Pancreatic Dyspepsia: A Place for Pancreatic Insufficiency in Dyspepsia*

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ABSTRACT

Dyspepsia refers to a condition of impaired digestion which has a yearly incidence of approximately 1%, and the prevalence of around 20-30%. Although the etiology of dyspepsia varies, an organic cause is found in only 40% of the patients. In the differential diagnosis of dyspepsia, cardiac, hepatobiliary, pancreatic, and intestinal disorders and gastroesophageal reflux disease can be eliminated as non-gastric causes. Inhibition of gastric acid secretion with proton pump inhibitors, use of an antidepressant drug in functional dyspeptic patients and prokinetics drugs are the approaches generally used in the treatment of dyspepsia regardless of the presence of gastric or non-gastric causes. Sometimes, despite all efforts, treatment of dyspepsia is unsuccessful. In those patients, pancreatic enzyme deficiency should be kept in mind and enzyme replacement therapy should be given.

Key words: Dyspepsia, Pancreas, Pancreatic insufficiency, Enzyme replacement therapy

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Dyspepsia (from the Greek dys "mal or impaired" and pepsis "digestion") refers to a condition of impaired digestion. According to the Rome III Consensus Conference, dyspepsia is described as pain and discomfort in the upper abdomen. Postprandial discomfort is described as early fullness, postprandial bloating, epigastric pain, and discomfort. The yearly incidence of dyspepsia is approximately 1%, and prevalence is 20-30%. While dyspepsia accounts for 40-70% of all gastrointestinal complaints, it is a very frequent complaint, seen in 4-8% of the patients who admit to primary care centers. Although the etiology of dyspepsia varies, an organic cause is found in only 40% of dyspeptic patients. Organic causes include peptic ulcer disease (15-25%), reflux esophagitis (5-15%), and gastric or esophageal cancer (< 2%). The other rare organic causes of dyspepsia are biliary tract disorders, gastroparesis, pancreatitis, carbohydrate malabsorptions (lactose, sorbitol, fructose, mannitol), drugs [acarbose, alcohol, alendronate, oral antibiotics such as erythromycin, codeine, corticosteroids, iron, herbal medicine such as garlic and ginkgo, metformin, miglitol, orlistat, risedronate, theophylline, non-steroid anti-inflammatory drugs including cyclooxygenase (COX)-2 inhibitors], infiltrative diseases of the stomach (Crohn's disease, sarcoidosis), metabolic disorders (hypercalcemia, hyperkalemia), hepatoma, ischemic intestinal disease, systemic diseases such as diabetes mellitus, thyroid, parathyroid and connective tissue diseases, intestinal parasites (Giardia), and other abdominal cancers. If functional dyspeptic patients are followed for a long period, organic causes of dyspepsia are detected in 20% of these patients.

In the differential diagnosis of dyspepsia, cardiac, hepatobiliary, pancreatic, and intestinal disorders and gastroesophageal reflux disease can be eliminated as non-gastric causes. After the non-gastric causes have been investigated and eliminated, investigation of Helicobacter pylori infection, performance of gastroscopy, or use of empirical proton pump inhibitors can be considered. There are some advantages and disadvantages to all approaches to dyspepsia. Inhibition of gastric acid secretion with proton pump inhibitors, use of an antidepressant drug in functional dyspeptic patients and prokinetics drugs are the approaches generally used in the treatment of dyspepsia regardless of the presence of gastric or non-gastric causes. Sometimes, despite all efforts, treatment of dyspepsia is unsuccessful.

Pancreatic enzymes are very important in the digestion of nutrients ingested orally. Pancreatic lipase, which hydrolyzes dietary fat molecules, is the most sensitive pancreatic enzyme. It is thus the most frequently used enzyme in the evaluation of pancreatic dysfunction. Deficiency in pancreatic lipase activity is not compensated in the body. In pancreatic lipase deficiency, maldigestion of dietary fat is seen. The amount of fat reaching the distal small intestine increases because of fat malabsorption. Increasing intraluminal fat amount accelerates gastric emptying and intestinal transit time. This situation still disrupts fat absorption. Thus, partial insufficiency in pancreatic lipase activity leads to disruption of fat absorption and increasing intestinal motility, causing the addition of malabsorption to maldigestion, and consequently, pancreatic lipase insufficiency becomes more evident.

The functions of the pancreas can be evaluated directly by the secretin stimulation test, which stimulates pancreatic enzyme and bicarbonate secretion, and then their levels can be measured in secretions obtained by duodenal tube. Today, the fecal elastase level is used to evaluate pancreatic functions indirectly. A level of fecal elastase lower than 20 μg/g of stool indicates pancreatic insufficiency, and a level lower than 100 μg/g of stool indicates a severe pancreatic insufficiency.

Causes of pancreatic dysfunction are classified into three groups:

1. Loss of functional pancreatic parenchyma such as in chronic pancreatitis, cystic fibrosis and pancreatic resection,
2. Decrease in pancreatic secretions in spite of functional parenchyma such as in pancreatic duct obstruction and reduction of endogenous stimulus [Celiac disease, Crohn's disease, diabetes mellitus, and intraluminal inactivation (gastrinoma)], and
3. Insufficient stimulation of enzymes and bicarbonate secretions such as in gastric resection, short bowel syndrome, Crohn's disease, and asynchrony after meals in diabetes mellitus. Cases of severe pancreatic enzyme deficiency are admitted with maldigestion, and cases of mild deficiency are admitted with dyspepsia. The results of the studies investigating the relationship between dyspepsia and pancreatic enzyme deficiency are conflicted, and its incidence is reported as ranging from 19-35%. This discrepancy between studies can be explained by the variety of definitions used for dyspepsia and the differences in
Pancreatic function insufficiency has been detected indirectly by using fecal chymotrypsin and elastase tests. According to these tests, pancreatic function insufficiency was found in 51% (26-74%) of type I diabetes mellitus patients and in 32% (28-36%) of type II diabetes mellitus patients in varying levels (mild to severe). Pancreatic enzyme insufficiency in dyspepsia should be considered in patients with diarrhea resistant to treatment and in those who are elderly, underweight or diabetic. Pancreatic enzyme insufficiency should also be considered in patients resistant to functional dyspepsia treatment with IBS-D, in dyspeptic elderly patients, in thin, diarrheic and dyspeptic patients, and in thin, dyspeptic, diarrheic, and diabetic patients.

**Pancreatic Enzyme Replacement**

The treatment of pancreatic enzyme deficiency is PERT. The main goal of PERT is to provide the presence of pancreatic enzymes in an adequate amount in the right place at the right time. The properties of an ideal preparation for PERT include an activity in the intestines for two hours, rapid enzyme excretion at approximately pH 6 levels, particle size less than 1.7 mm for crossing the pylorus concurrently, large specific surface area, a similar activity with each use, resistance to gastric acidity, and approved drug content. Pharmaceutical properties are very important for providing these conditions. Enteric-coated tablets are resistant to gastric acidity, but poor distribution and delay in emptying of the stomach are the disadvantages of these medicines. Microspheres or mini-microspheres are also resistant to gastric acidity, and they have superiority due to crossing the pylorus concurrently and the homogeneous distribution of the pancreatic enzymes in the chymus. Enzyme preparations should be given with meals, and gastric acid inhibition should absolutely be provided concurrently. While the activity of enzymes given before meals is around 50%, it increases to 63% with meals. The use of proton pump inhibitors increases the activity to 80%.

In summary, in patients with persistent dyspepsia and IBS-D, a pancreatic enzyme deficiency should be considered. Even the mild form of pancreatic enzyme deficiency (< 200 µg/mL) is capable of causing symptoms. When pancreatic enzyme deficiency is suspected, PERT should be given according to the symptoms; in this regard, mini-microspheres might be more active than enteric-coated tablets pharmacologically. Pancreatic enzyme deficiency should be kept in mind especially in patients with functional dyspepsia resistant to prior treatments and IBS-D, in elderly patients with dyspepsia, and in underweight diabetic patients with dyspepsia and diarrhea.
REFERENCES


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