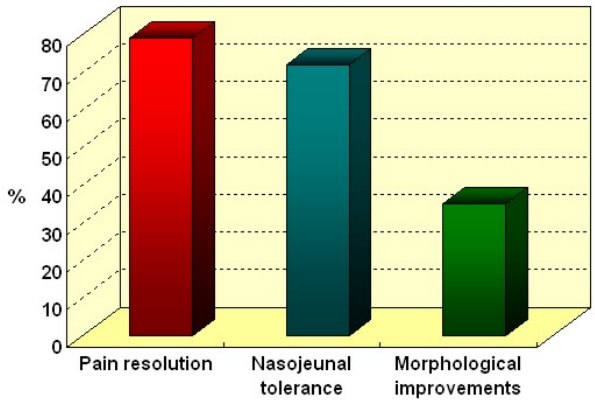

Figure 1. The outcome following nasojejunal nutrition in this cohort of patients with chronic pancreatitis.

Weight Effects

The patient's median weight prior to initiation of nasojejunal feeding was 60.0 kg (range: 42-123 kg) and 61.5 kg (range: 48-108 kg) at post-nasojejunal feeding review. Median weight change was +1 kg (range: from -24 to +27 kg; P=0.454). There was no association between aetiology and change in weight (P=0.130).

A comparison of those patients experiencing a prolonged weight gain with those experiencing minimal weight gain, no weight gain or weight loss demonstrates that the former were more likely to be younger, male and have an alcohol aetiology; further, the use of nasojejunal feeding was more likely to be associated with improvements in pain in weight gain chronic pancreatitis patients (although none of the aforementioned results reached statistical significance; Table 1).

Analgesic Effect

All patients presented with abdominal pain, requiring at least weekly opiate derivatives as analgesia. Forty-six patients (79.3%) reported resolution of their abdominal pain and cessation of opioid analgesia intake over the nasojejunal feeding period (Figure 1); although some patients underwent additional procedures for the management of acute complications. Upon discharge, 35 (60.3%) patients were still taking regular simple analgesia (paracetamol/ibuprofen) and 12 patients (20.7%) were still taking at least weekly opioid derivatives.

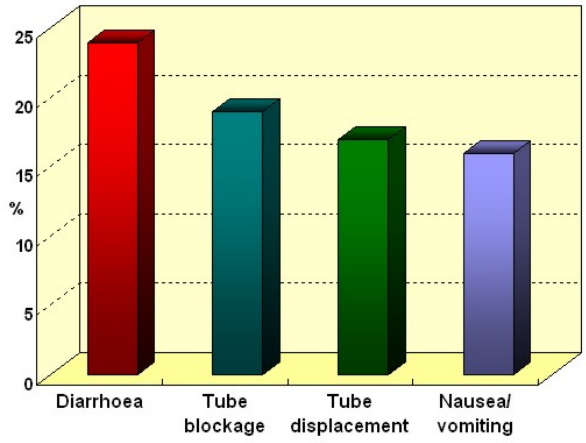

Figure 2. Complications associated with nasojejunal nutrition in this cohort of patients with chronic pancreatitis.

Twelve (20.7%) patients reported significant pain recurrence during the follow-up period (median time to recurrence 4 months; range: 1-25 months). There was no association between aetiology and analgesic effect.

Tolerance and Complications

Forty-two (72.4%) patients reported their tolerance of the feeding regime as 'good' or 'excellent' (Figure 1). Only 4 (7%) patients reported their tolerance of the feeding regime as 'poor'.

Complications were largely minor and infrequent, with diarrhoea (as per subjective patient assessment of alteration in bowel habit to looser or more frequent) occurring in 14 patients (24.1%) and nausea (as per subjective patient assessment) in a further 9 patients (15.5%) (Figure 2). Eleven (19.0%) patients required re-admission for tube blockage and 10 (17.2%) for tube displacement, mandating catheter reinsertion or re-positioning. There were no complications associated with nasojejunal catheter insertion and there was no association between aetiology and tolerance or complications (data not shown).

Pancreatic Morphology

Twenty patients (34.5%) showed radiological improvement in their pancreatic morphology, as assessed on routine computed tomography (Figure 1).

Blood Tests

Thirty-nine patients (67.2%) had blood tests on both the day of nasojejunal feeding commencement and cessation. Over the period of the nasojejunal feeding, significant improvements were seen in many blood and serum parameters, including sodium (from 134.8 to 138.1 mEq/L; P<0.001), urea (from 3.4 to 5.1 mmol/L; P<0.001), creatinine (from 58.3 to 60.3 µmol/L; P<0.001), corrected calcium (from 2.24 to 2.35 mmol/L; P=0.018), albumin (from 34.5 to 38.7 g/L; P=0.002), CRP (from 73.0 to 25.5 mg/L; P=0.006), and haemoglobin (from 11.8 to 12.4 g/dL; P=0.036) (Table 2).

Phosphate measured at 24 hours for assessment of refeeding syndrome was 1.31±0.22 mmol/L while the values measured before feeding were 1.40±0.25 mmol/L (P=0.098).

Outcome

Twelve patients (20.7%) went on to have definitive surgical management of their chronic pancreatitis during the follow-up period.

DISCUSSION

In mild chronic pancreatitis, abstinence from alcohol and effective analgesia can often be sufficient to control pain and enable nutritional improvements through oral intake. Replacement of pancreatic enzymes and acid suppression are of modest effectiveness in treating pain [5]; and frequent small meals, low in fat but rich in carbohydrates, calories and protein, are important to maintain adequate nutrition [22]. Fat soluble vitamins and other micronutrients should be supplemented as clinically indicated. More than 80% of patients can usually be treated adequately with standard food supplemented by pancreatic enzymes [1], only 10-15% of patients will require oral nutritional supplements and enteral tube feeding is only indicated in approximately 5% [1, 23], usually for treatment of severe pain, significant weight loss or acute complications.

A recent plethora of investigations, although mainly focusing upon acute pancreatitis, have shown that enteral nutrition is associated with attenuation of the acute phase response [24], a lower rate of sepsis-related complications (particularly extra-pancreatic) [25, 26], improved glucose control [25], decreased financial cost [26], possible reduced length of hospital stay [27, 28] and possible reduced mortality rates [27]. The enteral

Table 2. Various blood parameters (mean±SD; n=39) measured on the day of nasojejunal feeding commencement, and the day of nasojejunal feeding cessation, reveal significant improvements over the duration of nasojejunal feeding.

	Pre-feeding	Post-feeding	P value [a]
Electrolytes			
Sodium (mEq/L)	134.8±3.2	138.1±3.4	<0.001
Potassium (mEq/L)	4.4±0.5	4.3±0.5	0.124
Urea (mmol/L)	3.4±1.8	5.1±1.9	<0.001
Creatinine (µmol/L)	58.3±15.0	60.3±12.5	<0.001
Albumin (g/L)	34.5±7.9	38.7±7.4	0.002
Corrected calcium (mmol/L)	2.24±0.20	2.35±0.17	0.018
Phosphate (mmol/L)	1.40±0.25	1.31±0.22	0.098
C-reactive protein (mg/L)	73.0±90.5	25.5±40.2	0.006
Blood count			
Haemoglobin (g/dL)	11.8±2.2	12.4±2.2	0.036
Mean corpuscular volume (fL)	91.2±5.5	90.4±15.2	0.651
White cell count (10^9/L)	10.0±4.4	11.5±13.6	0.469
Platelet count (10^9/L)	392±190	356±150	0.283

[a] Paired Student's t test

route may also be useful in preventing gut compromise as this may serve as a trigger and perpetuator of multiple organ failure or sepsis in pancreatitis [29]. This observational study demonstrates that the use of nasojejunal nutrition in patients with chronic pancreatitis can be safely commenced in hospital and continued following discharge. Further, its use is associated with improvements in weight and blood parameters, as well as being well-tolerated and associated with minimal complications.

Our findings mirror the few studies investigating the role of nasojejunal feeding in chronic pancreatitis. Hamvas *et al*. observed 19 patients with necrotising chronic pancreatitis to show that 12 fed via a nasojejunal route recovered more quickly and required less interventions than 7 patients fed via a parenteral route [30, 31]. Similarly, Stanga *et al*. [23] retrospectively analysed 57 chronic pancreatitis patients (median duration of jejunal feeding 113 days) to illustrate an average weight increase of 4.3 kg ($P<0.05$) and a decrease in the proportion of patients with significant abdominal pain (96% to 23%; $P<0.05$), as well as noting that complications were largely minor and infrequent. Interestingly, patients with non-alcoholic pancreatitis suffered from ongoing weight loss and failure to put on weight as well as a higher number of physician visits due to abdominal pain and gastrointestinal complications. The authors concluded that reduced pancreatic gland stimulation may be the key to producing these effects, although the critical underlying mechanisms remained unclear. Ogara *et al*. [32] utilised nasojejunal feeding catheters in 30 chronic pancreatitis patients for a median duration of 4.6 months and median follow-up of 7.5 months. Nine out of 20 patients that had reported uncontrolled pain at initial evaluation reported pain levels that were completely, or nearly completely, resolved following treatment with jejunal feeds alone ($P=0.0008$). However, the cohort underwent a mean weight loss of 1.6 kg ($P=0.27$) (although some patients had suspected malignancy) and 12 patients suffered complications in total.

Pain associated with chronic pancreatitis is extremely challenging to manage and remains largely resistant to therapy, partly because the mechanisms underlying it are poorly understood. Elevated cholecystokinin (CCK) levels are one of the proposed mechanisms leading to pain in chronic pancreatitis [33] and feeding low in the gastrointestinal tract may invoke a minimal degree of pancreatic stimulation [34], thus decreasing CCK levels. However, Keith *et al*. investigated two patients with chronic pancreatitis to illustrate no change in volume or amylase output in response to intra-jejunal infusion of an elemental formula [35]. Further, despite the fact that the concept of resting the pancreas by decreasing its stimulatory activity makes physiological sense, it remains difficult to definitively prove any beneficial effects upon pain relief or outcome [12, 36, 37] and the fact that at least minor baseline pancreatic enzyme secretion occurs means that the pancreas is never fully 'rested' [38]. However, jejunal feeding may help to reduce other gastrointestinal complications that may contribute to pain [23], such as gastric paresis with associated symptoms such as nausea, vomiting and abdominal pain [39, 40, 41]. Elemental and semi-elemental feeds are more effective at reducing exocrine secretion than standard feeds with intact proteins at oral [42, 43], duodenal [44] and jejunal [45] levels. Elemental formulae also lead to decreased gastric acid production and further decreased pancreatic stimulation [46].

Although there are no studies correlating the degree of undernutrition with the course of disease in chronic pancreatitis, poor nutritional status is likely to contribute to a negative outcome [1]. Nutritional assessment and management therefore remains crucial not only in the context of outcome from disease but also in planning any future intervention. Improvements in certain blood parameters in this study, such as CRP, platelets and haemoglobin, require interpretation in the context of the patient's improving disease profile during the study period and caution should be taken in attributing them directly to the use of nasojejunal feeding alone. However, hyponatremia is one of the commonest abnormalities found in hospital in-patients [47] and its presence in many critically ill patients is associated with an increased risk of death and illness-associated morbidity [48, 49]. Under normal circumstances, the plasma sodium concentration is maintained within a narrow range; however, chronic inflammatory diseases, such as chronic pancreatitis, may affect this balance by producing an excess of interleukin-6 [50], while alcoholism and liver cirrhosis can also lead to hyponatremia. Thus, chronic pancreatitis patients may be at significant risk of hyponatraemia and nasojejunal feeding may be an effective way of correcting this imbalance. Significant increases in albumin, urea and creatinine were also observed in this study; however, such surrogate markers of nutrition and malnutrition have often been used with contention and their clinical relevance debated [51, 52]. Less contentious would be their use as surrogate markers for gain in lean body weight, an expected result of an appropriate feeding regime. However, whilst a gain in weight was seen (and inferred from the biochemical results to be lean body mass) this was not significant; although an initial weight loss period during the acute phase of the disease may have reduced the overall net weight gain effect. In future studies, serial, objective measures of muscle mass may be useful to circumvent this issue [53].

Refeeding syndrome is also a concern in the initiation of feeding in the malnourished or starved and is characterised by hypophospahatemia and hypokalemia [54, 55]. Whilst mean phosphate levels declined during the first 24 hours of feeding (from 1.40 to 1.31 mmol/L; $P=0.098$), none fell below the normal range and nasojejunal feeding in this population does not seem to be associated with an increased risk of refeeding syndrome.

CONCLUSION

Reduction in malnutrition, adequate energy and calorie intake, and relief of pain are the main goals of therapy in chronic pancreatitis, all of which can be aided via the delivery of nasojejunal nutrition. However, all home-based or long-term nutrition programmes for chronic pancreatitis should be developed in a multi-disciplinary setting with the involvement of gastroenterology, radiology, dietician and nursing colleagues. Aetiological factors, complications, and changing severity and nutritional requirements mandates that nutrition teams work closely with surgical and gastroenterological colleagues to swiftly resolve the disease process and reduce the likelihood of long-term complications.

The limitations of this and other studies, including the retrospective nature of the cohorts, and the lack of objective pain assessments and control groups, mandates future randomised controlled trials to further assess the effect of nasojejunal feeding in chronic pancreatitis.

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Conflict of interest All authors declare that they have no competing interests

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