

## Original article

# The value of elastase evaluation in comparison with amylase and lipase in prediction and diagnosis of post-ERCP pancreatitis

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## SUMMARY

Pancreatitis is the most common of the serious complications of ERCP, with rates between 2 and 40%. The aim of this study was to evaluate the significance of serum levels of amylase, lipase and elastase after ERCP, in the prediction and diagnosis of pancreatitis.

**Patients:** Forty three consecutive patients underwent ERCP for various indications.

**Methods:** Serum samples were taken before, one hour and six hours after the procedure. Amylase was evaluated with enzymatic colourimetric test (Olympus, normal <200 U/L), lipase with kinetic ultraviolet method (Boehringer, normal <190 U/L) and elastase with ELISA (Schebo Tech, normal <3,5 ng/ml).

**Results:** Two patients (4%) developed mild pancreatitis and one (2%) had fever for 48 hours. The others had normal course. Nineteen patients (44%) had serum amylase elevation (>2N) the first hour and 26 (60%) the sixth. Twenty seven (62%) had serum lipase elevation (>2N) the first hour and 30 (70%) the sixth. Four (9%) had increased elastase (>2N) the first hour and 2 (4%) the sixth. The only enzyme that was significantly elevated in the patients who developed pancreatitis compared to those who did not, was serum elastase at one hour post-ERCP ( $p=0,025$ ). In the first hour, sensitivity for amylase, lipase and elastase was 50%, 100% and 100% respectively, specificity 60%, 40% and 95%,

positive predictive value (PPV) 5%, 7% and 50% and negative predictive value (NPV) 96%, 100% and 100%. In the sixth hour sensitivity was 100%, 100% and 100%, specificity 40%, 30% and 98%, PPV 4%, 3% and 50% and NPV 100%, 100% and 100% respectively.

**Conclusions:** Although serum amylase and lipase evaluation are good methods to exclude the diagnosis of pancreatitis, they do not assist in prediction and documentation of diagnosis. In contrast, serum elastase evaluation is more reliable in prediction and diagnosis of post-ERCP pancreatitis.

**Key words:** ERCP, pancreatitis, amylase, lipase, elastase

## INTRODUCTION

Pancreatitis is a common serious complication of endoscopic retrograde cholangio-pancreatography (ERCP) with reported incidence rates from 2 to 40%.<sup>1</sup> Prediction of post-ERCP pancreatitis and its severity is useful for planning treatment strategy (surveillance, intensive care therapy, use of novel drugs like platelet activating factor antagonist, parenteral nutrition). The commonly used criteria of severity (Ranson's, APACHE, Glasgow, CT, CRP) need several days to be evaluated. Investigators have tried to discover an inexpensive, easy to perform and credible test which could predict quickly the severity of pancreatitis.<sup>2-4</sup> We assessed the usefulness of serum pancreatic enzyme measurement during the first hours after ERCP, in detecting and predicting the severity of post-ERCP pancreatitis.

## PATIENTS AND METHODS

Forty three consecutive patients, 23 men and 20 women, mean age 60 years, range 19-85 years, underwent

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ERCP for the following indications: recent cholangitis 7 (16%), recent pancreatitis 4 (9%), possible choledocholithiasis 15 (34%), jaundice 9 (21%), biliary colic 3 (7%), pancreatic head enlargement 2 (4%), possible sclerosing cholangitis 2 (4%) and liver cystadenoma with jaundice 1 (2%).

Serum samples were taken before, one hour and six hours after ERCP. Amylase was evaluated with enzymatic colourimetric test (Olympus, normal <200 U/L), lipase with kinetic ultraviolet method (Boehringer, normal <190 U/L) and elastase with ELISA (Schebo Tech, normal <3,5 ng/ml). The ELISA technique was preferred to the commonly used radioimmunoassay (RIA)<sup>5,6</sup> because it is a relatively new, inexpensive and easily performed method, with reliable results, even though less precise.<sup>7</sup> The results were analyzed as per protocol, by Mann-Whitney test.

## RESULTS

Two patients (4%) developed mild pancreatitis (epigastric pain and vomiting for 24 hours) and one (2%) had fever for 48 hours. The other patients had normal course without symptoms of pancreatitis. Cholangiography was performed in 36 patients and pancreatography in 20. Seventeen patients underwent sphincterotomy. In one patient, who developed pancreatitis, only cholangiography was performed and in the other only pancreatography. None of them underwent sphincterotomy. Nineteen patients (44%) had serum amylase elevation (>2N) in the first hour and 26 (60%) in the sixth. Twenty seven patients (62%) had serum lipase elevation (>2N) in the first hour and 30 (70%) in the sixth. Four patients (9%) had increased elastase (>2N) in the first hour and 2 (4%) in the sixth. One patient with pancreatitis and two without had no serum sample taken in the sixth hour. Increasing the cut off value for an abnormal level for amylase, lipase and elastase to >3N, resulted in 12 pa-

tients (28%) with elevated serum amylase in the first hour and 15 (35%) in the sixth, 25 (58%) with elevated serum lipase in the first hour and 24 (56%) in the sixth and one patient (2,3%) with elevated elastase in the first and sixth hour.

Mean values for baseline amylase were  $142,7 \pm 95,5$  U/L for the non pancreatitis group and  $106 \pm 67,6$  U/L for the pancreatitis group ( $p=0,6$ ). The first hour amylase mean values were  $507,4 \pm 412$  U/L and  $104,6 \pm 102,6$  U/L ( $p=0,4$ ) and the sixth hour values were  $690,9 \pm 650,1$  U/L and  $2690$  U/L respectively. The respective mean lipase values were  $128,4 \pm 155,5$  U/L and  $151 \pm 196,6$  U/L at baseline ( $p=0,97$ ),  $1320 \pm 1615$  U/L and  $4260 \pm 3294$  U/L in the first hour ( $p=0,055$ ) and  $1478 \pm 2011$  U/L and  $8770$  U/L in the sixth hour. Likewise the respective mean elastase values were  $1,71 \pm 1,34$  ng/ml and  $2,9 \pm 2,97$  ng/ml at baseline ( $p=0,64$ ),  $2,82 \pm 2,08$  ng/ml and  $14,75 \pm 10,25$  ng/ml in the first hour ( $p=0,025$ ) and  $2,892 \pm 1,9$  ng/ml and  $18$  ng/ml in the sixth hour. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for each test are shown in table 1.

## DISCUSSION

The measurement of serum amylase has relatively low sensitivity and specificity for the diagnosis of pancreatitis, as is already known.<sup>8</sup> For post-ERCP pancreatitis in particular, the specificity of serum amylase is even lower than that estimated for other causes of pancreatitis, because hyperamylasemia without pancreatitis is very common (up to 70%).<sup>9</sup> In our study the sensitivity of serum amylase was 50% in the first hour and the specificity 60% in the first and 40% in the sixth hour. The PPV was also extremely low at 5% in the first and 4% in the sixth hour. Conversely the NPV was high at 96% and 100% respectively. Thus the serum amylase measurement can assist in the exclusion of diagnosis of pancreatitis although

**Table 1.** Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of serum amylase, lipase and elastase measurements for the diagnosis of post-ERCP pancreatitis.

	Sensitivity %		Specificity %		PPV%		NPV%	
	>2N	>3N	>2N	>3N	>2N	>3N	>2N	>3N
Amylase 1st hour	50	50	60	73	5	8	96	96
Amylase 6th hour	100	100	40	66	4	7	100	100
Lipase 1st hour	100	100	40	44	7	8	100	100
Lipase 6th hour	100	100	30	44	3	4	100	100
Elastase 1st hour	100	50	95	100	50	100	100	98
Elastase 6th hour	100	100	98	100	50	100	100	100

some authors report normoamylasemia in up to 20% of patients with acute pancreatitis.<sup>10</sup>

The measurement of serum lipase was comparable with that of amylase, although it was more sensitive than amylase in the first hour and equally sensitive with elastase. Change of the cut off value to >3N (which is more specific) did not result in substantial difference. Lipase is considered equally sensitive but more specific than amylase in the diagnosis of pancreatitis because it is originated almost solely in the pancreas,<sup>11</sup> in contrast to amylase which is widely distributed in the body. The reasons of false positive results in pancreatic enzyme measurements could be: silent invasion of the pancreas by microorganisms, bowel obstruction with reflux of enzymes into the pancreatic duct and diffusion across the duct wall, activation of trypsinogen in liver disease in excess of  $\alpha$ 1-antitrypsin secretion or focal subclinical pancreatitis secondary to intestinal obstruction, vascular diseases, uremia, dehydration or hypovolemia.<sup>8</sup> In one study, serum lipase was found to be more sensitive than both serum amylase and elastase in the detection of ERCP induced pancreatic damage.<sup>12</sup>

In our study the measurement of serum elastase proved to be the most sensitive and specific test, with very good NPV and good PPV, in the diagnosis of pancreatitis. Change of the cut-off value to >3N resulted in lower sensitivity. In a recent study elastase was shown to be moderately sensitive (66%) and relatively non specific (85%) for the diagnosis of acute pancreatitis, with little relation to disease severity and inaccurate prediction of complications.<sup>7</sup> Other authors claim that elastase correlates best with the clinical picture.<sup>6,13</sup> The causes of the discrepancy in various reports could be: methods of enzyme measurement with different sensitivity and specificity, selection of patient populations with variable rate of occurrence of pancreatitis, use of different reference ranges or cut-off points, or incorrect diagnosis.<sup>8</sup> Clearly, more studies are required to assess the usefulness of elastase and other novel agents, like leucocyte elastase, interleukin-6 and 8, or trypsinogen activation peptide, in the prediction of post-ERCP pancreatitis and its severity.

In summary, we found out that elastase seems more useful in prediction and diagnosis of post-ERCP pan-

creatitis than amylase and lipase, which can only be used to rule out the diagnosis.

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