Point-of-care Urine Trypsinogen-2 Test for Diagnosis of Acute Pancreatitis

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Abstract

Objectives: To assess a point-of-care urine trypsinogen-2 (UT) test for the diagnosis of acute pancreatitis.

Methods: This was a prospective study of patients presenting to the emergency department with abdominal pain suggestive of acute pancreatitis. A 3-minute point-of-care UT test (Actim Pancreatitis; Medix Biochemica, Kauniainen, Finland) was compared with final diagnosis of acute pancreatitis, which was based on suggestive clinical features, serum lipase and/or amylase levels and imaging.

Results: Of 124 patients included in this study, 69 patients had final diagnosis of acute pancreatitis. The sensitivity and specificity of UT were, respectively, 73.9% (95% CI 61.9% to 83.8%) and 94.6% (95% CI 84.9% to 98.9%).

Conclusions: The point-of-care UT test for acute pancreatitis had good sensitivity and specificity, and can be used reliably at the bedside to make a positive diagnosis.

Introduction

Acute pancreatitis accounts for up to 5% of patients presenting to the emergency department (ED) with abdominal pain, depending on age and other underlying factors. Although most patients with pancreatitis have mild disease that resolves spontaneously, 20% to 30% present with severe disease, which is characterized by a protracted clinical course, pancreatic necrosis and multi-organ failure, and is associated with increased morbidity and mortality.

Early diagnosis of pancreatitis is essential, because therapy may improve outcome. There is general acceptance that a diagnosis of acute pancreatitis requires two of the following three features: 1) abdominal pain characteristic of acute pancreatitis, 2) serum amylase and/or lipase ≥3 times the upper limit of normal, and 3) characteristic findings on CT scan.

Although serum amylase and lipase historically have been used for the diagnosis of pancreatitis, neither is a definitive test for pancreatitis and levels vary independent of disease and severity. Ultrasonography has a limited role in diagnosing acute pancreatitis because bowel gas may make visualization of the pancreas difficult; but the test may help identify gallstones and choledocholithiasis. Contrast-enhanced abdominal CT is considered the most accurate noninvasive imaging test for pancreatitis but is expensive, not universally available, contraindicated in those with allergies to contrast agents, and carries the risk of ionizing radiation and contrast-induced nephropathy.

Recently, a qualitative, 3-minute point-of-care test (Actim Pancreatitis; Medix Biochemica, Kauniainen, Finland) to detect trypsinogen-2 in urine was introduced in Finland to screen patients with abdominal pain for pancreatitis, and was shown to be accurate. Trypsinogen-2 is present in low concentration in the urine of healthy persons. It is strongly elevated in the early stages of acute pancreatitis and, importantly, remains elevated for several days or even weeks. We assessed the accuracy of the urine trypsinogen-2 (UT) test for diagnosis of acute pancreatitis in an Indian setting.

Methods

This was a prospective cohort study of a convenience sample of patients with symptoms consistent with acute pancreatitis.

The study population consisted of 124 patients with acute abdominal pain reporting to the emergency unit of 10 hospitals between July 2008 and October 2008. A final diagnosis of acute pancreatitis was made if at least two of the following three criteria were met: consistent clinical features (epigastric pain with or without nausea and vomiting), raised serum amylase and/or lipase levels (>3 times upper limit of normal reference values for the testing laboratory) and diagnostic findings on contrast-enhanced CT or ultrasonography. The choice of investigations was at the discretion of the treating clinician.

Since this was a pilot study, no formal sample size calculations had been done. All patients with symptoms consistent with a diagnosis of pancreatitis who consented to provide a urine sample for immediate UT testing were recruited. Patients with prior history of pancreatitis were not excluded.

Urine trypsinogen-2 test

The point-of-care test for urinary trypsinogen-2 is an immunochromatographic test. The test strip should be allowed to reach room temperature prior to use and the manufacturer recommends it be used on fresh urine sample. When the test strip is dipped into the urine sample, trypsinogen-2 is bound to monoclonal antibody-labeled blue latex particles, which migrate across a nitrocellulose membrane with a zone containing another antibody specific for another epitope on trypsinogen-2. At trypsinogen-2 concentrations higher than 50 μg/L, a blue line develops in this zone. The test is considered positive when a clear blue line is detected within 5 min. A control line is used to indicate proper functioning of the strip. If the control line is undetectable the assay needs to be repeated.

The criterion standard was a final diagnosis of acute pancreatitis made by the clinicians based on consistent clinical course (n=124), elevated amylase (n=114) / lipase (n=91) levels and imaging studies (n=109).

Data analysis

Data analysis was performed with GraphPad Instat (Version 3.06) to determine sensitivity and specificity with 95% confidence intervals (CI).
Future studies could assess the impact of UT testing on cost.

The UT test compares favorably with serum amylase and lipase.

Collection could not be monitored.

Room temperature prior to use and testing within 15 minutes.

This difference may be explained by the time to testing.

Pancreatitis at 48 hours.

Hwang et al. found that the UT had increased sensitivity for amylase/lipase when tested in patients who presented within 24 hours of symptom onset; with delayed testing (day 3 onwards) the sensitivity in our study also differed from those of the UT test (Table 1), but the specificity and PPV of the UT test were better.

The sensitivity and NPV of serum amylase and serum lipase tests were comparable to those of the UT test (Table 1), but the specificity and PPV of the UT test were better.

In a Finnish study on 525 patients presenting with acute abdominal pain, the test had higher sensitivity of 96% and specificity of 92%. The sensitivity in our study also differed from that in more recent studies among non-Scandinavian patients. This difference may be explained by the time to testing. Saez et al. found UT to be comparable to amylase and lipase, with a sensitivity of 68%, but performed UT within 24 hours of symptom onset. Likewise, Chen et al. showed that UT was comparable to amylase/lipase when tested in patients who presented within 24 hours of symptom onset; with delayed testing (day 3 onwards) the accuracy of the test diminished considerably. However, Hwang et al. found that the UT had increased sensitivity for pancreatitis at 48 hours.

We did not control for the time of UT testing relative to the onset of symptoms and our study may have included a more heterogeneous population.

This study had limitations. Since it assessed usefulness at point of care, variance in the interpretation of faint lines by different users may have led to false-negative results. Moreover, strict adherence to instructions of allowing the UT strips to reach room temperature prior to use and testing of urine within 15 minutes of collection could not be monitored.

Our study suggests that the 3-minute point-of-care Actim Pancreatitis test compares favorably with serum amylase and lipase values and may be useful as a bedside test for acute pancreatitis. Future studies could assess the impact of UT testing on cost-benefit and its use in the pediatric and pregnant populations.

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- Dr. M Agarwal, Austmangal Surgical Hospital, Ahmedabad
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- Dr. R Shah, Godrej Hospital, Mumbai
- Dr. AK Sharma, Sankalp Intensive Care Unit, Ahmedabad
- Dr. P Shinde and Dr. TY Sonavane, Bhagwati Hospital, Mumbai
- Dr. VN Thati, R.N.Cooper Hospital, Mumbai

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**References**


**Table 1**: Comparison of diagnostic accuracy of urinary trypsinogen-2 test and those of serum amylase, serum lipase and imaging to detect acute pancreatitis

<table>
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<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Positive likelihood ratio</th>
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<tbody>
<tr>
<td>Serum amylase ≥ 3</td>
<td>75.4%</td>
<td>87.8%</td>
<td>89.1%</td>
<td>72.9%</td>
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<td>ULN*</td>
<td>64.0%</td>
<td>90.2%</td>
<td>88.9%</td>
<td>67.3%</td>
<td>6.6</td>
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<tr>
<td>Serum lipase ≥ 3</td>
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<td>80.0%</td>
<td>82.9%</td>
<td>70.6%</td>
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<td>CT scan</td>
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<td>64.3%</td>
<td>81.5%</td>
<td>69.2%</td>
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<tr>
<td>Urinary trypsinogen-2</td>
<td>73.9%</td>
<td>94.6%</td>
<td>94.4%</td>
<td>74.3%</td>
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* Upper limit of normal