Medical nutrition therapy in chronic pancreatitis

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Abstract

Chronic pancreatitis is a complex disease associated with significant morbidity and mortality. Patients with chronic pancreatitis are at risk for malnutrition and nutrient deficiency caused primarily by malabsorption, inadequate intake, and inflammation. Poor nutritional status may negatively affect disease’s outcome. Medical nutrition therapy which include screening and assessment of malnutrition followed by optimal nutritional intervention for patient at risk should be the cornerstone of chronic pancreatitis multidisciplinary treatment. The dietary recommendation for malnourished chronic pancreatitis patients is high-calorie, high-protein, and low-fiber diet delivered in small frequent meals. Oral nutritional supplements, enteral, and/or parenteral nutrition should be considered respectively in the setting of failed oral nutritional intake to meet the energy and protein requirement.

Keywords: nutrition therapy, chronic pancreatitis, malnutrition, malabsorption

Introduction

The accelerated development in medicine still could not solve pancreatic problems such as inflammation, which is to date, difficult to treat.¹ Chronic pancreatitis occurs when there are recurrent inflammation episodes followed by the development of scar tissues, creating irreversible damages and pancreatic insufficiency that could potentially cause weight loss, malnutrition, diabetes, and other metabolic disturbances.¹–³ Globally, the prevalence of chronic pancreatitis is around 50 per 100,000 individuals, with an annual incidence of 5-12 per 100,000 individuals. The demographic distribution shows that higher numbers of chronic pancreatitis occur in tropical regions such as South India with 25-125 cases per 100,000 individuals.⁴

The consistency in managing pancreatitis is still puzzling as there are no effective treatments discovered. Generally, pancreatitis treatment is supportive, with nutrition as the main pillar aimed to prevent disease’s progressivity.² To this day, there has not been enough data to support optimal medical nutrition therapy for patients with chronic pancreatitis. Administering any dietary composition for chronic pancreatitis remain controversial, as questions arise between the use of balanced or low-fat diet, long or medium-chain triglycerides...
selection, adding or eliminating fibers, and the timing of micronutrient supplement administration. The variety of nutrition therapy on chronic pancreatitis is apparent in everyday practices, and therefore requires discourse in the administration of nutrient management based on evidence and available scientific data. The aim of this review is to highlight the optimal nutrition therapy for chronic pancreatitis based on current studies and recommendations.

**Chronic Pancreatitis**

Chronic pancreatitis is a collection of symptoms that is the result of progressive chronic inflammation on the pancreas, followed by fibrosis and scar tissues, resulting in the irreversible damage and loss of exocrine and endocrine cells. Although it is triggered by different risk factors, supporting data suggest that acute pancreatitis, recurrent acute pancreatitis, and chronic pancreatitis are one continuum of a disease. The TIGAR-O classification system groups the risk factors to intertwine among toxic-metabolic, idiopathic, genetic, auto-immune, heavy acute and recurrent pancreatitis, and obstruction as the causes of chronic pancreatitis. In most cases, there are more than one etiology.

Damages on acinar cells in alcohol-induced pancreatitis is caused by the metabolite, acetaldehyde. Smoking produces toxic metabolite nitrosamine ketone that can also damage the acinar cell. Mutation and genetic vulnerability correlate with the pancreatic defensive mechanism dysfunction against autodigestive processes. An intracellular trypsin activation triggers cascading inflammation, oxidative stress, and acinar autophagy disruption. The pancreatic stellate cells activation plays a role in chronic inflammation and fibrosis in acute pancreatitis. The history of acute pancreatitis and other risk factors can trigger the activation of the immune system that can either heal or progress to chronic pancreatitis.

Different from acute pancreatitis, chronic pancreatitis continues in several years. The main clinical manifestation is recurrent pain on the epigastrium spreading to the back, with food as the trigger for exacerbation in 80% of chronic pancreatitis patients. Other symptoms such as nausea, vomiting, diarrhea, steatorrhea, and fatigue hinder patients from maintaining adequate nutrition. Complications of chronic pancreatitis can result in glucose intolerance, gastrointestinal bleeding, jaundice, cholestasis, and biliary cirrhosis. Twenty years following chronic pancreatitis diagnosis, the cumulative risk towards pancreatic carcinoma is at 4%. The diagnosis of chronic pancreatitis is established using CT-Scan or MRI. The depiction of heavy chronic pancreatitis is marked by pancreatic calcification, atrophy, and dilating or irregular ductus. The combination of endoscopic ultrasound and pancreatic function tests used to detect chronic pancreatitis at the early stage are often inaccurate and difficult to do given there are no specific biomarkers to look for. Blood pancreatic enzymes can be normal or slightly elevated in chronic pancreatitis. Elevation in bilirubin serum and alkaline phosphatase can indicate secondary cholestasis due to common bile duct stricture on chronic inflammation. Glucose intolerance can also be indicated by the increase of fasting blood sugar level. Faecal elastase, pancreas’ specific enzyme that does not degrade during transport in the gut, and jejunum biopsy can be used to evaluate patients with steatorrhea suspected as the result of pancreatitis.

Chronic pancreatitis treatment involves modifying lifestyle that relates to the exacerbation of the disease, such as alcohol consumption and smoking, pain management, restoration of digestive and absorption functions, and overcoming endocrine insufficiency. As many as 30% of patients with chronic pancreatitis require endoscopic therapy and/or surgery. Resection procedure or drainage to manage pancreatic duct obstruction due to stones, stricture or both can reduce intraductal pressure and abdominal pain.

**Nutritional aspects**

Patients with chronic pancreatitis are at high risk of experiencing malnutrition due to pancreatic insufficiency and inadequate food intake. Other nutritional problems encountered in chronic pancreatitis include altered gastrointestinal function, recurrent abdominal pain that causes suboptimal food intake, increased resting energy expenditure...
(REE) and protein requirements, impaired energy utilization, as well as excessive alcohol consumption.\textsuperscript{2,9}

Malnutrition is often found in the advanced stages of chronic pancreatitis and is influenced by the severity, duration, and underlying cause of the disease. Loss of body weight and fat-free mass in chronic pancreatitis patients, as well as sarcopenia, will lead to decreased functional capacity and quality of life. Sarcopenia is found in 17\% of patients with chronic pancreatitis and is associated with a higher risk of hospital admission. The presence of pancreatic exocrine insufficiency (PEI) also increases the risk of bone loss and osteoporosis.\textsuperscript{2}

Pancreatic exocrine insufficiency in pancreatitis characterized by maldigestion and malabsorption of macro and micronutrients from insufficient secretion of pancreatic enzymes and bicarbonate.\textsuperscript{10} Symptomatic PEI manifests if 90\% of pancreatic exocrine function is lost. Severe PEI develop between 5–10 years from the initial diagnosis in 50\% chronic pancreatitis patients. Low levels fecal elastase (<200 μg/g stool) is often used to detect PEI.\textsuperscript{6}

Diabetes mellitus (DM) type 3c or pancreatogenic diabetes is a complication that occurs in 30-50\% of cases of chronic pancreatitis. Damage and loss of endocrine cell function in islet of Langerhans as a consequence of microvascular ischemia decreases the secretion of insulin and glucagon hormones which results in instability of blood glucose levels, so that patients can experience episodes of hyperglycemia or hypoglycemia. Hypoglycemia predominantly can result from malabsorption, decreased intake, and damage to pancreatic alpha cells.\textsuperscript{11}

Non-alcoholic fatty liver disease (NAFLD) is a complication of chronic pancreatitis that often goes undetected. The mechanism underlying the occurrence of NAFLD is related to the malabsorption of essential amino acids, such as choline, which causes a decrease in plasma concentrations of apoprotein B, the main component of VLDL.\textsuperscript{2}

Deficiency of vitamins A, D, E, and K correlates with the severity of steatorrhea in chronic pancreatitis, although it also can be caused by other mechanisms, such as inadequate intake, increased requirement, and high antioxidative activity.\textsuperscript{9,10} In chronic pancreatitis, the prevalence of vitamin A, D, E, and K deficiency are 3–14.5\%, 58–77.9\%, 9–24\%, and 13–63\%, respectively. Vitamin A deficiency with clinical manifestations of night blindness has been reported in some cases of chronic pancreatitis. Secondary thiamine deficiency may be considered in alcoholic pancreatitis. In addition, PEI can also cause deficiency of folic acid, zinc, selenium, and iron.\textsuperscript{2} The protease enzymes needed to release cyanocobalamin so that it can be absorbed in the terminal ileum have decreased secretions which in the long run lead to vitamin B12 deficiency.\textsuperscript{9}

Osteopathy, including osteoporosis, osteopenia, and osteomalacia, is found in at least 25\% of cases of chronic pancreatitis and is associated with malabsorption of vitamin D and calcium.\textsuperscript{9} However, in several studies, there was no direct relationship between serum vitamin D levels and low bone mineral density. Other factors that are thought to be involved in bone demineralization are smoking, low physical activity, and chronic inflammation in pancreatitis.\textsuperscript{2}

**Nutritional assessment**

Nutritional assessment is carried out through a multi-disciplinary approach, including clinical symptoms, organ function, anthropometry, and biochemical examinations.\textsuperscript{9} The method of assessing nutritional status based on body mass index (BMI) alone is considered inadequate to predict a decrease in muscle mass and functional status. Percentage of weight loss is rated as a better indicator of malnutrition and is associated with an increased risk of surgery for chronic pancreatitis. Sarcopenia in pancreatitis is associated with increased rate of hospitalization and mortality. Nutritional assessments should detect malnutrition, sarcopenia, and micronutrient deficiencies, and identify symptoms that have the potential to cause malnutrition.\textsuperscript{2} Routine anthropometric assessment in chronic pancreatitis patients should include weight changes, BMI, body composition, and handgrip strength.\textsuperscript{12}
Macro and micronutrient deficiency screening is performed every 12 months or more frequently for severe chronic pancreatitis with uncontrolled malabsorption. Routine screening forms the basis for determining which nutritional interventions should be given. Clinical symptoms of nutrient deficiency are difficult to find early in the disease, therefore routine screening are needed to detect early signs of deficiency. Chronic pancreatitis with PEI and malabsorption manifests in altered body composition and decreased markers of nutritional biochemical status, such as albumin, cholinesterase, prealbumin, retinol-binding protein, and magnesium.2

Dual-energy X-ray absorptiometry (DXA) can be used to identify chronic pancreatitis patients with osteopathy, especially in high-risk groups. Based on the recommendations, the group of patients at high risk of osteopathy are postmenopausal women, men over 50 years of age, a history of fractures due to minor trauma, and malabsorption. In patients with osteopenia, DXA examinations should be performed periodically every two years.11

Medical Nutrition Therapy

The main objective of medical nutrition therapy is to provide optimal nutritional support and reduce pain by minimizing exocrine stimulation of the pancreas. If post-prandial pain is a limiting factor for intake, administration of enteral nutrition therapy with minimal effect on elevated CCK levels may be an alternative. Nutritional counselling, administration of antioxidants, and pancreatic enzymes have a role in the effective management of chronic pancreatitis.8

Patients with chronic pancreatitis do not need dietary restrictions especially regarding fat intake, unless accompanied by symptoms of uncontrolled steatorrhea. A balanced diet is consistently recommended in patients of normal nutritional status. In patients with chronic pancreatitis and malnutrition, administration of 33% of energy derived from fat was well tolerated, and had an effect on improving nutritional status and pain control. The provision of a diet high in protein and energy in 5–6 small meals a day is also recommended in this patient group.2 Calorie needs are estimated to be up to 35 kcal/kg/day, with optimal protein administration of 1–1.5 g/kg/day and fat of 0.7–1 g/kg/day.13 On the other hand, high fiber consumption should be avoided because it is associated with worsening symptoms of flatulence and steatorrhea, and may interfere with pancreatic enzyme replacement therapy (PERT).2

As many as 20% of cases of chronic pancreatitis require oral nutritional supplementation (ONS) which is indicated in malnourished patients who are unable to meet the target calorie and protein needs through oral intake. In the presence of PEI, enteral formulas containing hydrolyzed nutrient components and a mixture of long-chain triglycerides (LCT) and medium-chain triglycerides (MCT) can be useful, because MCT absorption does not depend on lipase activity. However, substitution of fat in the diet with MCT has the potential to reduce energy intake due to its side effects, such as nausea and diarrhea. In patients treated with PERT, the use of the MCT formula was not considered superior to LCT.2

In general, dietary counselling and ONS administration are sufficient to improve the nutritional status of most patients with chronic pancreatitis. Enteral nutrition (EN) is indicated in 5% of malnourished patients who do not respond to ONS. Enteral nutrition therapy should be administered via the nasojejunal tube in patients with abdominal pain, delayed gastric emptying, persistent nausea and vomiting, and gastric outlet obstruction (GOO). Long-term jejunostomy access, percutaneous endoscopic gastrostomy with jejunal extension, direct percutaneous endoscopic jejunostomy, or surgical jejunostomy can be used when administering EN for more than 30 days. Semi-elemental formulas with MCT content can be selected if the standard formula cannot be tolerated. Pancreatic enzyme supplementation with EN should be given to patients with signs of exocrine failure.2

Another important benefit of EN is the maintenance of intestinal mucosal function and integrity. Parenteral nutrition (PN) is associated with an increased risk of hyperglycemia, infection, and sepsis, so it is only indicated in patients with GOO, complications of fistulas, or EN intolerance. The recommended route for PN administration is via central venous access.2 If total PN is indicated, intravenous administration of lipids and glucose
should not exceed 1.5 g/kg and 5 mg/kg/min, respectively.\textsuperscript{13}

Fat-soluble and water-soluble vitamins, such as vitamin B\textsubscript{12}, folic acid, thiamine, as well as minerals such as magnesium, iron, selenium, and zinc need to be evaluated and supplemented if deficiency is proven clinically or biochemically. To prevent osteopathy in chronic pancreatitis, several approaches can be taken, such as adequate calcium and vitamin D administration, PERT if indicated, regular weight training, and avoidance of smoking and alcohol. In patients with osteopathy, 800 IU of vitamin D and 500–1000 mg of calcium daily supplementation are recommended.\textsuperscript{2}

In chronic pancreatitis accompanied by PEI based on clinical diagnosis or investigation, it is recommended to initiate PERT. The goal of PERT is to improve symptoms of maldigestion and maintain body weight. Enteric-coated microsphere preparations protect the lipase, amylase, and protease enzymes mixture from gastric acid, so they can disintegrate at pH >5.5 in the duodenum. The efficacy of pancreatic enzyme supplements depends on the process of mixing enzymes and chemicals. The optimal timing of enzyme administration is during or after meals. The minimum dose of lipase is 20,000–50,000 PhU with large meals and half the dose with snacks. The efficacy of PERT can be evaluated through improvement of gastrointestinal symptoms and nutritional parameters, such as anthropometry and biochemistry markers. In patients who show no improvement, evaluation of pancreatic function by fecal fat excretion or breath test should be done. If there is still an inadequate clinical response, the PERT dose can be increased or accompanied by administration of proton pump inhibitor. If these methods fail, other causes of malabsorption such as small intestinal bacterial overgrowth should be ruled out.\textsuperscript{2}

Dietary counselling plays an important role in disease management. Chronic manifestations of nausea and vomiting can be reduced by a number of methods, such as eating dry food, drinking water several hours before or after meals, small frequent feedings, and avoiding consumption of alcohol or foods that have the potential to produce gas. In patients with PEI, diet containing MCT can be consumed along with simple carbohydrates to reduce unpleasant taste. In patients with pancreatogenic DM, it is necessary to control carbohydrate intake to prevent hyperglycemia.\textsuperscript{13}

**Conclusion**

Pancreatitis, characterized by chronic inflammation of the pancreas, is a prevalent disease associated with a significantly increased risk of malnutrition. Several mechanisms that occur due to inflammation and dysfunction of the pancreas underlie the changes in metabolism and nutritional status of patients with pancreatitis. A comprehensive nutritional assessment performed in a patient with pancreatitis can form the basis for a comprehensive management decision. Medical nutrition therapy is a vital component in the management of chronic pancreatitis which focuses on providing proper and optimal nutrition, both macro and micronutrients to increase food intake, reduce symptoms of pain and malabsorption, and prevent further damage to the pancreas.

**Conflict of Interest**

Authors declared no conflict of interest regarding this article.

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**References**


2. Arvanitakis M, Ockenga J, Bezmarevic M, Gianotti L,


