How Would You React to Intermediate Values of Lipase?

According to the American College of Gastroenterology, the diagnosis of acute pancreatitis requires at least 2 of the following 3 elements: characteristic abdominal pain, specific tomographic findings and a lipase level three times above the upper limit of normal. The aim of this study is to determine physicians’ interpretation of intermediate values of serum lipase (IVSL, a lipase level above the upper normal limit but below 3 times that value), and in which cases pancreatitis is diagnosed. The diagnosis of pancreatitis was more likely to be made when episodes of abdominal pain with IVSL were accompanied by either nausea and vomiting, serum lipase values at least 2 times above normal, concomitant elevations of serum amylase, or combinations thereof. These results suggest that diagnosing pancreatitis depends on the mindset of the treating physician, regardless of clinical, laboratory and imaging data.

**INTRODUCTION**

According to the American College of Gastroenterology, the diagnosis of acute pancreatitis requires the presence of at least 2 of the following 3 elements: characteristic abdominal pain, specific computed tomography (CT) findings, and a lipase level elevated three times above the upper limit of normal. In the setting of normal serum lipase most physicians would probably exclude the diagnosis of pancreatitis. Conversely, if the serum lipase value is three times above the upper normal limit, most physicians would likely diagnose pancreatitis. Being that an intermediate level of serum lipase alone (IVSL) is not sufficient to diagnose acute pancreatitis, this retrospective study aims to determine what additional parameters are utilized by physicians to establish the diagnosis of pancreatitis.

**MATERIAL AND METHODS**

The study was undertaken at Lyndon B. Johnson Hospital (LBJH), a tertiary care center in Houston, Texas, after obtaining Institutional Review Board approval; patient consent requirements were waived. From October 2010 to June 2011, 1091 abnormal lipase values in 1041 patients were collected.

The study consisted of a retrospective chart review. Considering normal lipase values as 114 to 286 U/L, 883 patients had intermediate values of serum lipase (IVSL) (between 286 and 3 times above normal, 858). Patients whose first lipase value was above 858 were (continued on page 44)
excluded as this finding confirms acute pancreatitis. Only patients who had at least 2 determinations of intermediate values of serum lipase (IVSL) per episode were included.

In February 2011, a new lipase test with a new set of reference values (73-393 U/L) was implemented at LBTH. To assess eligibility and to analyze laboratory data among patients with the new values, data were tabulated after using a factor to convert them into the old reference range.

A standardized questionnaire was implemented to retrieve information from the electronic medical records regarding demographic, clinical, laboratory, and imaging data. Included were: exposure to alcohol or medications, history of gallstones, diabetes mellitus, obesity, hypertriglyceridemia, and concomitant amylase levels (normal= 25-115 U/L).

The use of complementary studies in each event, such as abdominal X ray, abdominal ultrasound, abdominal computerized tomography (CT) or magnetic resonance (MRI), magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP) and/or intraoperative cholangiogram was evaluated. The need for surgery was also noted.

The medical decision-making portion of the chart was examined to assess whether an explanation for the elevated lipase was offered, and if so, if pancreatitis was included in the differential diagnosis, regardless of the lipase values.

An episode of IVSL was defined as any event with at least 2 lipase determinations in a month period or shorter. When the determinations were more than 1 month apart, they were considered as belonging to separate episodes.

Statistics
Categorical variables were analyzed using the Fisher exact test, and discrete variables were analyzed using the Student t test for unpaired samples. A two-sided P < 0.05 was considered indicative of statistical significance.

RESULTS
Ninety episodes of persistent intermediate values of serum lipase in 88 patients were documented.

In 34 events among 33 patients the final diagnosis was acute pancreatitis (group P). In 56 events in 55 patients the final diagnosis was not acute pancreatitis (group NP). The age (44±14 for P and 43±14 for NP, P=1.00), gender (21 men for P and 28 for NP, P=0.64) and racial distribution were comparable.

When comparing groups P and NP, there were no significant differences in the presence of obesity, type 1 or type 2 diabetes, hypertriglyceridemia, previous diagnosis of gallstones, ingestion of more than 20 g/day of ethanol, recent abdominal surgery or use of drugs known to be associated with acute pancreatitis.

With respect to clinical presentation, patients in group P were more likely to complain of nausea and vomiting than those in group NP (76% vs. 50%, P=0.01; and 71% vs. 43%, P=0.01), whereas abdominal distention or pain, jaundice, evidence of gastrointestinal bleeding, hypotension, fever (greater than 38ºC), tachycardia, ascites and dehydration were about the same in both groups. The APACHE II score for both groups was also comparable (3.47±4.11 vs. 4.45±4.55, P=0.53).

The patients in group P were more likely to have had previous episodes of IVSL (62% vs. 21%, P=0.0002). Most of the patients in both groups were admitted to the hospital (88% in the group P vs. 80% in the group NP, P=0.36) with virtually no difference in their length of stay.

Patients in groups P and NP underwent similar percentages of radiologic or endoscopic evaluations: abdominal X rays (9% vs. 16%, P=0.53), abdominal CT scans (41% vs. 48%, P=0.66), MRI (6% vs. 2%, P=0.55), abdominal ultrasound (47% vs. 41%, P=0.66) and ERCP (15% vs. 12%, P=0.76). The percentage of cholecystectomy and operative cholangiogram was also similar (24% vs. 14%, P=0.27; and 24% vs. 11%, P=0.13).

Because abdominal CT contributes to the diagnosis of pancreatitis, positive tomographic findings in both groups were analyzed. Four of 14 patients in group P had tomographic findings that confirmed the diagnosis of acute pancreatitis (29%) whereas the positive findings in group NP were 2 of 27 (8%, P=0.16).

There were no significant differences in the number of patients from both groups presenting with serum bilirubin higher than 2 mg%, glucose above 200 mg%, calcium higher than 11 mg%, creatinine above 2 mg%, lactic acidosis, hypertriglyceridemia and total leukocyte counts above 15,000/mL.

The patients in group P had significantly higher initial and peak lipase levels when compared with the NP patients (484±146 vs. 403±123, P=0.0061, and
529±163 vs. 442±136, P=0.0078). More patients in group P than in NP had values between 2 and 3 times above the upper normal level (35% vs. 14%, P=0.03). In addition, more patients in group P had serum amylase values above normal (29% vs. 5%, P=0.003), although never 3 times above normal. The change in the range of normal lipase made no difference in the selection of patients as belonging to group P or NP.

DISCUSSION

In this retrospective study, physicians were likely to diagnose acute pancreatitis when episodes of abdominal pain were accompanied by serum lipase at least twice normal. Moreover, nausea and vomiting, or concomitant elevations of serum amylase, or both also prompted a final diagnosis of acute pancreatitis. Small elevations of pancreatic enzymes (less than three times above the upper normal level) have been considered diagnostic of pancreatitis previously as long as concomitant elevations of amylase are present.

Classical risk factors for acute pancreatitis had no effect on physicians’ diagnoses but having had previous similar events did. Patients in group P had previous episodes of IVSL more frequently than those in group NP. Although the workup for both groups was similar, 92% of patients in the NP group who underwent abdominal CT had no tomographic findings of pancreatitis. This absence of CT specific abnormalities likely accounts for the patients being allocated to group NP.

The American College of Gastroenterology (ACG) guidelines recommend using abdominal CT when lipase values are less than three times above the upper normal limit either to support the diagnosis of pancreatitis or to broaden the diagnostic considerations. Other authors assign less value to abdominal CT believing that it is associated with increased length of stay and is of no diagnostic or management benefit to patients with pancreatitis.

The main limitation of this study is its retrospective nature, which prevents confirming the presence of subjective symptoms (pain, nausea, vomiting) or clearly ascertaining the thought process of the attending physician. It can be suggested, however, that since lipase levels were ordered, pancreatitis was at least being considered in the differential.

CONCLUSION

In conclusion, the diagnosis of acute pancreatitis depends primarily on the mindset of the treating physician, regardless of clinical, laboratory and imaging data. How would you react to an intermediate level of serum lipase?

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References

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