

Module 14.2

Nutritional Support in Chronic Pancreatitis

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Learning Objectives

- To know about the physiology and pathophysiology of CP (chronic pancreatitis);
- To know the treatment goals in CP with respect to nutrition;
- To understand the indications for different nutritional interventions in CP.

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2. Pancreatic physiology
3. Pathophysiology of chronic pancreatitis
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Key Messages

- Exocrine pancreatic function is necessary for adequate digestion of ingested food;
- The major exocrine function of the pancreas is to secrete bicarbonate and digestive enzymes like lipase, proteinase, and amylase as ingested food enters the duodenum;
- CP is characterized by a progressive loss of acinar and duct cells with a consequent decline in exocrine secretions;
- The main clinical consequences of exocrine pancreatic insufficiency (noted in 25% - 45% of CP patients) are fat maldigestion and steatorrhea;
- Chronic and especially postprandial pain is a hallmark of CP (60% - 90% of patients) and is a major reason for anorexia;
- Endocrine pancreatic insufficiency (diabetes) usually develops late in the course of the disease;
- Increased energy expenditure due to chronic inflammation can cause further deterioration in nutritional status;
- Nutritional treatment is only a part of the multimodal treatment in CP, next in importance to pain control and oral pancreatic enzyme replacement;
- Nutritional assessment should be documented during follow up;

- Nutritional objectives are firstly to provide optimal energy, substrates and vitamins, and secondly to avoid causing pancreatic pain;
- Adequate substitution of pancreatic enzymes is the mainstay of nutritional care in CP patients with exocrine pancreatic insufficiency;
- Nutritional therapy should consist of a high calorie (35 kcal/kg/24 hour), high protein (1.0 to 1.5 g/kg/24 hour), and carbohydrate-rich diet with moderate amounts of fat (0.7 to 1.0 g/kg/24 hour) diet;
- Dietary modification of fat intake (e.g. medium chain triglycerides) is only necessary if pancreatic enzyme therapy fails;
- Supplementary enteral nutrition (sip- or tube-feeding) is indicated if oral feeding doesn't reach the therapeutic goals;
- During a severe acute bout of pancreatitis the patient should be treated as for acute pancreatitis (see module 14.1).

1. Introduction

The incidence of chronic pancreatitis has increased over the last 60 years (Fig. 1) and now has now an incidence of up to 10 per 100,000 person years in industrialized countries. This observation may be due to better diagnosis, but may also be due to major change in life-style in western industrialised countries. In developed countries almost 70 - 80% of CP patients have a long history of high alcohol intake (> 80 g/day). Next to alcohol, smoking seems to be an additional risk factor and it is obvious, that almost all patients with high alcohol intake are heavy smokers. Several other aetiological factors, including a genetic predisposition to CP have been identified, but despite extensive investigation, in about 20% of patients a specific cause cannot be established, and these patients are classified as idiopathic pancreatitis.

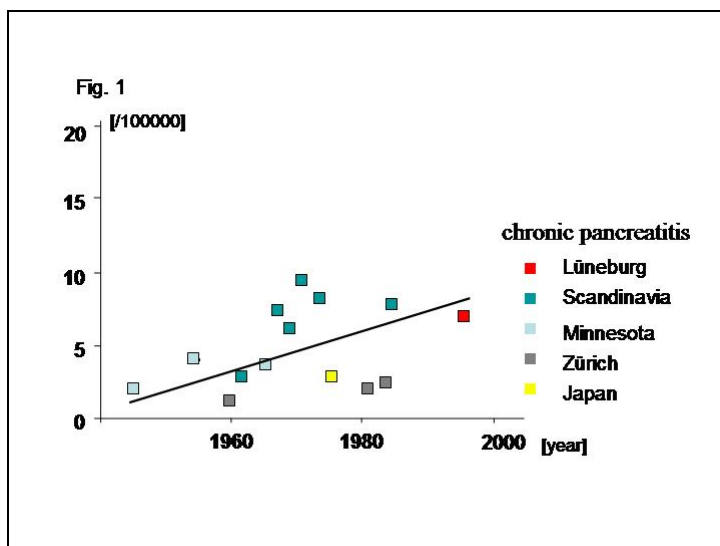


Figure 1

In the following text only the consequences and treatment of CP on the exocrine pancreas will be described. For specific treatment of endocrine pancreatic insufficiency please consult the diabetes chapter (Topic 21).

2. Pancreatic physiology

The exocrine response of the exocrine pancreas is time depend (Fig. 2) and related to several factors (Fig.3). The exocrine pancreas consists mostly of acinar, but additionally of centroacinar and duct cells. Whereas the acinar cells synthesize > 10 digestive enzymes, the duct cells are responsible for generation of bicarbonate, which is necessary to neutralize gastric acid and to raise the pH in the duodenum to obtain an optimal alkaline milieu for the pancreatic enzymes as well as for the jejunal digestive brush border enzymes.

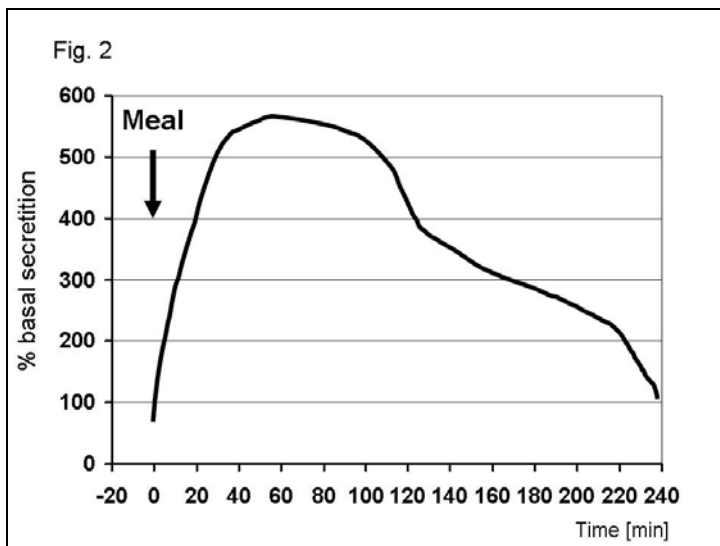


Figure 2

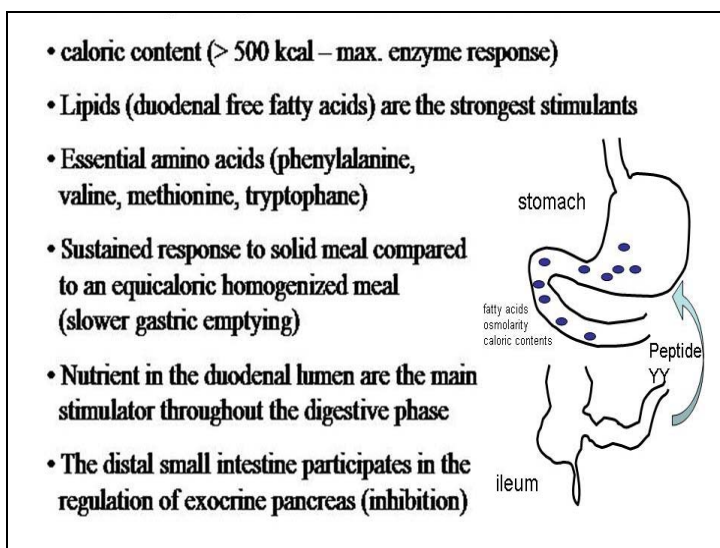


Figure 3 Factors regulating exocrine pancreatic secretion.

The vagus nerve and the hormones secretin and cholecystokinin (CCK) are responsible for stimulation of the exocrine pancreas. The pancreatic enzymes digest starch (amylase), lipids (lipase), and protein (trypsin and other proteolytic enzymes).

The most important stimulus for pancreatic secretion is the presence of nutrients in the duodenal lumen. It is not only the quantity but also the composition of nutrients in the duodenal lumen which influences the pancreatic secretory response (Fig. 3).

3. Pathophysiology of chronic pancreatitis

Due to the loss of acinar and duct cells (Fig. 4) the secretory capacity of the exocrine pancreas decreases. The large physiological reserve of the pancreas is the reason why clinical signs of fat maldigestion occur late in the course of CP, when 80 % of the secretory capacity of the pancreas has been lost.

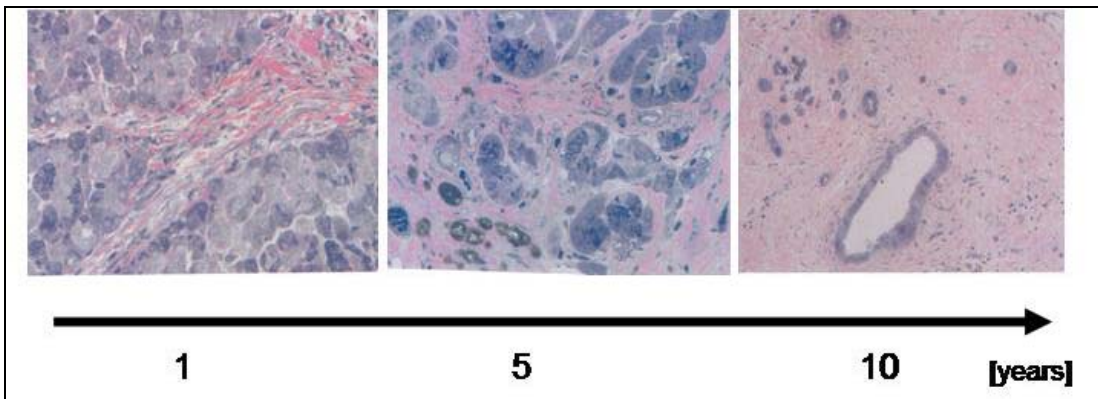


Figure 4 Loss of functional pancreatic tissue

Fat maldigestion (steatorrhea; > 10 g of stool fat per 24 hours) is the major problem in these patients. Steatorrhea is caused by (i) reduced pancreatic bicarbonate secretion leading to more rapid and complete inactivation of lipase in the acidic duodenum; (ii) further impairment of lipid absorption by bile acid denaturation within the acidic duodenum; (iii) rapid degradation of lipase in the small intestine lumen due to its greater vulnerability to proteolysis - thereby reducing the period of lipase activity ; (iv) limited capacity of extrapancreatic lipase (gastric); (v) no compensating triglyceride-digesting enzymes in the intestinal brush border. Because fat is the major source of energy, fat maldigestion not only creates a high risk of protein-energy malnutrition, but also of micronutrient and vitamin deficiency.

Creatorrhoea (>2.5 g of stool nitrogen per 24 hours) only occurs when trypsin output is less than 10% of normal. The problem with nitrogen balance studies is the difficulty of separating the contribution to nitrogen loss in the stool of ingested protein compared with that from proteins secreted into the GI tract and that derived from bacteria. The effect of enzyme supplementation on protein maldigestion has not therefore been well characterized.

As well as the increased risk of malnutrition, the increased stool volume and fat content cause abdominal symptoms such as pain, fullness, distension, diarrhea, meteorism, and flatulence. 20 - 25 % of cases with exocrine pancreatic insufficiency may also be complicated by bacterial overgrowth, which can further contribute to diarrhoea and other GI symptoms.

4. Clinical features of chronic pancreatitis

The cardinal symptom of CP is pain, which can present either as repeated mild or moderate attacks or as persistent and intractable abdominal and back pain.

The median latency between onset of first symptoms and signs of maldigestion is about 8-9 years in alcoholic chronic pancreatitis and more than 15 years in idiopathic non-alcoholic pancreatitis. In a minority of patients the clinical signs of exocrine pancreatic precede the other features of the condition.

Patients with significant steatorrhea typically report loose, greasy, foul-smelling voluminous stools, which are difficult to flush. Further clinical manifestations and complications of CP are given in Table 1.

Table 1 Chronic pancreatitis

Chronic pancreatitis: Clinical manifestation and complications
Pain (main symptom)
Los of exocrine function, with concomitant steatorrhea
Weight loss
Jaundice
Pancreatic calcification
Pancreatic pseudocyst
Splenic vein thrombosis
Loss of endocrine function, resulting in diabetes

5. Nutritional status in CP

5.1 Body weight and body composition

Weight loss occurs in those patients with maldigestion or in those with reduced food intake due to pancreatic pain. Although, weight loss is a frequent symptom in CP, only limited data on nutritional status in CP patients are available. Patients with symptomatic CP have a lower body mass index, reduced lean body mass and fat mass compared to healthy controls.

Malnutrition is associated with higher morbidity (e.g. higher incidence of postoperative complications after surgery for chronic pancreatitis). Therefore, those patients with malnutrition should be identified and treated.

Nutritional assessment is easy to perform. Weight loss over time, body mass index, anthropometry and some laboratory values are useful parameters. Furthermore, nutritional screening scores, e.g. subjective global assessment (SGA), ESPEN nutritional risk score (ESPEN-NRS; see www.espen.ch) are available for detecting those patients with nutritional deficiencies who are at risk of developing complications.

5.2 Metabolic situation

In patients with chronic pancreatitis, resting energy expenditure is increased by up to 30-50%. The loss of endocrine function in the late state of the disease also leads to glucose intolerance and eventually to frank diabetes. Glucose intolerance occurs in 40-90% of all cases with severe chronic pancreatitis during the course of disease. In 20-30% of all patients insulin-dependant diabetes develops. This is also associated with impaired glucagon release and reduced counter-regulatory capacity in the event of insulin induced hypoglycaemia.

5.3 Minerals, micronutrients and vitamins

Circulating levels of minerals, micronutrients and vitamins are reduced in CP patients with fat maldigestion, e.g. magnesium, calcium, essential fatty acids, and vitamin A, D, E, and K. In particular, vitamin D and calcium deficiencies are associated with an increased risk of osteomalacia and osteoporosis.

6 Nutrition related treatment

Due to the multifactorial nature of the nutritional problems in patients with CP, it is important to make an individual analysis of the underlying causes of weight loss in each patient before attempting treatment. Nutritional treatment is always part of a multimodal treatment plan addressing all aspects of the patient's condition.

6.1 Therapeutic goals

The goals of nutritional intervention are not only to treat established malnutrition but also to address the underlying cause. E.g. maldigestion and malabsorption, in order to prevent further malnutrition developing.

6.2 Pancreatic enzyme replacement

The administration of an adequate quantity of exogenous pancreatic enzymes is necessary to correct protein and lipid maldigestion (Fig.5). A suitable amount of lipase per meal (up to 80 000 U) is necessary to provide adequate lipolysis. There is no defined dose for these enzyme supplements. Usually, the amount of enzyme supplements needed depends on the degree of steatorrhea, not of azotorrhea. Symptomatic relief of steatorrhoea and weight control are practical endpoints for this therapy. The decrease in 72-hour faecal fat excretion is a more objective parameter, but due to the inconvenience for the patient, not so easy to handle. It is important to give the enzymes before and during the meal to ensure adequate mixing. If the enzyme treatment response is not satisfactory, the addition of an acid inhibitor (proton pump inhibitor) can be tried. Decreasing the duodenal acid load can prevent the inactivation of lipase in the small bowel. Because bacterial overgrowth is a frequent problem in advanced CP this should be considered only in those patients with treatment failure.

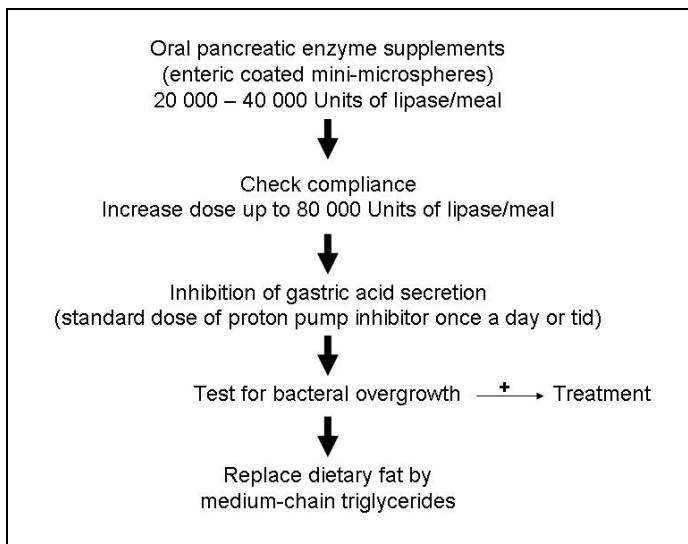


Figure 5 Treatment algorithm for exocrine pancreatic insufficiency.

6.3 Pain treatment

Pain is one of the cardinal symptoms of CP and has major impact on quality of life. Therefore, successful pain management is the first step in treatment of CP. Pain control is an essential basis for the success of other aspects of treatment including nutritional. Each patient should keep a pain diary to assist in assessing the efficacy of analgesia.

The following substances or strategies are available for pain treatment which should be individualized according to each patient's response and circumstances.

- **Analgesics.** Anti-inflammatory, non-narcotic (and therefore nonaddicting) pain medicines are tried first. If these provide no relief, narcotics or morphine may be given in addition to relieve sudden episodes of inflammation. The risk of becoming depended is low in chronic pain.
- **Tricyclic antidepressants.** These medications are synergistic with other pain medication, particularly in those patients in whom pain and depression co-exist.
- **Pancreatic enzyme supplements.** A time limited trial of pancreatic enzyme supplementation can be tried, but if no pain relief has been observed after 4 weeks, the enzymes should be stopped, unless exocrine deficiency is also present.
- **Acid reducers.** H₂-receptor-blocking medicines and proton pump inhibitors may be given along with enzymes to reduce the production of stomach acid, which can stimulate the pancreas. But again, if this is not successful after 4 weeks, the acid reducer can be stopped.
- **ERCP.** Patients with an obstructed pancreatic duct or pancreatic stones may profit from an endoscopic retrograde cholangiopancreatography (ERCP) with stone extraction or placement of a stent in the narrowed pancreatic duct.
- **Coeliac plexus nerve block.** An injection of alcohol or corticosteroids into the retroperitoneal nerves (plexus) may provide temporary relief.
- **Surgery.** Pancreatic surgery (Whipple procedure or duodenum preserving pancreatic head resection) is the last treatment option for pain in CP patients. Those patients, in particular, who have had benefit from endoscopic procedures or have a pseudo-inflammatory mass of the pancreas, seem to benefit from surgery. It has to be noted, however that surgery also has some peri- and postoperative side effects.

6.4 Diet recommendations

A normal diet should be the target goal in CP patients. In general, the patients should maintain a diet with high energy (35 kcal/kg/24 hours), high protein (1.0 to 1.5 g/kg/24hours), rich in carbohydrates, and with moderate amounts of fat (0.7 to 1.0 g/kg/24 hours). A reduction in oral fat intake or the replacement of dietary fat with medium chain triglycerides (MCT) risks a reduction in energy intake and therefore, a negative energy balance. This treatment option should, therefore, only be considered if adequate enzyme supplementation and exclusion of bacterial overgrowth has not led to a relief of and maldigestion and its

accompanying symptoms (Fig. 5). MCTs are quite foul tasting and associated with adverse effects like cramps, nausea, and diarrhoea. If MCTs are being considered, their dose should be increased slowly depending on the patient's tolerance.

Fat soluble vitamins (A, D, E, K), and vitamin B12, as well as micronutrients and minerals should be replaced as clinically indicated. This means that those patients with signs of persistent maldigestion should automatically receive multivitamin and trace element supplements, although neither this nor the effect of MCT's has been proved in clinical trials. In CP, antioxidant capacity is decreased and oxidative stress seems to be a factor promoting CP. This has been considered as a rationale for interventions with antioxidants like selenium or vitamin C or E. Although, the results of a limited number of trials with different antioxidant strategies suggest some benefit, a general recommendation cannot presently be given due to the small sample size and heterogeneity of these trials.

6.5 Role of enteral feeding

The role of enteral feeding in CP is still controversial and has not been adequately investigated in appropriate randomised studies. Possible indications for enteral nutrition are listed in table 2. However, enteral sip feeding has the potential, in patients with severe malnutrition, to improve energy and protein intake. For this purpose enteral sip feeding products based only on carbohydrates and protein are promising. But the advantage of this composition compared to a conventional composition has not been proven in clinical trials. From clinical experience, enteral feeding via a gastric or jejunal tube is seldom necessary except during acute episodes of pancreatitis. As in acute pancreatitis, experience suggests that the optimal method of feeding is via the jejunal route. In long term nutritional enteral support, this can be maintained either by a percutaneous endoscopic gastrostomy with jejunal extension or by a direct percutaneous endoscopic jejunostomy. In uncontrolled observational studies an increase in body weight as well as relief of abdominal pain and other gastrointestinal symptoms has been observed in those patients. There are also no randomized studies to investigate the efficacy of different formulas (e.g. standard or peptide based with MCT). In the presence of exocrine pancreatic insufficiency enteral formulas consisting of pre-digested products and a mixture of long chain fatty acids and MCT would seem, theoretically, to have potential advantage. The positive effect of a peptide based MCT containing formula has been shown in a small prospective uncontrolled study and a decrease in circulating cholecystokinin (CCK) levels has been proposed as a possible mechanism.

Table 2

Indications for enteral nutrition in CP

- Oral food intake is not possible due to persistent pain
- Gastric outlet syndrome due to enlarged pancreatic head or pseudocyst formation
- Acute complication (e.g. acute flare-up, fistula)
- Before and after surgery
- Progressive weight loss despite adequate medical therapy

Parenteral nutrition (PN) is only indicated, if enteral nutrition is not possible. There are no specific considerations with regard to PN in patients with CP.

7. Summary

Malnutrition is a frequent feature in patients with CP with maldigestion and pain being the two major risk factors for its development. Nutritional therapy should always be considered as an integrated part of the overall multimodal medical and surgical therapy of chronic pancreatitis. A low fat diet is often prescribed, but carries the risk of a reduced total energy intake, thereby worsening the degree of malnutrition. In addition, this strategy, therefore, only be recommended in those patients in whom pain control and enzyme

supplementation fail to resolve the gastrointestinal symptoms. Sip or enteral tube feeding are options for patients not responding to medical therapy or for those undergoing surgery.

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