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Plasma Calprotectin Values in Acute Pancreatitis

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ÖZET

Akut pankreatitte plazma calprotektin değerleri

Amaç: Plasma calprotectin değerinin akut pankreatit tanısında kullanılabilirliğini araştırmak.

Gereç ve Yöntem: Bu prospektif çalışmaya akut pankreatit tanılı 84 hasta dahil edildi. Erkek/kadın oranı 36/48, ortlama yaş 44 (19-81)' idi. Kontrol grubuna kasık fıtığı ve pilonidal sinüs operasyonu olacak 30 hasta dahil edildi. Erkek/kadın oranı 20/10, ortalama yaş 31 idi (21-56). Kan örnekleri EDTA'lı tüpe alınıp plazmaları ayrıldıktan sonra -80°C'de saklandı. Plasma cal değeri ELISA yöntemi ile çalışıldı.

Bulgular: Cal değerleri 32 ile 490 ng/ml arasında değişken ve AP vakalarında kontrol grubuna oranla belirgin bir şekilde yüksekti (p=0.001). Cal ve WBC değerleri (r=0.423 p=0.0001), cal ve CRP değerleri (r=0.282 p=0.012), cal ve amilaz değerleri (r=0.675 p=0.0001), cal ve lipaz değerleri (r=0.595 p=0.0001) arasında istatistiksel olarak anlamlı, pozitif bir ilişki vardı.

Sonuç: Plasma calprotectin seviyesi akut pankreatitte nonspesifik olarak artmaktadır. Pankreatitin şiddetini değerlendirmede sınıflandırılmış hasta grupları üzerinde çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Plazma calprotectin, akut pankreatit, tanı

ABSTRACT

Plasma calprotectin values in acute pancreatitis

Objective: To investigate the usefulness of the plasma calprotectin values for diagnosis of acute pancreatitis.

Material and Methods: 84 patients who have been diagnosed as acute pancreatitis (AP) were included in this prospective study. Control group (CG) included 30 patients with elective surgery for inguinal hernia or pilonidal sinus. Male to female ratio was 36/48 with a mean age of 44 (19-81) for AP group and male to female ratio was 20/10 with a mean age of 31 (21-56) for control group. Blood samples were taken to EDTA coated tube and then aliquots of serum were stored at -80°C for assaying. Serum Cal was determined using Cal ELISA Kit.

Results: Cal values were significantly higher in AP cases than in control group (p=0.001), value range from 32 to 490 ng/ml. There was a statistically positive significant relationship between cal and WBC values (r=0.423 p=0.0001), between cal and CRP values (r=0.282 p=0.012), between cal and amylase values (r=0.675 p=0.0001), between cal and lipase values (r=0.595 p=0.0001).

Conclusions: Plasma calprotectin levels increase nonspecifically with AP. Further studies are needed with larger number of patients who were classified according to the severity of AP.

Key words: Plasma calprotectin, acute pancreatitis, diagnosis

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INTRODUCTION

Calprotectin (Cal) S-100 is a 36 kD weighing heterodimer belonging to the family of calcium binding proteins, which is composed of light (MRP 8) and heavy (MRP 14) chains. It was first identified as an antimicrobial protein in granules of neutrophils (1). Cal forms 60% of the total cytosolic protein in neutrophils (2). Yui et al. found that, the reason for the increase was the migration of leucocyte to the site where an inflammation and tissue disruption occurs (3-5). It's released from stimulated neutrophils and monocytes during cell death and cell rupture. It's also found in plasma, urine and various body fluids as dissolved, from as well as in the intestinal fluid and stool (1). Cal levels in serum and various body fluids can be used as a marker of inflammation. In the presence of an ongoing cycle of inflammation increased levels of Cal can

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be detected in plasma, synovial fluid, urine, and stool (6-8). Cal is a marker specific to acute inflammation (9). Fecal Cal value increases with colorectal cancer, inflammatory bowel disease, necrotizing enterocolitis and celiac diseases. Fecal cal may be used as non-invasive, non-specific marker for diagnosis of these diseases (10-14). Also fecal Cal value could be important for observation of activation and remission phases of ulcerative colitis and Crohn's disease (15-17).

Majority of the studies focused on fecal Cal values. Cal levels in plasma were conducted for several organic disorders acute inflammation for the cystic fibrosis, lung infections and some of the rheumatic diseases. These studies suggest that Cal can be used as a marker for an acute inflammatory process (18-23).

There are few studies which indicate that in acute inflammation Cal increases systemically so can be used as a specific marker. In this study we aim to show effectively of Cal levels in plasma for acute pancreatitis (AP).

MATERIAL AND METHODS

In this prospective study, 84 patients with AP diagnosis who had been hospitalized in our General Surgery Clinic between Jan 2013-May 2013, were included. 30 patients were chosen as control group. Study was approved by ethic committee of our hospital (02-2013).

Male to female ratio was 36/48 with a mean age of 44 (19-81) for AP group and male to female ratio was 20/10 with a mean age of 31 (21-56) for control group. Physical examinations, urinanalysis, chest x-rays and abdominal ultrasonographies were performed to all patients in AP group. Infections other than pancreatitis was eliminated regarding the diagnostic tests. Blood samples were obtained before any treatment for Cal levels.

Blood samples for control group were obtained from the elective pilonidal sinus and inguinal hernia patients who were operated at our clinic. No local, systemic inflammation or incarceration was observed in control group patients. Patients with normal leukocyte (WBC), C-reactive protein (CRP) values were included in the control group.

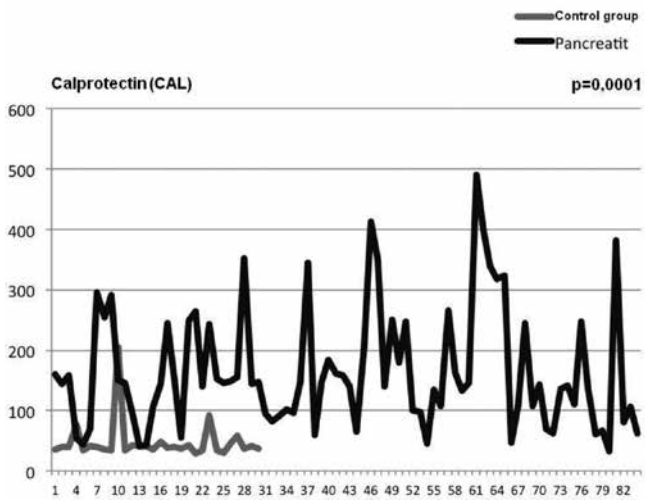
Age, WBC glucose, aspartate aminotransferase (AST), lactate dehydrogenase (LDH), CRP values of patients who has high plasma amylase and lipase were measured and Ranson scores were recorded. For measuring plasma Cal values, blood samples were taken to EDTA coated tube and then aliquots of serum were stored at -80°C for assaying. Blood samples were obtained for measurement of Cal from both groups. The blood samples were centrifuged for 15 minutes at 2000xg. Serum Cal was determined using Cal ELISA Kit (Cat no: CK-E90177), purchased from Eastbiopharm (China) following the manufacturer's instructions. The Human Cal ELISA was an enzyme-linked immunosorbent assay for the quantitative detection of human Cal. Cal levels were expressed as ng/ml. The limit of detection of Cal was determined to be 20 ng/ml. The intra-assay and inter-assay coefficient variations were <8.1% and <7.6%, respectively.

Statistical Analysis

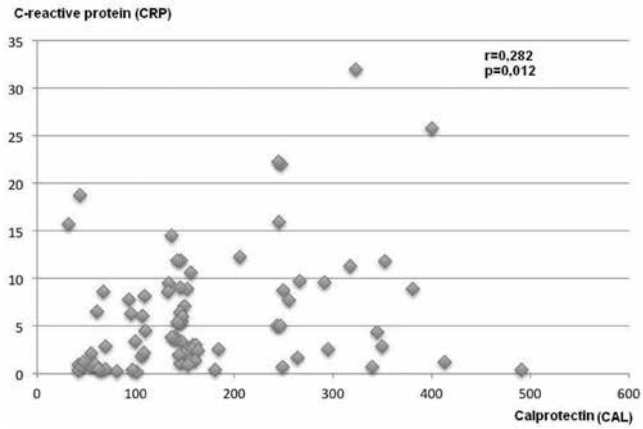
In this study, statistical analysis was performed with the package Statistical Software (Utah, USA). NCSS (Number Cruncher Statistical System) 2007. Mann-Whitney-U test used for the comparison of two groups and descriptive statistical methods (mean, standard deviation) for statistical analysis, the qualitative data compared with Chi-square test, relationships between variables determined with the Pearson correlation test. The results of $p<0.05$ was accepted for the evaluation of significance.

RESULTS

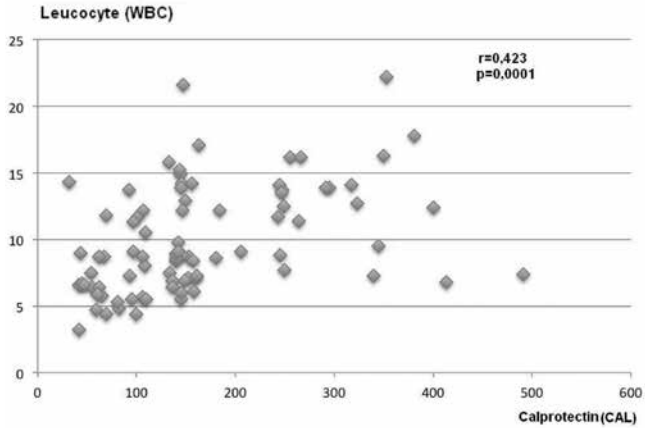
Cal values were significantly higher in AP cases than in control group ($p=0.001$), value range from 32 to 490 ng/ml (Graphic 1). There was a statistically positive significant relationship between cal and WBC values (Graphic 2)



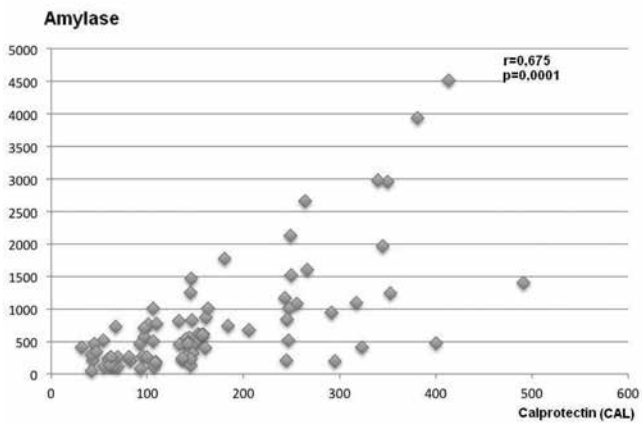
Graphic 1: Acute pancreatit and control group Calprotectin values



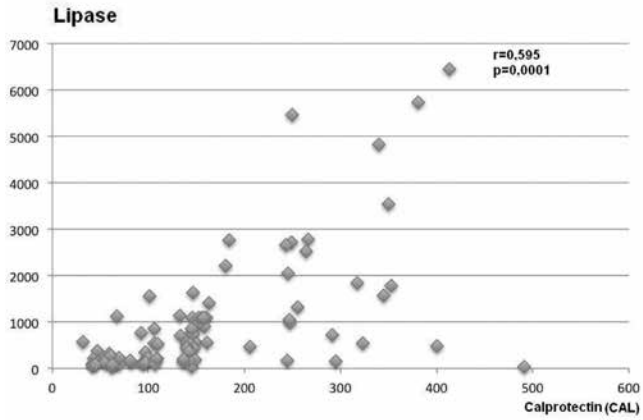
Graphic 2: CRP and Calprotectin values for Acute pancreatitis



Graphic 3: Leucocyte and Calprotectin values for Acute pancreatitis



Graphic 4: Amylase and Calprotectin values for Acute pancreatitis



Graphic 5: Lipase and Calprotectin values for Acute pancreatitis

Table 1: Laboratory results of groups

Dunn's Multiple Comparison Test	Lipase	Calprotectin	AST	ALT	GGT	LDH
Ranson 0/Ranson 1	0.029	0.011	0.033	0.434	0.360	0.002
Ranson 0/Ranson 2	0.049	0.016	0.0001	0.0001	0.004	0.0001
Ranson 1/Ranson 2	0.799	0.524	0.0001	0.001	0.008	0.005

(r=0.423 p=0.0001), between cal and CRP values (Graphic 3) (r=0.282 p=0.012), between cal and amylase values (Graphic 4) (r=0.675 p=0.0001), between cal and lipase values (Graphic 5) (r=0.595 p=0.0001).

Also there was statistically significant differences of calprotectin values between Ranson 0, Ranson 1 and Ranson 2 groups (p=0.021). Calprotectin values of Ranson 0 group was significantly lower than Ranson 1 and Ranson 2 groups (p=0.011, p=0.016). There was no statistically significant difference between calprotectin levels of Ranson 1 and Ranson 2 groups (p=0.524) (Table 1).

Area under the ROC curve was calculated (0.962±0.016) for demonstration of the power of Cal in detecting AP. Cal was a safe variable in the differentiation of AP. Cutoff point for Cal>52.19, sensitivity 91.67, specificity 90, positive predictive value 96.2, and negative predictive value 79.4, LR + value was 9.17. Which means that the possibility of AP in a patient with Cal value >52.19 is 9.17 times more likely than a patient with Cal value <52.19.

DISCUSSION

Cal values increase in acute infections. Alteration of fecal cal value is used as an indicator in inflammatory bowel disease especially activation and remission phases. It is stated that, increased levels of plasma Cal values can be a promising marker with WBC and CRP for diagnosis of AA (24). Plasma Cal value increases with AP. Cal is found in mainly 60% of neutrophils cytosole and also found within the cells of pancreas (25). There are studies suggesting that in acute inflammation Cal increases systemically. In this study we have recruited patients with AP which has no other systemic or local infection and WBC, CRP values were evaluated only according to severity of AP. Alterations of WBC, CRP values and relationships with plasma Cal were statistically significant, suggesting that cal increases in acute inflammation. Rising values of amylase and lipase represents pancreatic tissue damage. Also there was a statistical significant relationship between plasma cal values and amylase, lipase levels which is another important consequence that represents cal increases in pancreatic tissue destruction and inflammation. WBC and CRP levels are the parameters which are commonly used in the diagnosis and follow-up of local or systemic acute inflammatory processes. Our results show that Cal can be used as a marker of acute inflammation by these means. Increase in the value plasma Cal is not specific for AP. Further studies needed to be designed with larger number of patients which classified according to the AP severity for figuring out the use of cal value as a parameter for predicting the severity of AP.

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