COLLEGE of AMERICAN PATHOLOGISTS

Lipase in the Diagnosis of Acute Pancreatitis

SYNOPSIS AND RELEVANCE

Acute pancreatitis, an inflammation of the pancreas, is one of the most frequent gastrointestinal causes of hospital admissions. Lipase is a digestive enzyme that is stored by the pancreas and released into the intestines after a meal. In acute pancreatitis, lipase levels in plasma/serum rise within a few hours of symptoms and stay elevated for several days. Lipase is more specific than amylase and is the preferred biochemical marker for diagnosis of acute pancreatitis.

INSIGHTS

1. Lipase is more specific and preferred over amylase in the diagnosis of acute pancreatitis.
2. Amylase is not needed for the diagnosis of acute pancreatitis.
3. Repeat or serial monitoring of lipase is unnecessary.

BACKGROUND

Lipase is an enzyme that hydrolyzes triglycerides to glycerol and free fatty acids. Lipase plays a key role in the digestion of dietary fats.[1,2] Lipase in pancreatic secretions is the primary lipase in the body. Pancreatic lipase is responsible for fat digestion, but lipases are also important to the processing and transport of lipids in the body. There are several types of lipases; hepatic lipase in the liver, hormone-sensitive lipases in fat cells, lipoprotein lipase in the vascular endothelial surface as well as pancreatic lipase in the intestine.[3,4] These lipases are responsible for formation and transport of triglycerides and lipoproteins from the liver to the tissues, as well as metabolism of triglycerides in fat cells. Lipase requires bile acids and colipase as a cofactor for full enzyme activity. Laboratory assays utilizing colipase are selective for pancreatic lipase over other lipases in the sample. Lipase is usually present in small amounts in the plasma/serum, but when the pancreas is injured, higher concentrations of lipase can be seen.[1]

Amylase is a group of enzymes that hydrolyze starch into sugars. α-Amylase cleaves long-chain starches at different α-1,4 glycoside bonds along the starch molecule.[1] α-Amylase is produced by humans and mammals. α-Amylase is the primary enzyme produced by the pancreas and salivary gland that breaks down dietary starches to disaccharides and trisaccharides during digestion. These sugars ultimately produce glucose used to supply energy to the body. α-Amylase is normally only present in small amounts in the plasma/serum, but increased amounts are released when the pancreas is injured. Increased levels of both amylase and lipase can be seen with pancreatitis and pancreatic duct obstruction.

While amylase levels in plasma/serum are sensitive for pancreatic disease, the test is not specific. Up to 60% of the total serum/plasma amylase originates from non-pancreatic sources.[5,6] Few studies have evaluated whether measuring the pancreatic isoenzyme improves the diagnostic accuracy of acute pancreatitis, so the pancreatic isoenzyme is not routinely measured.[7,8] Amylase can increase in a number of conditions including; pancreatic disease (pancreatitis or pancreatic trauma), abdominal diseases (intestinal obstruction, mesenteric infarct, perforated ulcers, gastritis, duodenitis, ruptured aortic aneurysm, appendicitis, peritonitis, and trauma), genitourinary disease (ectopic pregnancy, salpingitis, ovarian malignancy and renal insufficiency), human immunodeficiency viruses (HIV), salivary gland lesions, alcohol abuse, diabetic ketoacidosis, septic shock, cardiac surgery, tumors and drugs.[1] Both amylase and lipase are cleared in the urine, but lipase is reabsorbed. In cases of acute pancreatitis, serum activity of both enzymes is greatly increased. However, the lipase elevation is prolonged creating a wider diagnostic window than amylase. This is an advantage in diagnosing patients with delayed presentation (>24 hours) from onset of pancreatitis.[5,7,8] Serum amylase rises within 5 - 8 hours of the onset of acute pancreatitis, has a half-life of 10–12 hours and returns to normal in 1-5 days.[1,5] Elevations in amylase greater than (>) 2-6 times the upper limit of the reference interval has optimal diagnostic accuracy with sensitivity for diagnosis of acute pancreatitis of 67–83 percent but low specificity of 20–60%, because increased values are found in a number of intraabdominal disorders and extrapancreatic conditions.[1,5] Lipase elevations occur within 4–8 hours, peak at 24 hours and return to normal in 7–14 days.[1,5] Increases in lipase between 2 and 50 times the upper limit of the reference interval have been reported with a clinical sensitivity between 80 – 100% and clinical specificity of 80–100% for diagnosis of acute pancreatitis depending on the selected cutoff.[1,9] Sensitivity and specificity for either amylase or lipase varies with different diagnostic thresholds. Increasing the diagnostic cutoff will increase specificity of the test, but decrease the sensitivity.[9] Due to limitations in the sensitivity, specificity, and positive and negative predictive value, serum amylase alone cannot be used to reliably diagnose acute pancreatitis.[9,10] The specificity of lipase has been shown to be higher

than amylase in several studies.[5,7,8,11,12] Measurement of lipase is recommended over amylase as the initial diagnostic test for acute pancreatitis.[1,5,10,13-15]

There are several cases when lipase is preferred in the diagnosis of acute pancreatitis. In hyperlipidemic acute pancreatitis, lipase has better diagnostic accuracy (92%) compared to amylase (40%).[13,16,17] Hyperlipidemia may cause analytical interference and false normal amylase levels. Patients with alcoholic pancreatitis tend to have elevated lipase with normal levels of amylase.[13,18,19] Patients presenting greater than 24 hours after onset of symptoms can show high levels of lipase, but normal levels of amylase. Late presentation accounts for up to a third of normal amylase levels in acute pancreatitis.[20,21] On the other hand, elevated amylase levels may be misinterpreted as pancreatitis due to renal failure and decreased enzyme clearance. This and the number of cases where acute pancreatitis presents with normal amylase make amylase an unnecessary test for patients presenting with acute abdominal pain.

Ordering a combination of amylase and lipase is a common practice but does not increase the sensitivity over a single test and ordering both tests is inefficient.[5] Measuring both lipase and amylase has been suggested as a means to determine the etiology of acute pancreatitis.[5,13] Ratios of lipase to amylase greater than 2:1 have been proposed to be indicative of alcoholic acute pancreatitis while a ratio of less than 1:2 is more likely gallstones.[5] However, the effectiveness of the lipase to amylase ratio in determining the source of acute pancreatitis remains questionable.[13] Several studies have examined the economic outcomes and indicate that ordering only lipase could result in significant savings.[13,22-24] The simultaneous measurement of both amylase and lipase is not necessary, results in test overutilization, and adds to the financial burden of patient care.[1,13,25]

The magnitude of amylase and lipase elevation does not predict disease severity and levels do not indicate if the pancreatitis is mild, moderate or severe.[1,5] There are cases where normal levels of amylase and lipase were found in gallstone, alcohol induced, and even severe necrotizing acute pancreatitis.[26] Normal levels have also been seen in acute pancreatitis with hypertriglyceridemia.[26] In chronic pancreatitis, pancreatic tissue can demonstrate a substantial decline in both amylase and lipase activity that is reflected in lower serum/plasma levels in acute on chronic pancreatitis. In renal insufficiency, both amylase and lipase may be elevated. Macroamylasemia is amylase bound to immune complexes, mostly IgG and IgA.[1] The size of the complex cannot be filtered by the glomerulus elevating plasma/serum amylase levels. No clinical symptoms are associated with this disorder, but some cases have been discovered when investigating abdominal pain.[1] Lipase levels should be checked on initial presentation to diagnose acute pancreatitis. There is no role in trending lipase levels on a daily basis once the diagnosis is made, as it is not useful for monitoring clinical improvement or guiding treatment.[27] Monitoring levels serially during hospitalization does not reflect disease prognosis. Repeat or serial measurement of amylase or lipase should not be used to guide disease progression or resolution.[5]

REFERENCES

1. Rifai N, Horvath AR, Wittwer CT (editors). *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*, 6th ed. Elsevier; 2018.
2. Cerk IK, Wechselberger L, Oberer M. Adipose triglyceride lipase regulation: an overview. *Curr Protein Pept Sci*. 2018;19(2):221-233.
3. Waldmann E, Parhofer KG. Apheresis for severe hypercholesterolaemia and elevated lipoprotein(a). *Pathology.* 2019;51(2):227-232.
4. Lotta LA, Stewart ID, Sharp SJ, et al. Association of genetically enhanced lipoprotein lipase-mediated lipolysis and low-density lipoprotein cholesterol-lowering alleles with risk of coronary disease and type 2 diabetes. *JAMA Cardiol*. 2018;3(10):957-966.
5. Basnayake C, Ratnum. Blood tests for acute pancreatitis. *Aust Prescr.* 2015;38:128-130.
6. Pieper-Bifelow C, Strocchi A, Levitt MD. Where does serum amylase come from and where does it go? *Gastroenterol Clin North Am*. 1990;19:793.
7. Lippi G, Valentino M, Cervellin G. Laboratory diagnosis of acute pancreatitis: in search of the Holy Grail. *Crit Rev Clin Lab Sci.* 2012;49:18-31.
8. Yadav D, Agarwal N, Pitchumoni CS. A critical evaluation of laboratory tests in acute pancreatitis. *Am J Gastroenterol*. 2002;97:1309-1318.
9. Esmaili HA, Mehramus B, Maroufi P, Ghasemi A, Pourlak T. Diagnostic value of amylase and lipase in diagnosis of acute pancreatitis. *Biomed & Pharmacol J.* 2017;10(1):389-394.
10. Tenner S, Baillie J, DeWitt J, Vege SS; American College of Gastroenterology. American College of Gastroenterology guideline: management of acute pancreatitis [published correction appears in *Am J Gastroenterol*. 2014;109(2):302]. *Am J Gastroenterol*. 2013;108(9):1400-1416. doi:10.1038/ajg.2013.218
11. Fossard JL, Steer ML, Pastor CM. Acute pancreatitis. *Lancet.* 2008;371:143-152.

12. Banks PA, Nollen TL, Dervenis C, et al. Classification of acute pancreatitis - 2012: revision of the Atlanta classification and definitions by international consensus. *Gut.* 2013;62:102-111.
13. Ismail OZ, Bhayana V. Lipase or amylase for the diagnosis of acute pancreatitis? *Clin Biochem*. 2017;50:1275-1280.
14. Chang JWY, Chung CH. Diagnosing acute pancreatitis: amylase or lipase? *Hong Kong J Emerg Med*.2011;18:20-25.
15. Choosing Wisely. ABIM Foundation. September 16, 2020. Accessed December 1, 2022. www.choosingwisely.org/clinician-lists/american-society-clinical-pathology-testing-for-amylase/
16. Yin G, Cang X, Yu G, et al. Different clinical presentations of hyperlipidemic acute pancreatitis: a retrospective study. *Pancreas.* 2015;44(7):1105-1110.
17. Tsuang W, Navaneethan U, Ruiz L, Palascak JB, Gelrud A. Hypertriglyceridemic pancreatitis: presentation and management. *Am J Gastroenterol*. 2009;104(4):984-991.
18. Orebaugh, SI. Normal amylase levels in the presentation of acute pancreatitis. *Am J Emerg Med.* 1994;12(1):21-24.
19. Spechler SJ, Dalton JW, Robbins AH, et al. Prevalence of normal serum amylase levels in patients with acute alcoholic pancreatitis. *Dig Dis Sci*.1983;28(10):865-869.
20. Matull WR, Pereira SP, O'Donohue JW. Biochemical markers of acute pancreatitis. *J Clin Pathol*. 2006; 59:340-344.
21. Clavien PA, Robert J, Meyer P, et. al. Acute pancreatitis and normoamylasemia. Not an uncommon combination. *Ann Surg*. 2989;210(5):614-620.
22. Gomez D, Addison A, De Rosa A, Brooks A, Cameron IC. Retrospective study of patients with acute pancreatitis: Is serum amylase still required? *BMJ Open*. 2012;2(5):e001471.
23. Sutton PA, Humes DJ, Purcell G, et al. The role of routine assays of serum amylase and lipase for the diagnosis of acute abdominal pain. *Ann R Coll Surg Engl.* 2009;91(5):381-384.
24. Barbieri JS, Riggio JM, Jaffe R. Reducing co-ordering of amylase and lipase testing at an academic medical center: a quality improvement project. *Am J Med Qual*. 2016;31(3):286-287.
25. Phillip V, Steiner JM, Algül H. Early phase of acute pancreatitis: Assessment and management. *World J Gastrointest Pathophysiol.* 2014;5(3):158-168.
26. Shah AM, Eddi R, Kothari ST, Maksoud C, DiGiacomo WS, Baddoura W. Acute pancreatitis with normal serum lipase: a case series. *JOP.* 2010;11(4):369-372.
27. Hoang L. Amylase and lipase: to trend or not to trend in acute pancreatitis. *Gastroenterol Hepatol Open Access.* 4(2): 00094. doi: 10.15406/ghoa.2016.04.00094