The Significance of the 4-Hours Post-ERCP Serum Amylase Level to Predict Post-ERCP Pancreatitis

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Abstract

ERCP is a very important therapeutic tool and Acute Pancreatitis remains the most common and feared complication. The recognition of the risk factors for post ERCP pancreatitis and the high risk patients is highly desirable & in this study we evaluate the relation between post ERCP serum amylase level and the incidence of post procedure acute pancreatitis.

Patients and Methods: The study was performed on 100 patients exposed to the ERCP in endoscopy unit of internal medicine hospital, Kasr Al-Ainy Hospitals either therapeutic or diagnostic over a period of 18 month and a blood sample for serum amylase 4-hours later was measured and then the patients were followed up for occurrence of acute pancreatitis.

Results: 9% of the patients developed acute pancreatitis with a positive correlation was found between the incidence of pancreatitis and 4-hours post ERCP amylase level & the study showed high incidence of pancreatitis with other ERCP parameters.

Conclusion: From our study that showed the relation between serum amylase level and incidence of post ERCP acute pancreatitis, we found that 4 hours post ERCP serum amylase level estimation is helpful to guide us and to predict patients with high risk of acute pancreatitis.

Key Words: ERCP – Acute pancreatitis – Serum amylase.

Introduction

ENDOSCOPIC Retrograde Cholangio–pancreatography (ERCP) is a technique that uses a combination of luminal endoscopy and fluoroscopic imaging to diagnose and treat conditions associated with the pancreato-biliary system, and it is a very important therapeutic tool [1].

Despite all the advances and improvement in ERCP techniques, post-ERCP acute pancreatitis remains the most feared and common complication, being associated with high morbidity and mortality.

Acute pancreatitis varies from 1-7% and up to 12-31% in some studies [2].

Most of post ERCP pancreatitis is mild pancreatitis which usually resolves spontaneously without serious complications. The incidence of severe pancreatitis ranges from 0.3% to 0.6% [1]. Several factors such as mechanical, chemical, hydrostatic, enzymatic, microbiologic, allergic and thermal insult are implicated in the etiology of post-ERCP pancreatitis [3].

We aimed in our study to find out the significance of four hours post ERCP serum amylase level in prediction of post ERCP pancreatitis and we aimed also to highlight the other factors that precipitate to post procedure pancreatitis.

Patients and Methods

Over a period of 18 month and between year 2013 and 2014, one hundred patients exposed to ERCP procedure were randomly selected from El-Ebrashi’s center of Gastro-enterology and Hepatology, Internal Medicine Department, Kasr Al-Ainy Hospitals, Cairo University, 46 of them were males and 54 were females with a mean age 48.85 years.

The patients who were excluded from this study are those who had previous attacks of pancreatitis, Patients with elevated serum amylase level diagnosed before the ERCP. Patients having any history of problems that cause elevation of amylase level not related to ERCP as (renal impairment, salivary disorders, other causes of acute abdomen like appendicitis, ectopic pregnancy, rupture ovarian cyst and intestinal obstruction, etc). And Patients with contraindication to ERCP like bleeding tendency.
All patients were subjected to Clinical evaluation. A detailed history was taken from each patient, with emphasis on the duration of illness, abdominal pain, fever, bleeding tendency, history of contrast dye anaphylaxis, previous attack of pancreatitis, ERCP or surgery on the biliary tract and Laboratory investigations were done in the form of Complete blood picture, liver function tests, pre and 4 hours post ERCP serum amylase level and abdominal sonography was done with special emphasis on the pancreas and biliary system to confirm the presence of biliary obstruction and diagnose its cause. Some of the patients had abdominal CT and/or MRCP data available to help reaching the diagnosis.

All ERCP procedures were performed by using the Olympus lateral view endoscope TJF 160 VR.

Patients were placed in the prone position and sedated with propofol with or without midazolam under the supervision of an anesthesiologist. Arterial oxygen saturation, heart rate, and blood pressure were closely monitored during the procedure.

Selective cannulation of the common bile duct was done using a double lumen sphincterotome Olympus KD211Q with a short nose (7mm) and a (30mm) clever cutting wire and was aided in difficult cases by a slippery guide wire. The contrast material used for cholangiopancreatography was urographin in most cases it was diluted with saline. In case of failed cannulation using papillotome and guide wire a precut papillotomy was done using the needle knife.

Papillotomy was done using the CONMED system 2450 electro surgical unit using endocut blended current & using 40 watt cutting and 25 watt coagulation current. In case of biliary obstruction Trials for stone extraction were done using balloon, stone extraction basket or sometimes lithotripsy. In many cases stent insertion—either biliary or pancreatic was done for Bile drainage and to relieve obstruction.

Hyperamylasemia was defined as an increase of serum amylase of greater than the upper limit of normal (>100 IU/dl). Acute pancreatitis was diagnosed by abdominal pain persistent for at least 24 hours, associated with serum amylase equal to or greater than three times the upper normal limit.

**Statistical analysis:**

Analysis of data was done by IBM computer using SPSS (statistical program for social science version 12). Description of quantitative variables as mean, SD and range 27.

- Description of qualitative variables as number and percentage.
- Chi-square test was used to compare qualitative variables between groups.
- Unpaired t-test was used to compare quantitative variables, in parametric data (SD <50% mean).
- Mann Whitney test was used instead of t-test in non parametric data SD >50% mean.
- Spearman Correlation co-efficient test was used to rank variables versus each other positively or inversely p-value >0.05 insignificant p<0.05 significant and p<0.01 highly significant.

**Results**

Among the 100 patients in our study, 13 (13%) patients had normal post ERCP amylase level & 87 (87%) patients had hyperamylasemia (amylase more than 100 IU/L) and only 9 of them developed acute pancreatitis.

Regarding the age, the mean age of the pancreatitis group was 47.44 with SD of 8.71 years while the mean age of the non pancreatitis group was 48.99 with SD of 12.59 years. No relation was found between the age of patients and the occurrence of pancreatitis. Table (1) shows the mean age of patients that experienced post ERCP acute pancreatitis.

Regarding the 4 hours post ERCP amylase level and the incidence of acute pancreatitis, 100% of patients who developed pancreatitis had elevated amylase level versus the non pancreatitis patients with p-value of 0.034 which is considered statistically significant. This is expressed in Table (2).

In our study the ROC curve analysis put the cut off value of 4 hours post ERCP serum amylase level >260 IU/L, at this amylase level more than or equal 260 the incidence of acute pancreatitis increases with p-value <0.001.

Table (3) showed that a 4 hours post ERCP serum amylase level in prediction of post ERCP pancreatitis had a sensitivity of 88.89%, specificity of 94.51%, positive predictive value (PPV) of 61.50%, negative predictive value (NPV) of 98.9% and accuracy of 92% Fig (2) which is the Receiver operating characteristics curve was used to define the best cut off value of the post ERCP amylase which was >260 (micron/L), with sensitivity of 88.89%, specificity of 94.51%, positive predictive value of 61.50%, negative predictive value of 98.9% with diagnostic accuracy of 92%.
Table (1): The age group in both males and females that have acute pancreatitis.

<table>
<thead>
<tr>
<th>Post ERCP pancreatitis</th>
<th>Age</th>
<th>t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Yes</td>
<td>9</td>
<td>47.44 ± 8.71</td>
</tr>
<tr>
<td>No</td>
<td>91</td>
<td>48.99 ± 12.59</td>
</tr>
</tbody>
</table>

Table (2): Comparison between yes and no (post ERCP pancreatitis) as regard amylase.

<table>
<thead>
<tr>
<th>Amylase</th>
<th>Post ERCP pancreatitis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal</td>
<td>9</td>
<td>78</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>91</td>
</tr>
<tr>
<td>X2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table (3): The statistical significance of 4 hours post ERCP amylase level in prediction of acute pancreatitis.

| Cut off ≤260 | Sens. 88.89% | Spec. 94.51% | PPV 61.50% | NPV 98.9% | Accuracy 92% |

Fig. (1): The ROC curve analysis showing the diagnostic performance of all studied parameters discriminating post ERCP pancreatitis and amylase from patients group.

Fig. (2): Interactive dot diagram showing the best cut off value of the post ERCP amylase level.

**Discussion**

ERCP is a very important maneuver in the diagnosis and management of different pancreatico-biliary diseases and despite all the advances and improvement in ERCP techniques, post-ERCP acute pancreatitis remains the most feared and common complication, being associated with high morbidity and mortality. Acute pancreatitis varies from 1-7% and up to 12-31% in some studies [4].

Regarding the age, the mean age of the pancreatitis group was 47.44 with SD of 8.71 years while the mean age of the non pancreatitis group was 48.99 with SD of 12.59 years. No relation was found between the age of patients and the occurrence of pancreatitis, other studies showed high variation in determining the age group at risk. Studies by Masci et al., [5] and Cooper and Slivka [6] reported that patients under the age of 60 years were found to be at higher risk of post-ERCP pancreatitis.

Another study by Thomas and Sengupta, 2001 reported that age less than 25 years was a high risk factor for post ERCP pancreatitis [7].

Another study by Nishino et al., [8] concluded that one of the patient related risk factors was age more than 65 years. Obviously, determining the age group at risk for post ERCP pancreatitis needs a large number of patients.

In this study although the female patients had higher rates of both hyperamylasemia and acute pancreatitis than male patients, yet, this was statistically insignificant. Most of the authors reported that females appear to be at higher risk for developing post ERCP pancreatitis compared to males [9,10,11].
Post-ERCP hyperamylasemia is reported by many authors to be extremely common reaching up to 70% [12-16].

Nine patients among the 100 patients had developed acute pancreatitis diagnosed by the classic symptoms of pancreatic abdominal pain plus raise in serum amylase at least 3 times the upper limit of normal (up to 100 IU/L). None of the patients developed rise in amylase level less than 3 times the upper normal limit had clinically relevant acute pancreatitis. These results are harmonious with the previous authors who found out that increased amylase level more than three times the upper normal limit is predictive of acute pancreatitis [13,15,16,17].

Regarding the 4 hours post ERCP amylase level and the incidence of acute pancreatitis, 100% of patients who developed pancreatitis had elevated amylase level versus the non pancreatitis patients with $p$-value of 0.034 which is considered statistically significant.

According to ROC curve analysis it was found that the cut off value of 4 hours post ERCP serum amylase level is $>260$ IU/L. at this amylase level more than or equal 260 the incidence of acute pancreatitis increases with $p$-value $< 0.001$.

The 4 hours post ERCP serum amylase level in prediction of post ERCP pancreatitis had a sensitivity of 88.89%, specificity of 94.51%, positive predictive value (PPV) of 61.50%, negative predictive value (NPV) of 98.9% and accuracy of 92%.

In a retrospective study Verity R Sutton et al. [18] also studied the significance of post ERCP serum amylase level in prediction of acute pancreatitis and they put a cut off value of 2.5 of upper limit range in case of pancreatogram with sensitivity 80% and specificity 80.4% and a cut off value of 5 of ULR in case of no pancreatogram with sensitivity 100% and specificity 91.8%.

**Conclusion:**

From our study we found that 4 hours post ERCP serum amylase level estimation is important to guide us and to predict patients with high risk of acute pancreatitis.

**Recommendations:**

The 4 hours post ERCP amylase level is advised in all patients undergoing this maneuver for early prediction of acute pancreatitis.

**References**


**الملخص العربي**

يدخل النتائج من أهم وأخطر المضاعفات الناتجة عن تنظير القناوات العصبية وذلك أصبه التعرف على عوامل الخطورة التي تتزامن من احتمالات حدوث التهاب البنكرياس بعد تنظير القناوات العصبية إذا أظهرت التحاليل باللغة حتى يمكن تحديد المضاعفات وكم متابعة هذه الحالات باهتمام أكبر بعد إجراء المنظار.

هدف البحث: تقييم عوامل الخطورة المسببة لالتهاب البنكرياس بعد التنظير القناوات العصبية مع التركيز على قياس نسبة أنيزم الانزيم في المراضي بعد أربعة ساعات من المنظار وتحديد مدى اهمية وفعالية في تحديد حدوث التهاب البنكرياسي الحاد من عدمه.

خطوة وطرق البحث: أجري هذا البحث على مائة مريضاً من مستشفى الأمراض الباطنية بمستشفى المبرة الحدي (وحدة الإشراشة للمناظير والجهاز الهضمي) والذين تم عمل منظار قنوات مراوية لهم سؤال تشخيصي أو علاجي أو كلاهما. تضمنت الحالات (100 حالة) عدد 45 أثلي و47 ذكر متوسط اعمارهما 48.8 عام. تم تسجيل التاريخ المنظري، وإجراء فحص كليكيسيومي، اجراءات صلبة على البطن، وقياس مستوي الاميليز بالدم قبل إجراء المنظار.

بعد إجراء المنظار تم قياس مستوي أنيزم الانزيم في الدم المنظري، وتم متابعة المرضى لتشخيص الأصابات بالتهاب البنكرياس الحاد.

النتائج: أظهرت النتائج بعد المنظار أن 87% من المرضى أظهروا ارتفاع في مستوي الاميليز عن معدل الطبيعي في حين أن 9% من المرضى أظهروا نقص في مستوي الاميلاز.

ToUpper:P

難了解: التهابsume: إخصائيات بين السن والنوع ونسبة حدوث التهاب البنكرياس. كذلك فان مستوى الصفراء وانزيما الكبد بالدم لم تكن من العوامل المؤثرة في حدوث التهاب البنكرياس.

وقد اظهرت الرسالة إخصائيات بين مستوي الاميلاز في مستوي البلوكتراكسي الحاد محسوبة قدرها 88.8% وخصوصية قدرها 88.9% والقيمة التنبؤية السالبة = 76.9% والقيمة التنبؤية الموجبة = 95.4% ونسبة الحساسية = 92.8%.

الاستنتاج: من هذا البحث نستنتج أهمية قياس مستوي أنيزم الانزيم في الدم المنظري 4 ساعات بعد عمل منظار القناوات العصبية كما استنتجنا أن هناك العديد من عوامل الخطورة التي تصبح المنظار وتشير إلى زيادة فرص حدوث التهاب البنكرياس الحاد.