Lipase in the Diagnosis of Acute Pancreatitis

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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.

OBJECTIVES

1. Promote appropriate utilization of lipase over amylase in the assessment of patients presenting with suspected acute pancreatitis.
2. Discourage overordering both lipase and amylase in the diagnosis of acute pancreatitis.
3. Understand the limited utility of repeat or serial lipase or amylase as neither enzyme biomarker correlates with severity of disease, patient outcome or prognosis during the treatment/hospitalization of acute pancreatitis.

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 not cost effective.[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]

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.

INTERVENTIONS

1. Endorse consensus guidelines for the appropriate use of amylase and lipase among medical staff (GI, ED, hospitalists, surgeons, etc.) in your hospital based on the ordering of lipase over amylase in the diagnosis of patients presenting with symptoms of acute pancreatitis.

2. Collect data on amylase and lipase utilization patterns, if available from information systems. If access to data is limited, use laboratory test logs over several weeks to collect information about the frequency of ordering both amylase and/or lipase. These data can be analyzed with a spreadsheet. Basic assessment should include amylase ordering practices by physician against your hospital's guidelines as an ongoing or intermittent monitor. Unless separated by location, tracking the amylase/lipase ratio (against a target of > 0.5) may be a better indicator of compliance with consensus guidelines than total number of amylase tests ordered.
3. Operationalize consensus guidelines into local practice by incorporating quick laboratory order sets or panels for patients presenting with acute abdominal pain to include lipase with other required tests (liver enzymes, pregnancy, etc.) but not amylase. Order sets could be customized by setting based on physician preferences. Review standing orders, panels, etc. that contain both amylase and lipase to confirm that they are appropriately designed and utilized. Modify or eliminate any order set for acute abdominal pain that includes both amylase and lipase.
4. Consider using order systems to develop soft stops if amylase is being ordered with lipase too frequently. Possible interventions include:
    a. Add comments to amylase order forms or order entry screens to inform clinicians about proper use of the test at the time of order, based on guidelines developed by the medical staff.
    b. Use different names for the same test to guide appropriate utilization. For example, pancreatic lipase or nonspecific total amylase might be considered.
    c. Create a "pop-up" or other alert (soft-stop) whenever amylase is ordered together with lipase.
    d. Create an order alert comment when amylase or lipase are ordered more than once per 3 days to provide feedback on consensus guidelines and evidence demonstrating lack of value for repeat testing. Alternatively, use a popup screen displaying the previous result and recommending a cancellation of the repeat order with evidence-based explanation.
    e. Consider adding an interpretive comment to normal amylase results that "normal result does not exclude acute pancreatitis".
    f. Have the chemistry analyzer check for hypertriglyceridemia (high triglyceride or L index) in patients with normal amylase through LIS middleware. If triglycerides are elevated post a result comment alerting physician of potential interference (false normal) amylase.
    g. Consider adding an interpretive comment to elevated amylase or lipase in patients with elevated creatinine (2.0 mg/dL) to warn about the potential for increased results with renal insufficiency.
5. Perform random audit of medical record of patients having amylase and/or lipase ordered to monitor the number of appropriate (eg, abdominal pain) and potentially inappropriate (asymptomatic) indications for testing.
6. Discontinue amylase testing. If the volume of testing has dwindled in light of lipase ordering and with most amylase testing ordered on inpatients, there will be cost savings from discontinuing the amylase test.

INTERVENTION ANALYSIS

Assess the utilization of amylase and lipase (see Appendix A):

1. Determine the number of incidents when amylase is ordered together with lipase over a period of time (eg, 12 months).
2. Determine the number of lipase tests performed, as determined by your guidelines, over the same period of time.
3. Identify providers and/or patient locations with the most amylase/lipase simultaneous orders.
4. Assess the potential impact of a potential reduction in unnecessary duplicate amylase/lipase orders .
5. After interventions have been implemented (eg, education, guidelines, order entry changes), determine the number of orders with both amylase and lipase over a suitable time interval (eg, 1 or 2 months).
6. Calculate the percent improvement in lipase utilization and the number of simultaneous amylase orders with lipase orders reduced annually (see Appendix B).

APPENDIX A: AMYLASE ORDERED WITH LIPASE VOLUME, PRE-INTERVENTION

Collect the data below for a defined period (1-12 months depending on ease of collection). This data will serve as a baseline measure for amylase and lipase utilization. The results will be compared to data obtained after interventions have been made to reduce the co-ordering of amylase with lipase. Record the time periods for documentation purposes.

Pre-Intervention:	
Total number of amylase and lipase tests ordered on the same day	A1
Total number of lipase tests	A2
Percent of inappropriate testing	(A2-A1)/A2 x 100% = A3%
Time period in months	A4

APPENDIX B: POST-INTERVENTION ASSESSMENT

Post-Intervention:	
Total number of amylase and lipase tests ordered on the same day	B1
Total number of lipase tests	B2
Percent of appropriate testing: post-intervention	(B2-B1)/B2 x 100% = B3%
Change in percent appropriate testing post-intervention	A3%-B3% = B4%
Time period in months	B5

QUESTIONS AND ANSWERS

QUESTION 1 OBJECTIVE:
Understand the clinical indications for lipase.

QUESTION 1
Lipase levels increase in plasma/serum in which conditions?
A. Peripheral vascular disease
B. Mumps
C. Acute pancreatitis
D. Congestive heart failure

The correct answer is C. Lipase levels increase occur within 4–8 hours, peak at 24 hours and return to normal in 7–14 days with acute pancreatitis.
A is incorrect. Lipase levels are not affected by peripheral vascular disease
B is incorrect. Lipase levels are not affected by mumps
D is incorrect. Lipase levels are not affected by congestive heart failure

REFERENCE
Basnayake C, Ratnum. Blood tests for acute pancreatitis. *Aust Prescr.* 2015;38:128-130.

QUESTION 2 OBJECTIVE
Understand the frequency for ordering lipase.

QUESTION 2
How frequently should lipase be ordered?
A. Once on presentation of a patient presenting with symptoms of acute pancreatitis
B. Serially to assess treatment and recovery from pancreatitis
C. To discharge a patient with acute pancreatitis from the hospital
D. To determine the severity of pancreatic disease

The correct answer is A. Lipase should be ordered to diagnose acute pancreatitis in a patient with abdominal pain.
B is incorrect. Serial measurement of lipase is not clinically useful
C is incorrect. Measurement of lipase is not useful after the initial diagnosis of pancreatitis is made
D is incorrect. Lipase levels do not correlate with the severity of pancreatitis

REFERENCE
Ismail OZ, Bhayana V. Lipase or amylase for the diagnosis of acute pancreatitis? *Clin Biochem.* 2017;50:1275-1280.

QUESTION 3 OBJECTIVE
Identify lipase as the preferred test in the diagnosis of acute pancreatitis.

QUESTION 3
This test is more specific in the diagnosis of acute pancreatitis
A. Amylase
B. Lipase
C. Creatine kinase
D. Lactate dehydrogenase

The correct answer is B. Lipase is more specific than amylase for the diagnosis of acute pancreatitis

A is incorrect. Amylase levels are increased in a number of pancreatic and non-pancreatic disorders
C is incorrect. Creatine kinase is an enzyme found in heart, brain and skeletal muscle that catalyzes the conversion of creatine to phosphocreatine using adenosine triphosphate.
D is incorrect. Lactate dehydrogenase is an enzyme of the glycolytic pathway that converts lactate to pyruvate

REFERENCE

Rifai N, Horvath AR, Wittwer CT (eds). *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*, 6th ed. Elsevier; 2018.

MODULE 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 6, 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