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Review

Lipase or amylase for the diagnosis of acute pancreatitis?

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ABSTRACT

Acute pancreatitis is a rapid onset of inflammation of the pancreas causing mild to severe life threatening conditions [1, 2]. In Canada, acute pancreatitis is the 5th most expensive digestive disease in Canada with a considerable economic burden on the health care system [3]. The diagnosis of acute pancreatitis is usually based on the presence of abdominal pain and elevated levels of serum amylase and/or lipase. Many health care centers use either serum amylase, lipase or both to diagnose acute pancreatitis without considering which one could provide a better diagnostic accuracy. The aim of this review is to investigate whether serum lipase alone is a sufficient biomarker for the diagnosis of acute pancreatitis. We have examined various studies looking at the utilization, sensitivity, specificity and cost associated savings of lipase and amylase in the diagnosis of acute pancreatitis. When comparing different studies, serum lipase offers a higher sensitivity than serum amylase in diagnosing acute pancreatitis. Lipase also offers a larger diagnostic window than amylase since it is elevated for a longer time, thus allowing it to be a useful diagnostic biomarker in early and late stages of acute pancreatitis. Several recent evidence-based guidelines recommend the use of lipase over amylase. Nevertheless, both lipase and amylase alone lack the ability to determine the severity and etiology of acute pancreatitis. The co-ordering of both tests has shown little to no increase in the diagnostic sensitivity and specificity. Thus, unnecessary testing and laboratory expenditures can be reduced by testing lipase alone.

1. Introduction

Acute pancreatitis, the inflammatory disorder of the pancreas, is one of the most frequent gastrointestinal causes of hospital admission. The annual incidence of acute pancreatitis visits range between 13 and 45 per 100,000 persons in the United States and Canada [4]. Acute pancreatitis can either resolve quickly, or cause a systematic inflammatory response leading to a multi-organ failure and death [5]. Despite improvements in the diagnosis of disease and treatment, the mortality rate of acute pancreatitis remains around 5% [5]. The average length of hospital stay for acute pancreatitis patients is eight days, with a mean cost per hospitalization of CAD $8896 [4]. Hence, acute pancreatitis is an economic burden to patients and the health care system.

2. Etiology and pathophysiology

The most common causes of acute pancreatitis are biliary tract obstruction by gallstone (up to 40% of cases) and alcohol abuse (up to 35% of cases) [1,6]. Mechanistically, pancreatic duct obstruction by gallstone leads to the blockage of pancreatic secretion and lysosomal dysfunction causing injury and inflammatory response. Alcohol abuse exerts toxic effect on several types of pancreatic cells, most notably acinar cells, which results in the generation of toxic metabolite and activation of signaling pathways promoting the injury of acinar cells [6]. Other less frequent causes of acute pancreatitis include post endoscopic retrograde cholangiopancreatography (ERCP), medication, infection, hypercalcemia (total serum calcium concentration of > 2.60 mmol/L), hypertriglyceridemia (triglyceride level of > 10 mmol/L), tumors, vascular abnormalities and abdominal trauma [1]. Genetic abnormalities such as mutations in the cystic fibrosis transmembrane conductance regulator allele have been shown to lead to pancreatic ductal obstruction and recurrent acute pancreatitis [7]. Other mutations in the pancreatic secretory cationic trypsinogen inhibitor gene have been linked to autosomal dominant hereditary pancreatitis which manifests as recurrent acute pancreatitis and develops to chronic pancreatitis [8].

3. Clinical signs and symptoms

The clinical presentation of acute pancreatitis involves a sudden

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onset of abdominal pain in the upper left quadrant that radiates to the back with nausea and vomiting [5,6]. Patients could also present fever, hypotension, tachycardia, abdominal distension, and/or jaundice. Since the clinical presentation of acute pancreatitis varies, a clinical classification system is used to assist in managing patients according to their disease severity. The most currently used classification system in guidelines and clinical diagnosis is the Revised Atlanta Classification [9]. This classifies the disease into two phases, early and late, with various severity index; mild, moderate and severe [9]. Mild acute pancreatitis is the most common form with no organ failure, local complications (such as necrosis and pseudocyst formation) or systematic complications [6,9,10]. Moderately severe acute pancreatitis is indicated by transient organ failure (lasting < 48 h) and/or local or systematic complications. Severe acute pancreatitis is classified by persistent single or multiple organ(s) failure (lasting for > 48 h). The revised Atlanta Classification diagnosis of acute pancreatitis entails the presence of at least two of three criteria; abdominal pain, serum lipase or amylase activity at least three times the upper limit of normal, or characteristic radiological findings by contrast-enhanced CT, transabdominal ultrasonography or MRI [6,9]. Both abdominal pain and elevated lipase or amylase serve as the first steps in diagnosing acute pancreatitis, with less reliance on radiological findings that increase medical costs. Predicting the course of acute pancreatitis is often difficult; thus it is necessary to start immediate basic treatment at its first signs. This often includes fluid resuscitation, oxygen supplementation, analgesia, and nutritional support [6]. In gallstone-associated acute pancreatitis patients, a cholecystectomy is generally performed [5].

4. Current diagnostic biomarkers for acute pancreatitis

An important part of acute pancreatitis' diagnosis and treatment is the assessment of pancreatic enzymes, specifically serum amylase and lipase.

4.1. Total and pancreatic amylase

Amylase is synthesized mostly by pancreatic acinar cells and salivary glands, and in negligible level by adipose tissue, the gonads, fallopian tubes and intestinal tract and skeletal muscles [1,11,12]. Humans only have one specific isoenzyme, the α-amylase, with different isoforms specific to the pancreatic or salivary gland. The use of specific monoclonal antibodies allows for the detection of specific pancreatic α-amylase in a serum test rather than total amylase level [13,14]. The measurement of pancreatic amylase has improved the sensitivity and specificity in the diagnosis of acute pancreatitis [15,16]. However, due to the increased cost associated with measuring pancreatic amylase and inconvenience when it comes to different instrumental platforms, the measurement of pancreatic amylase has been largely disregarded while the measurement of total amylase continues to be widely used in clinical laboratory [14,17,18]. Most of amylase is reabsorbed by the renal proximal tubules where the liver is responsible for breaking down most of the amylase with very little excreted through renal system [19,20]. Renal clearance of amylase refers to the rate of glomerular filtration and tubular reabsorption of amylase and is usually elevated in acute pancreatitis [21].

The serum amylase concentration usually reflects the balance between the rate of amylase synthesis and removal. In the case of acute pancreatitis, the rise in serum amylase level to at least three times the upper limit of normal occurs rapidly in the blood, with peaks at three to six hours following the onset of symptoms, a half-life of ten to twelve hours and persistent elevation for three to five days.

Hyperamylasemia could occur due to other pancreatic diseases, such as pancreatic obstruction and pancreatic cancer [1]. High amylase levels could also occur as a result of several malignant conditions, such as breast, colon, lung, and ovarian cancers [1]. The loss of bowel integrity, in conditions such as ulcers, intestinal perforation, perforated duodenal ulcer or ischemia and appendicitis, could lead to hyperamylasemia due to the reabsorption of amylase from the intestinal lumen [11,17]. In addition, decreased metabolic clearance of amylase as indicated by decrease renal filtration and reabsorption, causes an increase in serum amylase level [20,21]. This has been seen in conditions such as renal failure or macroamylasemia. Macroamylasemia is referred to the large complex formed between amylase and immunoglobulins (usually IgA), which usually leads to a decrease in renal function and prolong the presence of amylase in serum and subsequently an abnormal increase in the level of serum amylase [1,22]. Other non-pancreatic conditions causing elevated amylase include cystic fibrosis, burns, hepatitis, cirrhosis, acidosis, pregnancy, gynecological disorder, peritonitis, chronic alcoholism, acute aortic dissection, head injury and various drugs and infectious diseases [1]. Salivary diseases involving salivary glands could also increase the level of total amylase in serum by more than three folds, causing the need for more specific pancreas enzymes in order to determine the diagnosis of acute pancreatitis.

4.2. Lipase

Serum lipase is another pancreatic enzyme that is mainly produced by acinar cells and is at 100 times greater concentration than other isoforms of hepatic, endothelial and lipoprotein lipase [1]. In acute pancreatitis, the increased permeability of cells producing serum lipases allows the release of enzymes to circulate at a high level. Hence, the elevation of serum lipase arises within three to six hours of onset symptoms, peaks within 24 h, and has a persistent elevation of up to two weeks [1]. This gives lipase a larger diagnostic window in comparison to amylase. In addition, lipase has a higher specificity than amylase since it is mainly produced by pancreas. When the lipase test was first introduced in the 1930′s [13], it was difficult to measure and consequently had limited use due to interferences by lipoprotein lipase, intestinal lipase, hepatic lipase and carboxylesterase. However, the use of reagent systems that are specific for pancreatic lipase and addition of bile salts, colipase and calcium as cofactor has improved the specificity and sensitivity of the lipase test [5,13]. The specificity of the lipase test is still not perfect due to several cases of non-pancreatic related elevations in lipase with normal amylase levels and no abdominal discomfort. These cases are usually present in patients with renal insufficiency and high alcohol intake [5]. Similar to amylase, elevated serum lipases with abdominal discomfort could be due to other non-pancreatic diseases, such as trauma, appendicitis, diabetic ketoacidosis, inflammatory bowel disease, intestinal obstruction or infraction, fat embolism, liver, renal failure, and hypertriglyceridemia [1]. Other cases associated with abdominal pain were due to acute cholecystitis or esophagitis and non-pancreatic malignant tumors secreting lipolytic enzymes. In addition, numerous drugs and infections attribute to the non-pancreatic increase in lipase levels.

4.3. Limitation of the amylase and lipase tests

Despite the use of amylase or lipase to diagnose acute pancreatitis, there are several cases where symptoms and radiologic evidences point to acute pancreatitis with normal levels of lipase and amylase. In some of these cases, normal levels of amylase and lipase were found in gallstone and alcohol induced acute pancreatitis, and even in severe necrotizing acute pancreatitis [23]. Another cases have showed a normal level of lipase and amylase in acute pancreatitis patients with hypertriglyceridemia [6,23,24]. These normal levels could be related to the timing of patients' presentation to the emergency department where a very early or late presentations might give normal level results. Various studies suggested that an initial negative result of lipase and amylase tests is unlikely to yield a positive result, especially when the patient is presented to the emergency department within < 4 to 5 h of onset abdominal pain [25]. These cases highlight the importance of