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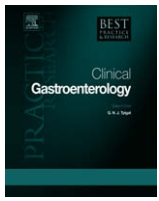

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Tests of pancreatic exocrine function – Clinical significance in pancreatic and non-pancreatic disorders

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The pancreas functions as the main factory for digestive enzymes and therefore enables food utilisation. Pancreatic exocrine insufficiency, partial or complete loss of digestive enzyme synthesis, occurs primarily in disorders directly affecting pancreatic tissue integrity. However, other disorders of the gastrointestinal tract, such as coeliac disease, inflammatory bowel disease, Zollinger-Ellison syndrome or gastric resection can either mimic or cause pancreatic exocrine insufficiency. The overt clinical symptoms of pancreatic exocrine insufficiency are steatorrhoea and maldigestion, which frequently become apparent in advanced stages. Several direct and indirect function tests are available for assessment of pancreatic function but until today diagnosis of excretory insufficiency is difficult as in mild impairment clinically available function tests show limitations of diagnostic accuracy. This review focuses on diagnosis of pancreatic exocrine insufficiency in pancreatic and non-pancreatic disorders.

Introduction

For centuries the pancreas was a *terra incognita* hidden behind the stomach and its pathophysiological role remained in the dark. Only in 1761 Jean-Baptista Morgagni described in his book "*de sedibus*

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et causis morborum'' the first case of chronic pancreatitis and it took 60 more years until Kuntzmann was able to connect fatty stool to diseases of the organ. Exocrine insufficiency usually results from reduced enzyme synthesis and secretion of the pancreatic juice which consists of a mixture of diverse proteases, lipase, amylase and bicarbonate, or from impaired enzyme function [1,2]. However, other mechanisms may also cause or contribute to pancreatic exocrine insufficiency (Table 1). Usually, clinically overt symptoms such as steatorrhoea and weight loss occur late in the clinical course of pancreatic disease as the exocrine pancreas has a high reserve capacity and symptoms arise only when functional reserve is spent by 90% [3]. Recognition of exocrine insufficiency is highly important to avoid complications of maldigestion with its related morbidity and mortality.

Pancreatic exocrine insufficiency

Pathophysiology and clinical symptoms

Steatorrhoea and azotorrhoea, an excessive discharge of nitrogenous substances in the feces, occur when secretion of lipase and trypsin fall below 5–10% of normal levels. In chronic pancreatitis, fat malabsorption develops earlier than malabsorption of proteins or carbohydrates. This is due to an earlier decrease in lipase secretion compared with amylase and proteases [5], higher susceptibility of lipase to acidic pH caused by concomitant impairment of bicarbonate secretion, higher susceptibility of lipase to proteolytic destruction during small intestinal transit, additional acidic denaturation of bile acids and marked inhibition of bile acid secretion in malabsorptive states [6]. Moreover, gastric lipase, the only extrapancreatic source of lipolytic activity in humans, does not compensate for pancreatic lipase deficiency efficiently although it may be elevated in patients with chronic pancreatitis compared to healthy individuals [7]. By contrast, more than 80% of carbohydrates can be digested and absorbed in the absence of pancreatic amylase activity [8] and the colonic flora can further metabolise malabsorbed carbohydrates. In consequence, stools usually do not contain carbohydrates [8].

In Western countries steatorrhoea is diagnosed when daily stool fat content exceeds 7 g during ingestion of a diet containing 100 g fat per day. This corresponds to a decrease of the enteral absorption rate to less than 93% [9]. Often steatorrhoea is accompanied by diarrhoea. This is partly caused by accelerated gastric emptying and intestinal transit in patients with exocrine insufficiency that can also be reversed by enzyme supplementation [10].

Fat excretion of patients with pancreatic steatorrhoea frequently exceeds that of patients with other causes of steatorrhoea such as coeliac disease, inflammatory bowel disease, or short bowel syndrome, with the exception of cystic fibrosis. Leaking oily stool from the anus is virtually pathognomonic of chronic pancreatitis. In general, weight loss is a cardinal symptom of pancreatic exocrine insufficiency with steatorrhoea, whereas hypoproteinemia or malabsorption of fat-soluble vitamins is less common. Overt steatorrhoea occurs in approximately 30% of patients with chronic calcific pancreatitis. Mild to

Table 1
Pancreatic and extrapancreatic mechanisms of exocrine insufficiency [6].

Loss of functioning parenchyma
• Chronic pancreatitis
• Cystic fibrosis
• Pancreatic tumours
• Pancreatic resections
• Diabetes mellitus?
Decreased secretion despite intact parenchyma
• Obstruction of pancreatic duct (tumour of the papilla)
• Decreased endogenous stimulation (coeliac disease, Crohn's disease, diabetes mellitus)
• Intraluminal inactivation (Zollinger-Ellison syndrome, tetrahydrolipstatin)
Post-cibal asynchrony
• Gastric resections
• Short bowel syndrome
• Crohn's disease? Diabetes mellitus?