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REVIEW ARTICLE

Diagnosing exocrine pancreatic insufficiency after surgery: when and which patients to treat

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Abstract

Exocrine pancreatic insufficiency (EPI) is a common problem after surgery of the pancreas and stomach. It is usually caused by inadequate pancreatic enzyme activity resulting from insufficient enzyme production, insufficient enzyme activation or disturbed enzyme deactivation. A variety of direct and indirect pancreatic function tests such as the secretin–cerulein test, the faecal elastase test and the ^{13}C-mixed triglyceride breath test are used to assess exocrine pancreatic function. Few studies have addressed pancreatic enzyme replacement therapy (PERT) following pancreatic surgery. These studies suggest beneficial effects of enzyme replacement after pancreatic resections. A number of studies have been performed to assess post-gastrectomy maldigestion and PERT. The treatment options remain controversial, although the published evidence is in favour of PERT leading to an overall improvement of symptoms. In conclusion, EPI following pancreatic surgery and total or partial gastrectomy remains a common clinical challenge. As a result of the lack of solid evidence, more clinical trials, particularly randomized, controlled clinical trials, are urgently needed.

Keywords

exocrine pancreatic insufficiency, pancreatic function tests, maldigestion, pancreatic enzyme replacement therapy, pancreatin

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Introduction

Exocrine pancreatic insufficiency (EPI) is a common clinical problem after pancreatic or gastric surgery.[1] It is defined as inadequate pancreatic enzyme activity for digestion, caused by insufficient enzyme production, insufficient enzyme activation or disturbed enzyme deactivation.[2] Other than post-surgery patients, EPI mostly affects infants and children suffering from cystic fibrosis, Shwachman–Diamond syndrome or pancreatic agenesis. In adults, the aetiology is diverse, with the underlying diseases being acute or chronic pancreatitis, pancreatic neoplasms, pancreatic resections (partial or total pancreatectomy), short bowel syndromes, hereditary haemochromatosis and partial or total gastrectomy. Importantly, elderly patients newly diagnosed with symptoms of EPI should undergo an immediate check-up for pancreatic cancer, particularly if co-morbid diabetes mellitus has also been newly diagnosed.[3] The symptoms of EPI are maldigestion or malabsorption and, specifically, malnutrition with weight loss, steatorrhoea, vitamin deficiencies (especially of vitamins A, D, E, K) and, of course, diabetes mellitus, which in turn may also be a cause of EPI.

Pancreatic function tests

The diagnosis of EPI is made by either direct or indirect pancreatic function tests (Table 1).[4,5] The cholecystokinin (CCK) test, the secretin test, the secretin–CCK test, the endoscopic pancreatic function test and the Lundh test are direct tests potentially available in clinical practice.[6] In the CCK test, the patient receives CCK or an analogue, and enzymes are collected using a duodenal tube during an 18-min test period.[7] The disadvantage of this test is that the determination of perfusion markers requires a specialized laboratory. The secretin test also makes use of a double-lumen gastroduodenal tube with which samples are collected at 15-min

Table 1 Summary of direct and indirect pancreatic function tests

Tests	Disadvantages
Direct tests	
CCK	Requires specialized laboratory
Secretin	1-h collection
Secretin–CCK	Potential for diluted, unreliable enzyme collections
Endoscopic pancreatic function	None
Lundh	Confounded in small bowel mucosal diseases
Indirect tests	
Faecal elastase-1	Poor sensitivity for early EPI
24-h and 72-h stool fat	Often inadequate patient compliance
Secretin-enhanced MRI	Limited assessment
Serum/urine pancreolauryl	Limited in bile salt deficiency, coeliac disease, renal failure and post-gastrectomy
^{13}C-mixed triglyceride	Currently under evaluation

CCK, cholecystokinin; EPI, exocrine pancreatic insufficiency; MRI, magnetic resonance imaging

intervals during a 1-h period after secretin simulation.[4,8] This test is relatively easy to perform and constitutes one of the most frequently used tests in the clinical setting. In addition, the secretin–CCK test can be performed; however, the secretin-induced rapid water flow may result in diluted and unreliable enzyme collections. In addition to these classical tests, the endoscopic pancreatic function test is sometimes used, with endoscopic aspirations at 0, 15, 30, 45 and 60 min. This test has recently attracted considerable clinical attention because it is preferred by many patients for the greater comfort with which it can be performed compared with other tests, and the availability of standardized endoscopy.[9] The Lundh test, in which a duodenal tube is necessary, is usually confounded in patients with small bowel mucosal diseases and is more complicated to carry out because it requires a liquid test meal as a stimulus.[10–12] However, these direct pancreatic function tests are less comfortable for the patient and therefore indirect pancreatic function tests are considered to be more acceptable to patients and their doctors.

The faecal elastase-1 test remains one of the most frequently used indirect tests in the clinical setting, although it has a poor sensitivity for early pancreatic insufficiency.[13,14] However, it is highly sensitive and specific for advanced EPI and is easily performed. The 24-h and 72-h stool fat tests are often affected by inadequate patient compliance and are therefore rarely used. In addition, there are novel indirect tests that have not yet been extensively studied, such as the secretin-enhanced magnetic resonance imaging test. The classical serum or urine pancreolauryl tests, which measure intraluminal pancreatic enzyme function, are limited in patients with bile salt deficiency, coeliac disease, renal failure and post-gastrectomy symptoms, and are therefore also being abandoned in the clinical setting.[15] Most recently, the ^{13}C-mixed triglyceride breath test has attracted considerable clinical attention and is being evaluated in clinical studies. Its results are promising; the test is simple and its findings are reliable.[16–19]

Treatment options

The therapeutic options for the treatment of EPI involve, firstly, nutritional changes, which include a high-carbohydrate diet, a normal fat diet and, optionally, medium-chain triglycerides, consumed in several (five to seven) small meals.[20] These changes are easily implemented and can be recommended for most patients suffering from EPI following surgery of the pancreas or stomach.

In addition, pancreatic enzyme replacement therapy (PERT) may be provided orally; the dose can be adapted to meals and should not fall below 25 000–50 000 units (U) of lipase/meal. As lipase is irreversibly deactivated by gastric acid, patients receiving uncoated enzyme preparations may require simultaneously administered proton pump inhibitors (PPIs).[21] Omitting PPIs is common because many patients are not aware of the importance of these drugs in conjunction with uncoated enzyme formulations. Enteric-coated enzyme preparations are resistant to gastric acid and in the majority of patients do not require concomitant PPI administration; however, in patients with EPI who have an incomplete response to PERT, the addition of a PPI may significantly improve and even normalize fat digestion.[21] To prevent low vitamin levels, especially in patients with severe diarrhoea, liposoluble vitamins (A, D, E, K) must be parenterally substituted.

Clinical considerations

Acute pancreatitis

Following acute pancreatitis, the incidence of EPI mostly depends on the severity of the attack, but it occurs in up to 86% of patients who have suffered from severe acute necrotizing pancreatitis.[22,23] Furthermore, the severity of the disease is not only associated with EPI, but, of course, also with endocrine pancreatic insufficiency.

Post-pancreatectomy EPI

Exocrine pancreatic insufficiency is common following pancreatic resections, including classical or pylorus-preserving Whipple