Serum Endocan and Procalcitonin Levels in Determining The Severity of Acute Pancreatitis

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Öz

Amaç: Skorlama sistemleri ve görüntüleme yöntemleri, akut pankreatitin (AP) şiddetini belirlemede yeterli bilgi sağlayamayabilir, diğer parametrelere ihtiyaç vardır. İnflamasyon akut pankreatit patogenezinde önemlibir rol oynar ve inflamasyon belirteçleri AP şiddetinin belirlenmesinde önemli olabilir.

Yöntem İlk AP atağı olan ardışık 52 yetişkin hasta (> 18 yaş) prospektif olarak çalışmaya dahil edildi. Akut pankreatit ciddiyeti Revize Atlanta kriterlerine göre belirlendi. Dolaşımdaki endokan ve prokalsitonin (PCT) seviyeleri ELISA yöntemi kullanılarak ölçüldü.

Bulgular İlk AP tanısıalan 52 sıralı yetişkin hasta AP ciddiyetine göre; 25hasta hafif- AP (% 48), 27'siorta – şiddetliAP (% 52) olmak üzere 2 gruba ayrıldı. Ortalama hasta yaşı ve kadın cinsiyet oranı orta - şiddetli AP grubunda hafif AP grubuna göre anlamlı derecede yüksekti (sırasıyla p = 0.04 ve 0.02). Bununla birlikte, gruplar biyokimyasal parametreler açısından anlamlı farklılık göstermedi ve grupl ar arasında serum prokalsitonin ve endokan düzeylerinde fark yoktu. Akut pankreatit ciddiyeti ile serum endokan ve prokalsitonin düzeyleri arasında korelasyon yoktu.

Sonuç Serum endokan ve PCT düzeyleri, ciddi AP ve hafif AP grupları arasında anlamlı bir farklılık göstermedi. Bu nedenle, bu belirteçler AP'nin ciddiyetini belirlemek için ek fayda sağlamayabilir

Anahtar Kelimeler: akut pankreatit, ciddiyet, serum endokan ve prokalsitonin

Abstract

Object Scoring systems and imaging methods could not provide sufficient information to determine the severity of acute pancreatitis (AP), other parameters are required. Inflammation plays an important role in the pathogenesis of acute pancreatitis and inflammation markers may be important for determining the severity of AP

Methods Fifty-two consecutive adult patients (>18 years) with a first AP episode were prospectively included in the study.The severity of acute pancreatitis was determined according to Revised Atlanta criteria. Circulating endocan and procalcitonin (PCT)levels were measured using ELISA.

Results Fifty-two consecutive adult patients with a first episode of AP who had been dividedinto two groups according to the severity of their AP; 25 were assigned to the mild- APgroup (48%) and 27 to the moderate-severe APgroup (52 %).The mean patient age and ratio female gender were significantly higher in the moderate - severe AP group than the mild AP group (respectively, p = 0.04 and 0.02). However, the groups did not differ significantly
with regard tobiochemical parameters and there was no difference in serum procalcitonin and endocan levels between the groups. There was no correlation between the severity of AP and serum endocanor procalcitonin levels.

Conclusion Serum endocan and PCT levels did not significantly differ between the moderate - severe AP and mild AP groups. Therefore, these markers may not provide additional benefits for determining the severity of AP.

Key words: acute pancreatit, severity, serum endocan and procalcitonin,

Introduction

Acute pancreatitis (AP) is an inflammatory condition that represents a spectrum of diseases ranging from those with mild,self-limiting course to severe cases such as fulminant illnesses that result in multiple organ dysfunction syndrome. AP has still a high risk of in- hospital mortality, particularly in severe cases over recent decades,due to its lack of a specific treatment regimen[1]. Endothelial cell-specific molecule 1 (endocan) is a soluble proteoglycan, mainly secreted by vascular endothelial cells. Therelationship between serum endocan levels with other inflammatory parameters (e.g., white blood cells and high-sensitivity C-reactive protein) supporting its role in systemic inflammation[2]. Increased circulating endocan levels have been demonstratedin several-diseasessuch as type 2 diabetes, hypertension hypothyroidism, obstructive sleep apnea syndrome, and coronary artery disease, in various cancers such as hepatocellular carcinoma, renal cell carcinoma, and in systemic inflammatory diseases such as systemic lupus erythematosus [3,4].

Procalcitonin (PCT) is a biochemical marker produced by the parafollicular C cells of the thyroid. Severalpreviousstudies have shown that PCT is superior to C-reactive protein, interleukin-6, and leukocyte counts in the early diagnosis of bacterial infections and is a highly specific marker of sepsis5. Elevatedserum PCT correlates closely with inflammatory responses that are secondaryto microbial infections. PCT has been observed as an early predictor of the severity and development of infected pancreatic necrosis in patients with acute pancreatitis[6,9].

Ourstudyaims to investigatethe relationshipbetween serum endocan and procalcitonin levels and the severity of APandits effect on in-hospital mortality.No study has yet assessed the relationship between serum PCT and endocan concentration and the severity of AP.

Material and methods

This study was approved by the local ethics committee of the RecepTayyip ErdoganUniversity-Hospital and the subjects gave informed oral and written consent before inclusion in the study. Fifty-two consecutive adult patients (>18 years) with a first episode of AP who were admitted to our emergency internal medicinedepartmentover a 20-month period (2015–2017) were prospectively included in the study and AP was definedif a patient had the presence of two of the three following criteria: 1) abdominal pain consistent with the disease, 2) serum amylase and/or lipase greater than three times the normal upper limit, and/or 3) abdominal imaging(transabdominal ultrasound and/or contrast-enhanced computed tomographic) findings in accordance with AP. Alcohol-induced AP was defined as daily consumption exceeding 30 g of alcohol for men, 20 g for women, or 50 g of alcohol/day one month prior to hospitalisation in accordance with the guidelines for alcohol consumption as issued by the Danish Medical Health Authorities[10], accompanied by the exclusion of gallstones in at least two of the followingexaminations: ultrasound (US), contrast-enhanced computerised tomography (CT) scan,and magnetic resonance imaging (MRI). Gallstone- induced AP was defined as a plasma level of aspartate aminotransferase (ASAT)>150 U/l in combination with the presence of gallstones or sludge identified via US MRI or endoscopic retrograde cholangiopancreatography (ERCP). The severity of acute pancreatitis was determined according to Revised Atlanta criteria.Moderate and severe AP were analysed together because of low number of patients in severe – AP Exclusion criteria were: pancreatic calcifications, cysts or other signs of chronic pancreatic defect; impaired glucose tolerance or type 1/type 2 diabetes; hypertension, hyperlipidaemia, active or chronic liver or renal failure, or congestive heart failure; a

history of coronary artery disease, or acute infection (within the previous 14 days); the presence of any chronic inflammatory and autoimmune disease, and known malignancy.

Blood samples for endocan from patients were collected in plain tubes and serum was separated after centrifugation at 1500g for 10 minutes and stored at 80°C until analysis. Blood samples from calcium–EDTA tubes were analysed in an autoanalyser and Endocan levels were determined using a commercially available sandwich enzyme-linked immunosorbent assay (ELISA) kit with high sensitivity and specificity for the detection of human endocan (Bester, Wuhan, China).

Samples for PCTwere centrifuged at 3,000 rpm for 10 minutes, and the serum was stored at –20°C until tested. PCT levels of were measured with LUMItestPCT, an immunoluminometric assay manufactured by BRAHMS Diagnostica GmbH (Berlin, Germany). The assay's analytic sensitivity was 0.1ng/ml and the functional sensitivity was approximately 0.3 ng/ml.

Statistical Analysis

Statistical analysis was performed using SPSS 21 (SPSS Inc., Chicago, Illinois). Data were tested for the normality of distribution using the Kolmogorov–Smirnov test. Continuous variables were presented as means with the standard deviation and categorical variables were presented as frequencies with percentages. Continuous variables between the two groups were compared using Student's t test for normally distributed data and the Mann–Whitney U test for non-normally distributed data, whilecategorical parameters were evaluated by chi-squared (2) test. Pearson rank tests were used to indicate the correlation of the severity of APwith endocan and PCT levels and a two-tailed $P \leq 0.05$ was considered significant

Results

Fifty-two consecutive adult patients (>18 years) with a first episode of AP were dividedinto twogroups according tothe severity of AP, meaning that25 were assigned to the mild-APgroup (48%) and 27 to the moderate - severe APgroup (52%).Alcohol was the only cause of AP in three (5.7%) patients, gallstones in 40 (76.9%) and others causes (e.g.cancer and hypertriglyceridemia) in the remaining nine (17.4%). No patientrequired treatment with an open surgical procedure.

The groups demographic and clinical characteristics are presented in Table 1. The mean patient age and ratio of female gender was significantly higher in the moderate - severe AP group than in the mild AP group (respectively, $p = 0.04$ and 0.02). However, the groups did not differ significantly with regard to biochemicalparameters. In addition, there was no difference in the serum procalcitonin and endocan levels between the groups and there was no correlation between the severity of AP and serum endocanor procalcitonin levels.

able1: The demographic and clinical characteristics of groups			
	Mildacutepancreatit(n=33)	evere acutepancreatit(n=19)	P value
Age, years	65,2±16,6	76,9±7,8	0,006
Female n, %	16(48,5)	13(68,4)	0,16
Etiology, n, % Alcohol Gallstone Others	 2(6,1) 27(81,8) 4(12,1)	 1(5,3) 13(68,4) 5(26,3)	0,42
Organ failure (n, %)	-	2(10,5)	
Glucose (mg/dl)	133,3±47,2	157,2±47,7	0,08
WBC count (103/L)	12668±4757	14596±1344	0,45
Hgb, g/dl	13,3±1,5	13,2±1,6	0,81
PLT count (103/L)	243±71	225±73	0,38
BUN, mmol/L	40,7±18,7	46,7±11,6	0,21
Cr,mg/L	0,91±0,36	0,90±0,23	0,91
CRP, mg/L	5,0±2,5	5,3±2,8	0,95
ALT, U/L	146,5± 29,1	174,7±35,5	0,59
AST, U/L	140,0±26,6	187,9±37,0	0,29
GGT, U/L	149,3±21,9	323,8±76,5	0,09
PCT,ng/dL	2,46±1,02	5,20±2,87	0,38
Endocan,ng/dl	9,8±6,0	10,8±5,9	0,56
WBC = whitebloodcell, Hgb =Haemoglobin, PLT = platelet, CRP = C-reactive protein, ALT=alanineaminotransferase, AST= aspertateaminotransferase, GGT=gamma- glutamyltransferase, PCT =procalcitonin, BUN = bloodureanitrogen, Cr = creatinine			

Three patients (5.7%) died during the first 10 days, two of whom were in the moderate - severe AP group due to organ failure and the other was in the mild AP group due to cancer. The serum endocan and procalcitonin levels were higher among the patients with APwho died (p=0.05 and p<0,001, respectively). However, serum endocan and procalcitonin levels did not predict death in logistic regression analysis.

Table 2: Correlation analysis between Ransons core and serum endocan and PCT levels in acute pancreatit		
	Correlationco-efficient	P value
Serum Endocan	r: 0,172	0,22
Serum PCT	r:0,091	0.52
PCT: procalcitonin		

Discussion

In this study, we found that there was no relationship between severity of AP and serum levels of endocan and procalcitonin.In addition, these biochemical markersdid not predict death secondary to AP.

Prediction of severity plays an important role in the management of acute pancreatitis. Severe AP occurs in approximately 15–20% of patients[11].The early recognition ofpatients is crucialto prevent-morbidity and mortality associated with severity. The 50% mortality relationship with severe acute pancreatitis could be decreased to 8% through early recognition[12].

It is difficult for physicians to predict whichpatients with AP will develop severe symptoms. Although several scoring systems have been developed to predict theseverity of acute pancreatitis, these have limitations and provide little additional informationfor the assessment of patients[13]. Imaging techniques can not reliably establish severity in the earlyperiodof AP, as necrosis is usually absentupon admission and may only occur after48 h [14]. Scoring systems and imaging methods could not provide sufficient information to determine the severity of AP, other parameters arerequired. The role of the inflammatory process in the basic pathophysiology of AP mean that inflammatory markers have been investigated in AP. Inflammatory mediators such as tumour necrosis factor- (TNF-), interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-8 (IL-8), platelet activating factor (PAF), intercellular adhesion molecule-1 (ICAM-1), growth related oncogene-a/cytokine- induced neutrophil chemoattractant (GRO- /CINC), monocyte chemoattractant protein-1 (MCP-1), interleukin 10 (IL-10), complement component C5a, substance P, hydrogen sulfide (H2S), and neutral endopeptidase (NEP)were investigated [15-17]. However, these mediators are not practically available or consistently accurate for severity predictions in patients with AP.

Neutrophil elastase (NE)is a serine proteinase in the same family as chymotrypsin and secreted by neutrophils and macrophages during inflammation. Several studies that investigated the plasma concentrations of NE have demonstrated it that plays a role in the development of AP [18,19]. In a study that investigated the role of neutrophil elastase in predicting the severity of acute pancreatitis,mean NE activity was significantly higher in patients with predicted severe AP than in those with predicted mild AP(20). In our study, serum endocan and procalcitonin levels did not differ between moderate-severe acute pancreatitis and mild pancreatitis. This situation may suggest that the mechanism of inflammation in variousdiseases may also differ. Serum PCT is secreted in the secondary inflammatory response to microbial infections, whereas endocan is released secondary to endothelial dysfunction and atherosclerosis.

Our study has several limitations; first, the sample size was relatively small, and we had no control group. Second,a single measurement of endocan and PCT may not reflect the lifetime status.

In conclusion, serum endocan and PCT levels did not differ significantly between severe AP and mild AP. Therefore, these markers may not provide additional benefit for determining the severity ofAP.

Conflict of Interest:
Authors declare no competing interest

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