

ประสิทธิภาพในการใช้ Pancreatic alpha amylase เป็นเครื่องมือในการคัดกรองโรคตับอ่อนอักเสบเฉียบพลัน (การศึกษานำร่อง)*

ชัยพร บุญเฉลิมวิเชียร¹, วิโรจน์ ไววานิขกิจ¹, ดวงพร ทองงาม², สัทธิพร แอทอง³,
นารา พรดิโกลี¹, แสงทิพา ชำนาญไพร¹

*นำเสนอในการประชุมวิชาการประจำปีครั้งที่ 41 คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

¹ ภาควิชาเวชศาสตร์ชั้นสูตโรค คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

² ภาควิชาสรีรวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

³ ภาควิชากายวิภาคศาสตร์ คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

A Pilot Study of Using Pancreatic Alpha Amylase in Screening for Acute Pancreatitis*

Boonchalermvichian C¹, Wiwanitkit V¹, Thongngarm D², Agthong S³,
Paritpokee N¹, Chamnarnapi S¹

*Presented at 41st Annual Scientific Meeting, Faculty of Medicine, Chulalongkorn University

¹ Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn University

² Department of Physiology, Faculty of Medicine, Chulalongkorn University

³ Department of Anatomy, Faculty of Medicine, Chulalongkorn University

Objective: To study effectiveness of serum pancreatic alpha amylase as a diagnostic marker in screening for acute pancreatitis

Methods: This study was set as a pilot study. Total 13 patients with elevation of serum alpha amylase level caused by diverse diseases were included. Serum from each subject was determined for alpha amylase, lipase and pancreatic amylase level. Diagnostic property of each chemical determination was presented as sensitivity, specificity, false positive and false negative.

Result: Considering serum alpha amylase determination, sensitivity, specificity, false positive and false negative were 100 % 60 % 40 % and 0 % orderly. Concerning serum lipase determination, sensitivity, specificity, false positive and false negative were 66.7 %, 50 %, 30 % and 33.3 % orderly. While sensitivity, specificity, false positive and false negative of pancreatic alpha amylase were 100 %, 70 %, 50 % and 0% respectively.

Conclusions: Pancreatic alpha amylase determination is overall similar to serum amylase determination in screening for acute pancreatitis. However, implication to other settings is still limited due to rather few subjects

วัตถุประสงค์: เพื่อศึกษาประสิทธิภาพในการใช้ Pancreatic alpha amylase เป็นเครื่องมือในการคัดกรองโรคตับอ่อนอักเสบแบบเฉียบพลัน

วิธีการ: การศึกษานี้เป็นการศึกษานำร่องโดยทำการศึกษาในผู้ป่วยที่มีระดับ serum alpha amylase สูงจำนวน 13 ราย เนื่องจากสาเหตุต่างๆ กันโดยเก็บตัวอย่างเลือดจากผู้ป่วยแต่ละรายเพื่อตรวจวัดระดับ alpha amylase, lipase และ pancreatic amylase ได้ทำการศึกษาค่าความไว ความจำเพาะ ผลบวกและผลลบของการตรวจแต่ละชนิดในการวินิจฉัยโรคตับอ่อนอักเสบแบบเฉียบพลัน

ผลการศึกษา: ค่าความไว ความจำเพาะ ผลบวกและผลลบของการตรวจ serum alpha amylase เท่ากับ 100%, 60%, 40% และ 0% ตามลำดับ ค่าความไว ความจำเพาะ ผลบวกและผลลบของการตรวจ serum lipase เท่ากับ 66.7%, 50%, 30% และ 33.3% ตามลำดับ ค่าความไว ความจำเพาะ ผลบวกและผลลบของการตรวจ serum pancreatic alpha amylase เท่ากับ 100%, 70%, 50%, และ 0% ตามลำดับ

สรุป: การตรวจวัดระดับ pancreatic alpha amylase ในเลือดให้ผลการตรวจคัดกรองได้ใกล้เคียงกับการตรวจระดับ alpha amylase อย่างไรก็ดีเนื่องจากกลุ่มประชากรที่ทำการศึกษามีจำนวนน้อย

according to the nature of pilot study. Further complete study is recommended.

Key word: acute pancreatitis, amylase

เนื่องจากการศึกษานำร่อง ดังนั้นการจำนำข้อมูลไปใช้จำเป็นต้องระมัดระวังและผลการศึกษาที่สมบูรณแบบเป็นสิ่งที่จำเป็น

คำสำคัญ: โรคตับอ่อนอักเสบแบบเฉียบพลัน, amylase

ศรีนครินทร์เวชสาร 2544; 16(3), 160-164 • Srinagarind Med J 2001; 16(3), 160-164

Given to the best of our knowledge, there are no official reports on the incidence or prevalence of pancreatic disease in Thai population. However, considering acute pancreatitis in the United States, there are about 5,000 new cases per year with a mortality rate of about 10 percent. These number maybe underestimate dramatically the true incidence and prevalence, since non alcoholinduced pancreatitis was largely ignored¹.

In addition, owing to the lack of specificity of symptoms and signs of pancreatic diseases and the difficulty in direct examination of pancreas, may necessitate the precise and early diagnosis of pancreatic disease². To certain extent, a presumptive diagnosis is mainly dependent on elevation of blood amylase levels, which in turn, is proven not a specific test, particularly, when used as a sole diagnostic test³. For instance, patients with acute pancreatitis and renal failure, single blood test is proven to be unreliable for the diagnosis of pancreatic disease⁴.

Since the clinical applications of pancreatic alpha amylase have not been studied systematically in Thailand. Its specificity and sensitivity in application for a variety of diseases should be studied thoroughly. In this study, the authors determined the effectiveness of serum pancreatic alpha amylase as a diagnostic marker in screening for acute pancreatitis comparing to other basic markers as serum amylase and serum lipase.

Materials and methods

This study was set as a pilot study. Total 13 patients with elevation of serum alpha amylase levels caused by diverse diseases were included (Table 1). Serum from each included subject was sent to the laboratory for new determination for alpha amylase, lipase and pancreatic amylase level. Diagnostic property of each chemical determination was presented as sensitivity, specificity, false positive and false negative.

Table 1. Details of subjects in this study.

Number	Sex	Serum amylase* (U/L)	Serum pancreatic amylase (U/L)	Serum lipase (U/L)	Acute pancreatitis**
1	Female	131	15	20	No
2	Female	238	99	99	No
3	Male	2077	934	1962	Yes
4	Male	1719	792	247	Yes
5	Female	239	97	53	Yes
6	Male	116	28	42	No
7	Female	107	22	18	No
8	Female	600	217	608	No
9	Male	99	12	22	No
10	Female	117	59	55	No
11	Female	328	60	55	No
12	Female	175	50	43	No
13	Female	224	74	489	No

Normal value

a.serum amylase, 0 - 220 U/L

b.serum pancreatic amylase, 0 - 60 U/L

c.serum lipase, 0 - 53 U/L

*new determination at the same time as the two left tests **definite diagnosis

Subject selection

Total 13 patients presented with hyperamylasemia were selected into this study. Finally, from 13 subjects, 3 subjects were definitively diagnosed to have acute pancreatitis by clinical diagnosis (clinical history, physical examination, laboratory investigation and imaging study). The other 10 left subjects were diagnosed to have other diseases: 2 with cholecystitis, 1 with chronic pancreatitis, 1 with cholangitis, 1 with spontaneous bacterial peritonitis, 1 with stomach cancer, 1 with choangiocarcinoma, 1 with pelvic fracture, 1 with pancreatic pseudocyst and 1 with systemic lupus erythematosus.

Laboratory investigation

The determinations for amylase and lipase levels in this study were performed by commercial assay kits (Boehringer Mannheim) on automated clinical analyzer, Hitachi. The pancreatic alpha amylase in this study was performed by a new enzymatic colorimetric assay (Boehringer Mannheim) on automated clinical chemistry analyzer, Hitachi. The activity of human salivary alpha amylase is inhibited by two different monoclonal antibodies (mouse) in the reagent without affecting the pancreatic alpha amylase in the first step. Then defined oligosaccharides such as 4,6 - ethylidene - (G7) p-nitrophenyl - (G1) - alpha, D - maltoheptoside (ethylidene - G, PNP) are cleaved under the catalytic action of pancreatic alpha amylases. The measuring/reportable range of this assay is 0 - 60 U/L.

Results

The details of 13 patients included in this study were presented in Table 1. There were 4 males and 9 females. Considering serum alpha amylase determination, sensitivity, specificity, false positive and false negative were 100 %, 60 %, 40 % and 0 % orderly (Table 2). Concerning serum lipase determination, sensitivity, specificity, false positive and false negative were 66.7 %, 50%, 30% and 33.3% orderly (Table 3). While sensitivity, specificity, false positive and false negative of pancreatic alpha amylase were 100 %, 70 %, 50 % and 0 % respectively (Table 4). Applying combination of the test, the diagnostic activities were shown in Table 4.

Discussion

In human serum, the alpha amylase (1,4-Dglucaglucanohydrolase, EC:3.2.1.1) consists of many isoenzymes which are produced mainly in pancreas (pancreatic alpha amylase) and salivary glands (salivary alpha amylase)⁵. These two isoenzymes share some common

Table 2. Diagnostic activity of serum alpha amylase in this study.

Level	Acute pancreatitis	
	yes	no
> 220 I/U	3	4
≤ 220 I/U	0	6

Table 3. Diagnostic activity of serum lipase in this study.

Level	Acute pancreatitis	
	yes	no
> 53 I/U	2	5
≤ 53 I/U	1	5

Table 4. Diagnostic activity of serum pancreatic alpha amylase in this study.

Level	Acute pancreatitis	
	yes	no
> 60 I/U	3	3
≤ 60 I/U	0	7

Table 5. Diagnostic activities from combination of the tests.

Combination	Sensitivity	Specificity
1. Amylase and lipase	66.7 %	88 %
2. Amylase and pancreatic amylase	100 %	80 %
3. Lipase and pancreatic amylase	66.7 %	85 %
4. Amylase and pancreatic amylase and lipase	66.7 %	94 %

properties, such as digestion of starch and glycogen, and possession of similar amino acids sequences but different carbohydrate moiety^{6,7}. The pathological processes, which occur in both pancreas and salivary glands, can change blood pancreatic alpha amylase level as well as blood salivary alpha amylase level⁸. The measurement of blood pancreatic alpha amylase level is more reliable to be used as a diagnostic marker for pancreatic diseases when compared to the total amylase level because it can help physicians to exclude nonpancreatic causes from others in case of hyperamylasemia⁹

Concerning clinical points of view, it is difficult to perform the direct examination of pancreas and the nonspecific symptoms and signs of pancreatic diseases do not aid the physician to arrive the correct diagnosis promptly. In case of boarder-line high amylase level without classic symptoms and signs, blood amylase seems not to be a good diagnostic marker^{2-4,10}. Many patients with chronic pancreatitis do not have elevated blood amylase levels¹¹. In such circumstances, neither blood amylase level nor pancreatic amylase can detect abnormality^{1,12}. Moreover, Total serum amylase levels are highly variable in chronic pancreatitis and carcinoma, therefore, they are of little diagnostic values¹³. Mergener and Baillis also emphasized on the problem of diagnosis of acute pancreatitis if too much reliance is placed on the serum amylase level, without careful attention to the relatively low specificity of the test. Furthermore, they also stated that many factors can lead to normal serum amylase levels even in the presence of severe necrotising pancreatitis¹⁴.

Another frequently used diagnostic marker for pancreatic diseases is lipase which is a glycoprotein with 420-449 amino acids residues and presents in the pancreas, intestines and a variety of other tissues¹⁵⁻¹⁷. The concentration gradient between pancreatic tissue and serum lipase is roughly 20,000-fold¹⁵. There are two molecular forms in the pancreas and three electrophoretic bands with lipolytic activity¹⁵. Some authors considered lipase determination in pancreatitis is superior to amylase determination¹⁸. Some authors refer it as a best single enzyme to measure for the diagnosis of acute pancreatitis¹⁹. However, the contradiction has been raised against the concept of using lipase to provide incremental information over amylase. Some authors pointed out that in the population they mentioned in their research, lipase was less specific and less sensitive than amylase for acute pancreatitis²⁰. This observation is also supported by Tetrault, that lipase is not specific for pancreatitis, and lipase assay needed to be evaluated for organ and tissue specificity²¹. Moreover, the source of increased serum lipase activity may be non-pancreatic tumor or even a cancer of pancreas, which results in chronic increased serum lipase²²⁻²³. In this clinical settings, lipase isoenzyme may be better diagnostic test for the diagnosis of pancreatic diseases²²⁻²⁴.

A recent study evaluated the sensitivity and specificity of five assays used to diagnose acute pancreatitis: two for amylase, one for lipase, one for trypsin like immunoreactivity (TLI), and one for pancreatic isomylase. In summary, (1) if the proper cutoff level were used, all these assays had equivalent specificities (2) that total serum amylase

was as good an indicator of acute pancreatitis as any alternatives. Nevertheless, some studies demonstrated the limitation of using serum amylase as a diagnostic marker due to low sensitivity (68 percent) and the detection and diagnosis of acute pancreatitis dependent on an elevated serum amylase levels. Ultimately, they recommend total serum amylase and serum lipase activities as screening tests for acute pancreatitis^(1,25).

Form this study, the sensitivity for serum amylase determination was 100 % according to the fact that serum amylase elevation is one of the criteria for diagnosis of acute pancreatitis. Interestingly, pancreatic alpha amylase determination is as effective as serum alpha amylase determination in screening for acute pancreatitis but it is better than serum lipase determination. Surprisingly, the lowest specificity was observed from detection for serum pancreatic alpha amylase. However, implication to other settings is still limited due to rather few subjects according to the nature of pilot study. Therefore, conclusion that pancreatic alpha amylase is not a good screening marker for acute pancreatitis was not set due to the rather few subjects in this study as a limitation. Further complete study is recommended.

In conclusion, in general situations, the efficacy of pancreatic alpha amylase in diagnosis of acute pancreatitis may be at least equivalent to total amylase level in blood or even inferior in certain selected conditions. Bearing on its limitation and dynamic activity-time-pattern, physicians are strongly recommended to interpret the laboratory results along with other supporting evidences such as symptoms and signs or other pertinent information carefully.

References

1. Toskes PP, Greenberger NJ. Approach to the patient with pancreatic disease. In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, Hauser SL, Longo DL, eds. *Harrison's Principles of Internal Medicine*. New York: McGraw-Hill, 1998: 1737-41
2. Toskes PP, Greenberger NJ. Approach to the patient with pancreatic disease. In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, eds. *Harrison's Principles of Internal Medicine*. New York: McGraw-Hill, 1994: 1516-20
3. Williamson RC. Early assessment of severity in acute pancreatitis. *Gut* 1984; 25: 1331-9
4. Kazmierczak SC. Gastrointestinal and pancreatic function. In: Anderson SC, Cockayne S, eds. *Clinical Chemistry Concepts and Applications*. Philadelphia: WB Saunders, 1993: 570-94
5. Moss DW, Henderson AR. Enzymes. In: Burtis CA, Ashwood

- ER, eds. Tietz Fundamental of Clinical Chemistry. Philadelphia: Philadelphia: WB Saunders, 1996: 138-9
6. Stiefel DJ, Keller PJ. Preparation and some properties of human pancreatic amylase. including a comparison with parotic amylase. *Biochim Biophys Acta* 1973; 345-61
7. Guyton AC. Digestion and absorption in the gastrointestinal tract. In: Guyton AC. eds *Guyton Textbook of Medical Physiology*. Philadelphia : WB Saunders, 1991: 726-8
8. Labon MHZ, Jones BJM. The Assessment of Gastrointestinal Function. In: Williams DL, Marks V, eds. *Scientific Foundations of Biochemistry in Clinical Practice*. Oxford: Butterworth-Heinemann, 1994 : 367-72
9. Kao YS, Liu FJ. Laboratory Diagnosis of Gastrointestinal Tract and Exocrine Pancreatic Disorders. In: Henry JB, eds. *Clinical Diagnosis and Management by laboratory methods*. Philadelphia: WB Saunders, 1991: 530-1
10. Lankisch PG, Burchard-Reckert S, Lehnick D. Underestimation of acute pancreatitis: patients with only a small increase in amylase/lipase levels can also have or develop severe acute pancreatitis. *Gut* 1990; 44: 542-4
11. Ravel R. Pancreatic Function. In: Ravel R, eds. *Clinical Laboratory Medicine*. St. Louis: Mosby-Yearbook, Inc. 1995: 450-3
12. Kitagawa M, Naruse S, Lshiguro H, Nakae Y, Kondo T, Hayakawa T. Evaluating exocrine function tests for diagnosing chronic pancreatitis. *Pancreas* 1997; 15: 402-8
13. Axon ATR, Mitchell CJ. Evaluation of Pancreatic Diseases. In: Bouchier IAD, Allan RN, Hodgson HJF, Keighley MRB, eds. *Gastroenterology*. London : WB Saunders, 1993: 1568-72
14. Mergener K, Baillie J. Acute Pancreatitis. *BMJ* 1998; 316: 44-8
15. NW Tietz, DF Shuey. Lipase in serum-the elusive enzyme: an overview. *Cline Chem* 1993; 39:746-56
16. Champe PC, Harvey RA. Cholesterol and steroid metabolism. In: Champe PC, Richard A, eds. *Harvey Lippincott's Illustrated reviews: Biochemistry*. Philadelphia : Lippincott - Raven, 1994 :205-28
17. Guess DA. Disorders of the liver biliary tract, and pancreas. In: Rund DA, Barkin RM, Rosen P, Sternback GI, eds. *Essentials of Emergency Medicine*. St. Louis: Mosby, 1996: 491-506
18. Soergel KH. Acute Pancreatitis. In: Sleisenger MH, Fordtran JS, Scharschmidt BF, Feldman M, eds. *Gastrointestinal Diseases Pathophysiology / Diagnosis / Management*. Philadelphia. : W.B. Saunders, 1993 : 1628-53
19. Carter DC. Acute Pancreatitis. In: Gilmore IT, Sheilds R, eds. *Gastrointestinal emergencies*. London: W.B.Saunders, 1992 : 123-41
20. Mangano MM, Theurer HA, Horowitz GL. Lack of added value of lipase in diagnosis of acute pancreatitis. *Clin Chem* 1990; 36:1123
21. Tetrault G. Serum lipase assayed on EKTACHEM 700 is not specific for pancreatitis in patients with elevated amylase or lipase. *Clin Chem* 1990; 36:1123
22. Donnelly JG, Ooi DS. Chronic increased serum lipase without evidence of pancreatitis: tumor-derived lipase? *Clin Chem* 1996; 42: 462-4
23. Munoz-Perez M, Sarrion-Pelous D, Jimenez-Jimenez J, Martinez-Montiel P, Gallego-Valdes M. Chronic increased serum lipase in a patient with suspected pancreatic adenocarcinoma. *Clin Chem* 1997; 43: 191-3.
24. Lott JA, Lu CJ. Lipase Isoforms and Amylase Isoenzymes: assays and Application in the Diagnosis of Acute Pancreatitis. *Clin Chem* 1991;37/3: 361-8
25. Forest JC, Turcotte G, Nadeau L, BergeronJ, Desluriers D, Fruteau B, Robitaille R. Serum lipase total and pancreatic amylases in the diagnosis of acute pancreatitis and other acute abdominal diseases in an emergency room setting. *Clin Chem*, 1990; 36:1124

