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A Practical Guide to the Nutritional Management of Chronic Pancreatitis

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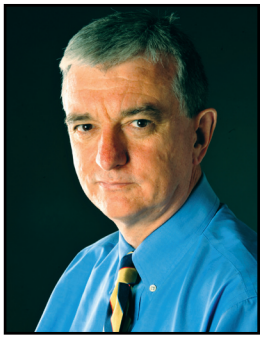

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Chronic pancreatitis is a progressive inflammatory disease that results in the irreversible deterioration of exocrine and endocrine function. Although research is limited, patients with chronic pancreatitis are deemed at high risk for malnutrition. Typical complications include maldigestion, malabsorption, abdominal pain, vitamin deficiency and poor bone health. The disease may be further complicated by the development of pancreatogenic (type 3) diabetes. Nutritional problems are exacerbated by poor dietary intake, pain, and possibly alcoholism. The aim of this review is to present the available evidence, highlight areas with recently published research, and to provide a framework for the management of patients with this nutritionally-challenging disease.

INTRODUCTION

Chronic pancreatitis (CP) results in progressive exocrine and endocrine dysfunction, thereby affecting the normal digestion, absorption, and utilization of nutrients. The nutrition research in pancreatitis has centered on acute pancreatitis, probably due to its life-threatening nature. In comparison, much of the evidence relating to nutrition in CP (with the exception of pancreatic enzymes) is older and of lower quality. Consequently, the available guidelines are similarly acute pancreatitis-focused. However, the lack of research does not mean that nutrition is of little consequence in CP. In fact, the opposite is true, and nutrition in CP has been described as a 'problem area'.[1] Issues of concern include vitamin deficiency, osteoporosis, brittle diabetes and malabsorption – all of which increases morbidity and affect patients' quality of life (QOL). As alcohol is a major etiological factor in CP, the effects of excess alcohol intake on nutritional competency may also be considerable.

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Pancreatic Exocrine Insufficiency

Assessing pancreatic exocrine function

A progressive loss of the exocrine acinar cells in CP results in the reduced production and secretion of pancreatic enzymes thereby causing nutrient maldigestion and malabsorption. Malabsorption of all macronutrients occurs, however fat malabsorption tends to be the most clinically evident. Gross fat malabsorption resulting in overt steatorrhea may only occur late in the disease

Table 1. Alternative Causes of PEI / Factors Affecting FE-1 Results

- Secondary PI resulting from primary gastrointestinal diseases
  - Autoimmune enteropathy
  - Indeterminate enteropathy
  - Post-infectious enteropathy
  - Tufting enteropathy
  - Food sensitive enteropathy
  - Food allergy without enteropathy
  - Short gut syndrome with enteropathy
  - Idiopathic inflammatory bowel disease (Crohn's disease)
- Surgical resection
  - Total pancreatectomy
  - Gastrointestinal and pancreatic surgical resection (e.g. gastrectomy or pancreaticoduodenectomy)
- Obstruction of the main pancreatic duct (e.g. pancreatic and ampullary tumours)
- Acid-mediated inactivation of pancreatic enzymes (e.g. Zollinger-Ellison syndrome)
- Decreased pancreatic stimulation (e.g. celiac disease)

process. Other symptoms of malabsorption which are less obvious are bloating, flatulence, failure to maintain/gain weight, nausea, and abdominal pain. Bloating and wind may be due to the passage of undigested carbohydrate into the colon, where fermentation by the colonic flora results in unacceptable symptoms. For the formal evaluation of exocrine function, there are both direct and indirect tests.[2] The secretin-pancreozymin test is the gold standard, but is time consuming, invasive and expensive. Indirect tests exist to measure the degree of fat malabsorption with varying effectiveness and practicality. The most accurate method is the 72-hour fecal fat study, which requires the consumption of 100 gram fat/day diet ideally, with a fairly accurate record of fat ingested during the 72-hour stool collection period.[3] However this is impractical, costly and painstaking, and therefore substitute tests for fat malabsorption are desired.[4] Pancreatic elastase-1 (fecal elastase-1, or FE-1) is a human-specific enzyme that is not degraded during intestinal transit, is enriched 5-6 fold in the faeces, and is therefore a good test of pancreatic exocrine function.[2] The fact that the ingestion of enzyme preparations do not interfere with the test, and that pancreatic enzyme replacement therapy (PERT) does not need to be interrupted for the purposes of testing pancreatic function adds to its practicality. While the test is not sensitive enough to adequately detect mild pancreatic exocrine insufficiency (PEI), it is highly sensitive for the determination of moderate-to-severe PEI.[5] Importantly, the patient does not need to ingest a specific substrate (i.e. fat) for its measurement, adding to its clinical application. A FE-1 level of <100 µg/g indicates severe PEI, and 100-200 µg/g indicates moderate PEI. FE-1 levels should be appraised in the context of a full clinical evaluation. See Table 1 for factors that may alter FE-1 results.

Pancreatic Enzyme Replacement Therapy (*PERT*)

A reduction in steatorrhea, along with adequate energy intake, are two of the most important principles of treatment for CP, and PERT is the mainstay of treatment for PEI.[6] PERT can be used to treat steatorrhea as well as the symptoms listed above, and is cost-effective[7] and safe.[8-9] Several recent randomized controlled trials have demonstrated an increase in fat and nitrogen absorption

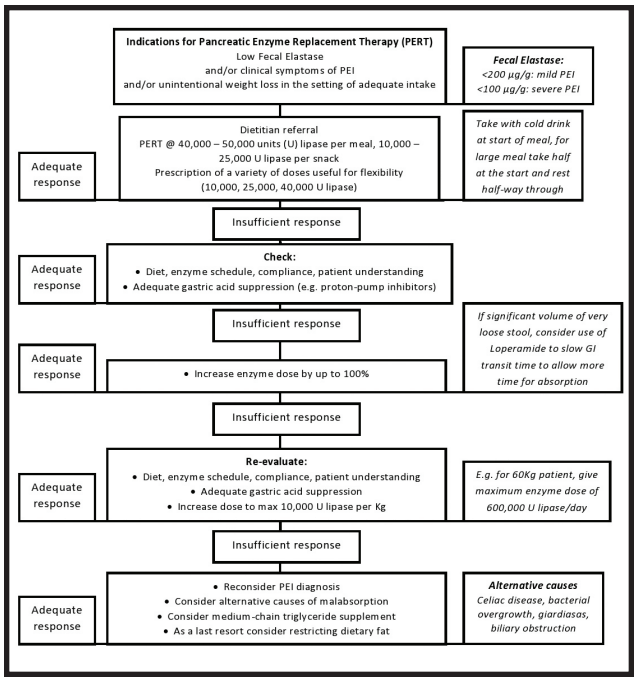

Figure 1. Algorithm for Pancreatic Enzyme Replacement Therapy in Chronic Pancreatitis[11-14]

Adapted with permission Centre for Pancreatico-Biliary Diseases, Tallaght Hospital, Dublin, Ireland, 2013.

for those taking PERT (up to 80,000 units [U] lipase with main meals) compared to a placebo.[8-9] Improvement in stool frequency, stool weight, abdominal pain and flatulence were also reported.

Guidelines for PERT

Patients with PEI tend to be undertreated, and PERT under-prescribed.[10] It is usually advisable to start with a dose of 40,000-50,000 U lipase per meal and 10,000 - 25,000 U lipase per snack,[11-12] and to increase in a stepwise manner depending on the patient's response [11-13] to an upper limit [14] of 10,000 U lipase / Kg body weight. Suppression of acid is often required[11] as pancreatic enzymes are denatured at a low pH. It is important to note that all but one of the pancreatic enzymes on the market are enteric-coated and meant to pass through the stomach unharmed to be released in the small bowel where the pH is much higher, the bicarbonate levels of patients with significant pancreatic insufficiency may be inadequate to allow release of the enteric-coated without the addition of acid suppression therapy. A detailed list of FDA approved enzymes and factors that may decrease the response to PERT was published in an article on nutrition in cystic fibrosis.[15]

Regular, detailed dietary assessment is vital to ensure appropriate and adequate usage and to improve patients' compliance. Intervention by a dietitian is considered essential.[14, 16] Figure 1 details the management of exocrine insufficiency in CP.

Type 3 Diabetes

Diabetes complicates CP in 30-50% of cases.[17] The pancreatogenic diabetes that develops in CP is termed type 3 (or type 3c), and is frequently misclassified as type 1 or 2, but is distinctly different from both of these.[18] Typically, those with type 3 diabetes are older than those with type 1, but not type 2 diabetes. They have lower BMI than in type 2 diabetes.[19] Many patients with type 3 diabetes have difficulty with labile glucose control. Hyperglycemia is frequent due to unsuppressed hepatic glucose production. Hypoglycemia is common due to enhanced peripheral insulin sensitivity and a decrease in glucagon production.[19] The risk of hypoglycemia is similar to that of type 1 diabetes, exacerbated in pancreatogenic diabetes by poor diet, malabsorption and, for some patients, persistent alcoholism.[18] There has been little guidance for the management of this diabetes subgroup to date. Nevertheless, the prevention of episodes of hypoglycaemia must be a priority of care, as well as a reduction in erratic swings in glucose control. Table 2 details the key principles of management and suggested strategies for patients with type 3 diabetes.

Fat Soluble Vitamin Deficiency

Guidelines on the nutritional management of CP advised that fat-soluble vitamin deficiency is common in chronic pancreatitis.[20-21] However, the studies to support this were mostly published in the 1980's and 1990's.[22-23] A recently-published study[24] reported a lower deficiency prevalence for vitamin A (3%) and vitamin E (10%). As deficiency of fat-soluble vitamins appears to have a variable prevalence, biochemical assessment of serum fat-soluble vitamin levels is advised and 'blind', routine supplementation should be avoided. There is little guidance on dosage for fat-soluble vitamin replacement for those who have detectable clinical or subclinical deficiencies, again due to a gap in the research. For patient with CP, one could take guidance from the recommendations for adults with cystic fibrosis[15], however caution is advised, particularly in the administration of mega-doses of fat-soluble vitamins.

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Vitamin D And Bone Health

Patients with CP may have low serum 25OHD (vitamin D) levels compared to controls[25], resulting in reduced absorption of dietary calcium and thereby negatively affect bone mineral density. However, vitamin D deficiency is just one of several risk factors for the development of osteoporosis in CP. Smoking, poor physical activity, poor diet and malabsorption all contribute to bone demineralization. Studies have reported a high prevalence of osteopathy (osteoporosis and osteopenia) in CP, ranging from 39%[26] to 74%[27]. The American Gastroenterological Association has recommended that patients with gastrointestinal conditions (inflammatory bowel disease, celiac disease and post-gastrectomy) should have a bone density assessment (by dual-energy X-ray absorptiometry, DXA) if they have at least one additional osteoporosis risk factor.[28] Therefore, as the risk of osteoporosis[27] and fracture[29] is at least as high in CP as in other gastrointestinal conditions, the same recommendations could apply. It seems prudent to request a DXA scan for those who have had a previous low-trauma fracture, are post-menopausal, >50 years for men, and / or have intractable malabsorption. Basic preventative measures should also be applied, including adequate dietary calcium and vitamin D (not only repletion where levels are low, but follow up to ensure serum levels are actually repleted), regular weight-bearing exercise, and smoking / alcohol avoidance.

Antioxidant Therapy

Pain is a major problem for patients with CP, for which there is no effective medical treatment. Pain may be at a debilitating level, greatly affecting QOL. The theory that free radical-induced pancreatic damage resulting in intractable pancreatic pain may be alleviated by taking a combined antioxidant preparation (selenium, beta-carotene, L-methionine, vitamin C and vitamin E) showed some initial promise. Improvements were demonstrated in QOL, pain and working days lost with the administration of a commercial antioxidant.[30] However, a more recent trial showed that despite an increase in blood antioxidant levels, there was no increase in QOL, nor was there a reduction in pain in an antioxidant treated group compared to the placebo group.[31] More research is required before definitive clinical recommendations can be made.

Diet And Oral Nutritional Supplements

The ongoing disease process in CP increases the requirement for nutrition. Resting energy expenditure is higher than normal by 30-50% and highest in the underweight and septic patient.[32-33] Consequently, a high calorie intake (35 kcal/Kg/day) is recommended.[21]

Table 2. Suggested Principles of Management and Management Strategies for Type 3 Diabetes in Chronic Pancreatitis

Principles of Management	Management Strategies
Prevent:	• Do not skip meals
• Hypoglycemia	• Take small, frequent meals
• Hyperglycemia	• Measure glucose levels frequently, particularly after physical activity, and if diet is poor
• Exacerbation of malnutrition	• Avoid alcohol
• Co-morbidities associated with diabetes (e.g. retinopathy, renal disease)	• Ensure adequacy of enzyme therapy
	• Minimize high-sugar/ high-glycemic index food or fluids
	• Consider a diary to record diet, glucose levels, enzymes, exercise, at least until acceptable glucose control is maintained
	• Dietitian assessment/ monitoring

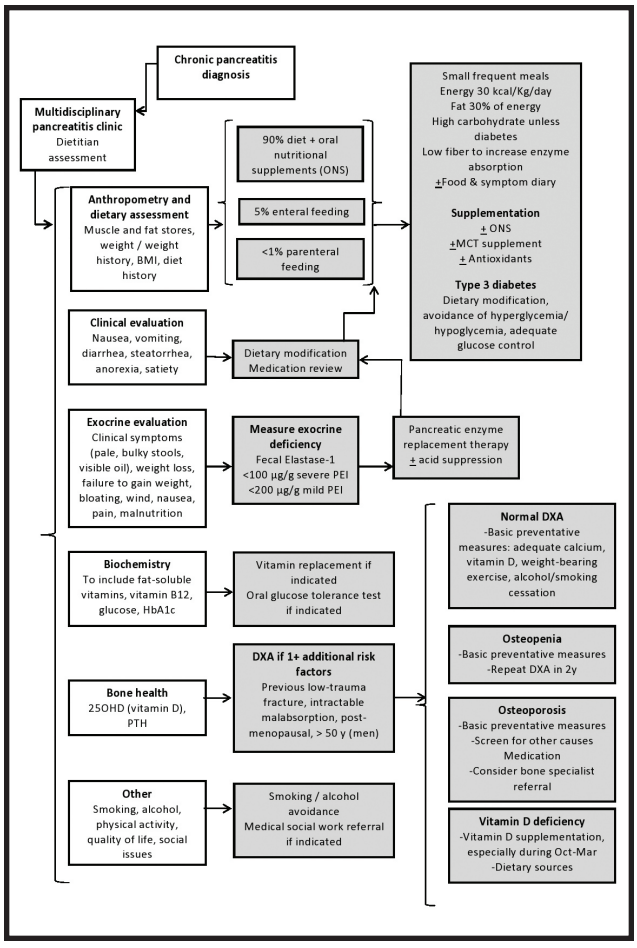

Figure 2. Algorithm for the Nutritional Management of Chronic Pancreatitis

Adapted and modified with permission from Duggan et al. Nutritional treatment of malnutrition and deficiency in chronic pancreatitis. Nutrition in Clinical Practice, 2010: 25 (4) 362-370.

Thirty percent of calories may be given as fat. Low-fat diets are neither palatable nor necessary and are not recommended. Rather, adequate PERT should be provided to allow for a moderate fat intake. There is no evidence that vegetable fat is better tolerated than animal fat.[20] A protein intake of 1-1.5 g/Kg/day should be provided.[21] In general, a high carbohydrate diet is recommended, although caution is advised in the diabetic patient. A high fiber diet may reduce the efficacy of pancreatic enzymes and therefore fiber intake should be reduced if enzyme therapy is suboptimal.[20, 34] Frequent meals of low volume are advised. Oral nutritional supplements (ONS) may be required for some patients.[21] Whole-protein ONS should be tried first before progressing to medium-chain triglyceride (MCT)-enriched or peptide-based ONS. MCTs require minimal digestion and are absorbed even in the absence of pancreatic lipase. However, they can cause cramps, nausea and diarrhoea, and may be unpalatable, and therefore should be increased slowly according to tolerance, and monitoring is advised. Food sources of MCT include coconut oil and palm kernel oil.

Nutrition Support

Enteral nutrition will be required for about 5% of patients.[21] Indications include the inability to ingest sufficient calories, weight loss despite apparently adequate diet, in the presence of acute complications (such as acute pancreatitis), and pre-surgery. Long-term jejunal feeding in selected patients may result in significant weight gain and a decrease in pain, with minimal complications.[35] Parenteral nutrition is necessary in < 1% of cases.[21] Indications include gastric outlet obstruction and jejunal access is unachievable, complex pancreatic fistulae, and in the severely malnourished patient pre-surgery, where enteral feeding is not possible.

CONCLUSION

Patients with CP have many risk factors for the development of malnutrition and nutrient deficiency. It is crucial that a standardized, evidence-based framework is followed when assessing and managing the nutritional issues for this disease. Figure 2[20] provides such a framework so that the nutritional competency of patients may be optimized. The role of the pancreatic dietitian is vital in the management of this challenging group. ■

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