

Management of Pancreatic Exocrine Insufficiency

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A 56-year-old obese Caucasian woman named M.B. reported experiencing anorexia and early satiety in the prior two months. She has lost 10 pounds in two weeks. No changes had been made to her type 2 diabetes medications, she took no other medications, and her exercise habits were unchanged. M.B. made an appointment with her primary care physician (PCP) and her physical examination was inconclusive. The complete blood count and chemistry panel were normal; however, a computed tomography scan of the abdomen showed a 3 cm abnormality in her pancreas with a question of involvement of her superior mesenteric artery. Her PCP suggested that she see a gastroenterologist for an endoscopy.

The gastroenterologist performed an endoscopic ultrasound (EUS) and blood work was conducted, including the cancer antigen 19-9 (CA 19-9) and carcinoembryonic antigen tumor marker tests. M.B.'s CA 19-9 was slightly elevated at 88 mg/dL, and the EUS procedure obtained several tissue specimens that were consistent with adenocarcinoma of the pancreas with no involvement of lymph nodes. She then saw an oncologic gastrointestinal surgeon who ordered a positron-emission tomography (PET) scan; the scan showed the tumor in the head of the pancreas involving major blood vessels. Based on these findings, her pancreatic cancer was determined to be locally advanced and unresectable.

M.B. was referred to a medical oncologist and reported several additional symptoms that she started to experience, including more frequent and very foul smelling stools as well as bloating with flatulence. She was continuing to lose weight because eating was so uncomfortable. Her oncologist asked a registered dietitian to consult with her. An initial diet history revealed that M.B. was eating a diet consisting of three

meals and two snacks daily; however, portions were smaller because she had early satiety.

At the request of the registered dietitian, M.B. completed an evaluation tool where she rated how often she experienced a variety of symptoms (see Figure 1). Her score was high, indicating that she had pancreatic exocrine insufficiency (PEI). The dietitian discussed instituting a trial of pancreatic enzymes with the oncologist. The objective was to see if the enzymes would be effective in decreasing the frequency and severity of pancreatic insufficiency symptoms. Samples of pancreatic enzymes were provided by the oncologist and specific dosing was determined in consultation with the dietitian after her detailed diet history. The dietitian asked M.B. to keep a food diary and to record the dose of enzymes taken with each meal and snack. Three weeks later, M.B. was asked to rate how often she was experiencing the symptoms now that she had been using pancreatic enzymes, and she reported a definite decrease in the frequency of symptoms. On subsequent visits, the dietitian updated M.B.'s history and discussed additional strategies to minimize symptoms of PEI. The dosing of enzymes also was tweaked several times. M.B. went on to receive chemotherapy and radiation and required continued reassessment and adjustment of diet and enzyme dosing by the dietitian.

Pathophysiology

The American Cancer Society ([ACS], 2013) estimated that 45,220 people will be diagnosed with pancreatic cancer in the United States in 2013. Pancreatic cancer is the 10th most common type of cancer and accounts for 7% of all cancer-related deaths (ACS, 2013).

The pancreas is a gland that is about two inches wide by six to eight inches

long and is positioned horizontally deep within the abdomen. Two different types of glandular tissue make up the bulk of the pancreas. The endocrine tissue accounts for about 5% of the pancreas and is involved in the production of the insulin and glucagon hormones. The exocrine tissue accounts for 95% of the pancreas and produces pancreatic enzymes to aid in the digestion of fat, protein, and carbohydrate (ACS, 2012).

Surgery

Surgical resection offers the only reasonable hope of long-term survival. Various surgical options are available for resecting pancreatic cancer, with tumor location being a major determining factor. Most pancreatic cancers occur in the head of the pancreas and the pancreaticoduodenectomy, or Whipple procedure, is the most common procedure. A Whipple procedure involves the removal of the head of the pancreas, the gastric antrum and pylorus, the duodenum, the gallbladder, and the common bile duct (Fernandez-del Castillo, Jimenez, & Steer, 2012). A total pancreatectomy is performed if diffuse carcinoma of the entire pancreas or multifocal tumors within the pancreas are found, whereas a distal pancreatectomy is performed if the tumor is located in the body or tail of the pancreas. A regional or radical pancreatectomy removes tumors located in the pancreatic head or periampullary region and is more extensive than the Whipple procedure (Dunphy, 2008). A patient who has had surgery for pancreatic cancer may experience a deficiency in the secretion of enzymes (Matsumoto & Traverso, 2006).

Gastric resection also may be associated with PEI because of impaired stimulation of cholecystokinin and insufficient mixing of gastric chyme, resulting from dumping syndrome or

rapid gastric emptying. Bowel surgery for colon cancer, perforated diverticuli, intestinal polyposis, colitis, Crohn's disease, and others can cause short bowel syndrome, which also is associated with PEI (Ali, Natasha, Gagloo, & Dhar, 2012).

Pancreatic Dysfunction

If the tumor is located in the head of the pancreas, the pancreatic duct may be obstructed and secretion of pancreatic enzymes and bicarbonate that are needed for digestion may be impaired. Therefore, patients who have locally advanced disease can have pancreatic insufficiency from the tumor itself because of obstruction of the duct or damage to the pancreas parenchyma. About 80%–85% of patients with pancreatic cancer are diagnosed with unresectable disease (Hruban & Ali, 2005). More than 60% of pancreatic duct involvement is needed before enzyme secretion is affected (Damerla, Gotlieb, Larson, & Saif, 2008).

Management

About 50%–92% of patients experience some degree of PEI during treatment for pancreatic cancer (Matsumoto & Traverso, 2006; Perez, Newcomer, Moertel, Go, & DiMagno, 1983; Watson, 2010). Once pancreatic cancer has been diagnosed, weight maintenance can improve overall survival and quality of life (Banim & Hart, 2010). To achieve weight maintenance, digestion of dietary fat, protein, and carbohydrates should be promoted through diet modification and, if necessary, pancreatic enzyme replacement therapy (PERT). Steatorrhea, the prevalent symptom of fat malabsorption, typically occurs when pancreatic enzyme production decreases to less than 10% of normal function (Owens & Greenon, 2007). If a patient is experiencing any symptoms of pancreatic insufficiency listed in the evaluation tool, a dietitian should be consulted to assess the patient's intake and evaluate the extent of symptoms of pancreatic insufficiency. No means of assessing PEI existed; therefore,

the tool in Figure 1 was developed and used clinically at the authors' institution but has not yet been validated or determined to be reliable. Diagnostic tests do exist for PEI, but they often are cumbersome, not readily available, and expensive. They include direct measurement of enzymes via endoscopy, a 72-hour fecal fat test, and breath tests (Stevens & Conwell, 2012).

Typical recommendations would be to divide intake into smaller, more frequent meals. Distributing fat intake throughout the day also is important. Because many patients diagnosed with pancreatic cancer have lost weight prior to diagnosis, fat restriction usually is not advocated. Patients also may be dealing with managing labile diabetes mellitus. If the patient has had recent GI surgery, they may be experiencing symptoms of lactose intolerance for the first time (Lindsey, 2006).

When dietary modification is not effective in reducing symptoms of pancreatic insufficiency, PERT should be considered. A detailed diet history is obtained by the dietitian to assess the patient's caloric and nutrient intake. Although the pancreatic enzymes contain lipase, protease, and amylase, the dose

of pancreatic enzymes reflects the units of lipase contained in the product (e.g., Zenpep® 10,000 units contain 10,000 units lipase per capsule; Creon® 12,000 units contain 12,000 units lipase). If a patient is motivated and willing to count fat grams consumed in meals and snacks, 4,000 units of lipase per 5–7 grams of fat is recommended (O'tery, 1996). If counting fat grams is not realistic, a patient may be initiated on 20,000–40,000 units of lipase per meal and 10,000–20,000 units of lipase per snack, based on the patient's weight and the dietitian's assessment of usual fat grams consumed (Damerla et al., 2008). Patient symptoms of pancreatic insufficiency should be reevaluated frequently when enzymes are initiated to assess the effectiveness of the enzymes. Dosing may need to be increased gradually and/or dietary intake habits may need to be adjusted to minimize symptoms of insufficiency. Patient education guidelines for the use of pancreatic enzymes can be found in Figure 2.

Of note, porcine lipase is used in all commercially prepared pancreatic enzyme products that are currently available. These products are not appropriate

Rating Scale: 1 = never, 2 = rarely, 3 = sometimes, 4 = often, 5 = always

Symptoms of Pancreatic Enzyme Insufficiency	Baseline: Rate Presence of Symptoms Following Meals					Rate Presence of Symptoms Following Meals After PERT				
1. Feelings of indigestion	①	②	③	④	⑤	①	②	③	④	⑤
2. Abdominal cramps after meals	①	②	③	④	⑤	①	②	③	④	⑤
3. Large amounts of gas	①	②	③	④	⑤	①	②	③	④	⑤
4. Foul smelling gas or stools	①	②	③	④	⑤	①	②	③	④	⑤
5. Floating or greasy or fatty stools	①	②	③	④	⑤	①	②	③	④	⑤
6. Frequent stools	①	②	③	④	⑤	①	②	③	④	⑤
7. Loose stools	①	②	③	④	⑤	①	②	③	④	⑤
8. Weight loss	①	②	③	④	⑤	①	②	③	④	⑤

Patient name _____

Name of pancreatic enzyme _____

Physician _____

Quantity of enzyme used _____

Dates of ratings _____

Note. Validity and reliability of this tool have not been established.

Figure 1. Evaluation Tool for Rating Presence of Pancreatic Exocrine Insufficiency Before and After Pancreatic Enzyme Replacement Therapy (PERT)

Note. Tool courtesy of Hackensack University Medical Center. Reprinted with permission.

How to take enzymes

- Enzymes should be taken at the beginning of a meal or snack. They do not work as well if taken during or at the end of a meal.
- Enzymes should be taken with liquid, ideally water, and swallowed whole. They should not be chewed or crushed.
- If you are unable to swallow the enzymes, the capsule can be opened and the contents mixed into applesauce. The applesauce should be eaten right away, and swallowed immediately once in the mouth. Drink some water after you finish the applesauce to be sure no enzyme residue is left in your mouth.
- Monitor enzyme expiration dates, taking those that will expire first. Do not mix old capsules with new capsules.

Diet tips

- If you expect a meal will be prolonged, such as a catered event where courses are

spaced out over an hour or more, enzyme intake should be spaced out as well.

- “Grazing” type food habits can make enzyme dosing difficult. Eating actual meals and snacks is recommended.
- If you plan to consume a glass of milk or another dairy product such as pudding or ice cream, alone and not as part of a meal, take the enzyme tablet with water about 15 minutes before you consume the dairy product.
- If you continue to have a problem with flatulence, with or without burping, when the other symptoms of pancreatic insufficiency have decreased, eliminate the following items for several days to see if avoiding them decreases your symptoms: raw or cooked broccoli, cauliflower, cabbage, Brussels sprouts, onions, and garlic. During this time period, also avoid legumes (hard beans and peas, such as navy beans, kidney beans, chick peas, lentils, etc.). Carbonated beverages

should also be avoided. (You can have them if you allow the bubbles to escape before drinking.)

- Some foods that may not require enzymes include fruit, fruit juice, tea (no milk), black coffee, sour balls and lollipops and similar hard candies, jelly beans, chewing gum, and frozen fruit pops and ices that do not contain milk.

Precautions

- Enzymes may reduce the effectiveness of two oral diabetic medications: acarbose (Precose®) and miglitol (Glyset®). If you take either of these medications, monitor your blood sugar levels closely and if they start to increase, contact the physician who prescribes the diabetes medications.
- The effectiveness of pancreatic enzymes can be reduced if taken with antacids or supplements that have calcium or magnesium.
- If the enzyme dose that you are taking is too high, you may experience constipation.

Figure 2. Patient Education Guidelines for Using Pancreatic Enzymes

Note. Based on information from Conlon, 2010; Damerla et al., 2008; Smith, 2008.

for patients with a pork allergy. Patients should be informed of the source of the lipase in case they avoid pork for religious or other reasons. Over-the-counter products that do not contain porcine-derived enzymes do exist; however, they are not well studied.

Nursing Implications

The case study represents an uncommon clinical challenge in oncology that can have a dramatic effect on a patient's quality of life. As stated, patients who

maintain their weight live longer and have a higher quality of life. Identifying PEI is important not only in the patient who has had a surgical procedure, but also for those patients who have unresectable disease that renders their pancreas dysfunctional in regard to enzyme secretion.

Anorexia and weight loss often are attributed to the disease process and not pancreatic insufficiency. Careful assessment can identify those patients who will benefit from PERT. Close coordination of care with the registered dietitian is needed to identify patients as well as monitor them while on PERT. Oncology nurses who do not have access to a registered dietitian often are responsible for working with the oncologist to initiate and monitor PERT use and dietary modifications.

Two significant factors in caring for patients on PERT include the cost of the enzymes and patient compliance. Some insurance companies do not fully reimburse for the cost of these enzymes (often as much as \$300 per month). This will adversely affect patient compliance because some patients will eat less often or under dose the enzymes to save money. Patient assistance programs to help patients gain access to these enzymes are in place (see Figure 3). According to Dominguez-Munoz (2011), “Prescribing the appropriate dose of enzymes and ensuring patient compliance are the

two key factors for optimizing enzyme therapy. This therapy should also be individualized, with the aim of normalizing digestion and optimizing a patient's nutritional status” (p. 403).

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Abbott Laboratories
<http://bit.ly/W2JQEn>

- Creon® co-pay assistance program

Aptalis Pharma
<http://bit.ly/W2JUUB>

- Zenpep® and Ultresa® assistance form

<http://bit.ly/Vvx9AS>

- Viokace® patient assistance program

Digestive Care

<http://bit.ly/V05IPv>

- Pertzye® co-pay assistance program

Janssen Pharmaceuticals

<http://bit.ly/10UxwLI>

- Pancreaze® patient assistance program

Figure 3. Assistance Programs for Enzyme Replacement

Pancreatic Exocrine Insufficiency

Common Causes

- Pancreatic dysfunction causes an insufficient secretion of digestive enzymes and/or bicarbonate.
- The presence of a tumor or inflammation causes obstruction or narrowing of intrapancreatic ducts, the main pancreatic duct, and/or the biliary duct.
- Gastric, pancreatic, and colon surgery can result in a change in the mechanical or secretory process of the pancreas.

Symptoms

- Feelings of indigestion
- Cramping after meals
- Large amount of foul smelling gas
- Floating or greasy/fatty stools (steatorrhea) which may be foul smelling
- Frequent or loose stools
- Weight loss (Pancreatic Cancer Action Network, 2012)

Primary Dietary Interventions

- Eat five to six smaller meals and snacks evenly spaced throughout the day that contain some fat and protein.
- If a patient has been losing weight, do not restrict fat intake. Start with about 30% of daily kcals coming from fat; increase fat intake gradually, and distribute fat intake in the five to six feedings per day.
- Eat calorically and nutrient-dense foods.
- If new-onset lactose intolerance is reported, have the patient change to lactaid milk and take lactaid pills prior to consumption of dairy products. Reevaluate lactose intolerance several months later as the intolerance may be temporary.
- After a Whipple procedure, refined carbohydrates should be limited and spread throughout the day to minimize symptoms of dumping syndrome (Conlon, 2010; Pancreatic Action Network, 2012; Smith, 2008).

Pharmacologic Interventions

- If loose stools persist after dietary interventions are initiated, antidiarrheal use may be appropriate: loperamide, atropine and diphenoxylate, tincture of opium, and, in severe cases, octreotide injection.

- If gastroparesis occurs after pancreatic surgery and does not resolve on its own, metoclopramide or domperidone may be used (Conlon, 2010).

Use of Pancreatic Enzyme Replacement Therapy

- If dietary modification is not effective, a trial of pancreatic enzymes should be considered.
- A detailed diet history is necessary to estimate the number of fat grams consumed at each meal and each snack.
- 4,000 units of lipase per 5–7 grams of fat is a starting dose. Dosing may need to be gradually adjusted upward if the recommended starting doses are only moderately effective in reducing symptoms of pancreatic exocrine insufficiency (Ottyer, 1996).
- Several brands of enzyme products are available. All enzymes are dosed based on the units of lipase that the product contains.
- Choosing which brand to start with a patient is a preference of the practitioner and ideal lipase dose for meals and snacks is based on the desired dosing. (Creon® is dosed in multiples of 6,000 units of lipase, Zenpep® in 5,000 units of lipase, and Pertzye® in 8,000 units of lipase.) Unless an adverse reaction occurs, such as urticaria, adjust the dose of the initiated enzyme and only use another brand if the initial one is ineffective.
- Patient compliance is very important in enzyme effectiveness. The patient education guidelines in this article have been used by the authors and have helped to reinforce patient compliance.

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