Original Article

Comparison of ranson criteria with paraoxonase, oxidative stress index and CRP in patients with acute pancreatitis

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ABSRACT

Objective: We aimed to compare paraoxonase levels, total antioxidant levels, total oxidant levels, oxidative stress index between Ranson score and C-reactive protein levels in acute pancreatitis.

Methodology: Thirty two patients were included in the study. Their Ranson scores were recorded upon arrival at the hospital and at the 48th hour. During the recovery period (6th week), CRP, paraoxonase and oxidative stress index levels were simultaneously checked.

Results: Mean first ranson score of patients were 1.4±1.4, mean paraoxonase levels of patients paraoksonaz were 176.5±108, and mean CRP levels of patients were 49±51. When the paraoxonase levels of the patients with systemic diseases and patients without systemic diseases were compared, no difference was detected in the arrival levels of paraoxonase, while differences were observed in paraoxonase-II (182.3 ± 38.5, 192 ± 28.2) and paraoxonase-III (158 ± 28.7, 230.9 ± 33.1) levels. However, this was not statistically significant. A positive correlation was observed among patients CRP, paraoxonase levels and oxidative stress index and Ranson criteria.

Conclusion: Paraoxonase and oxidative stress index can be used as new parameters for predicting clinical outcome of acute pancreatitis.

KEY WORDS: Acute pancreatitis, Antioxidant levels, Ranson score, CRP.

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INTRODUCTION

Acute pancreatitis is a disease which has no special treatment and is characterized by the damage of the activated, by whatever reason, enzymes in pancreas to the peripheral tissue and pervasive inflammation. In humans, acute and chronic pancreatitis with different etiologies, oxidative stress is important in the development and progression of the disease.[1]

During acute pancreatitis, platelet activating factor, bradykinin, complement, free oxygen radicals (FOR) and cytokines are released from acinar cells of pancreas, capillary endothel, mast cells.[2] When the balance between production and elimination of free radical is broken oxidative stress develops.[3] Development of oxidative stress in critically ill patients is associated with poor prognosis.[4] In acute pancreatitis, lipid peroxidation increases and there is a correlation between oxidative stress and severity of pancreatitis.[5] Cellular lipid peroxides hydrolyze LDL by human serum paraoxonase (PON) and reduce their uptake of macrophages.[6] A standard parameter to define the redox status was not found. Therefore, potential representative parameters of

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anti-oxidant and oxidizing biomolecules must be examined.[7]

Total Oxidant Capacity (TOC) that can be taken directly outside the body or might be generated during reactions in the body. Total peroxide, serum oxidant activity is synonymous with the molecules of reactive oxygen.[8] Total Antioxidant Capacity (TAC) is the defense mechanism of the body against to oxidative stress consisting of a variety of substances such as enzymes and vitamins. Prevents the formation of free radicals, and repair cell damage.[9]

Oxidative Stress Index (OSI) is calculated by dividing Total Oxidant Capacity (TOS) / Total Antioxidant Capacity (TAC)[10] which when high indicates that oxidative stress has increased.[11,12] Effects of free radicals on lipids cause peroxidation, on proteins cause change of structure and function, to carbohydrates cause various diseases[13], to DNA cause a mutation and cell death.[14]

Paraoxonase is an enzyme involved in the hydrolysis of organophosphates. There are three genotypes. Paraoxonase 1 Paraoxonase 2 Paraoxonase 3 Paraoxonase 1 (PON-1) is an enzyme which is mainly synthesized in the liver. PON-1 circulates in the blood bound to HDL and delays or prevents the oxidation of LDL.[15] In many organs, tissues and serum PON-1 is present.[16] Serum PON-1 activity is decreased in clinical conditions associated with low high-density lipoprotein cholesterol (HDL-C), increased lipid peroxidation and low-grade chronic Inflammation.[17] Enzyme activity decrease with increasing age. PON-1 enzyme activity is influenced by genetic and environmental factors, different populations and different intervals.[18] In recent years, enzyme activities were determined in several diseases because of the antioxidant effects.[19] In some cases, increase in oxidants and decrease in antioxidants are unavoidable. As a result, oxidative stress cause more than 100 disease.[20]

It may be valuable to measure free radicals to predict the severity of acute pancreatitis.[21] In this study, we aimed to compare the levels of PON, TOC, TAC, OSI with Ranson scores and C reactive protein (CRP) levels measured in three different phases: at the beginning of the disease, 48th hour and 6th week of the recovery period.

METHODOLOGY

Ethical committee approval was obtained for this study. In this prospective study, we have examined 32 patients admitted to our hospital that are of age between 28-85, have no known renal failure, their high level amylase and lipase cannot be associated to any other reason, have *classical* belt type *abdominal pain, less than 6 hours has passed from the beginning of their abdominal pain. The patients were assessed in terms of their glucose, white cells, lactic dehydrogenase (LDH), alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), lipid profile (total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG), C-reactive protein (CRP), amylase, lipase, urea (BUN), creatinine levels on the admission, and in terms of their hematocrit, blood urea nitrogen (BUN), calcium levels, partial pressure of oxygen, base deficit and fluid deficit at the 48th hours of the admission. Ranson criterias were calculated and complications that emerged recorded. Ten cc. serum samples were taken from patients to the tubes for the measurement of* TAC, TOC, *PON at the application (TAC1, TOC1, PON), TAC2, TOC2, PON II at the 48th hours and TAC3, TOC3, PON III at the 6th week. These tubes were kept at the room temperature for two hours and then centrifuged and kept at -80 C. OSI was calculated.* TAC levels were measured spectrophotometrically by a fully automated method in an automated analyzer which is developed by *Erel.*[10] TOC levels were measured by a fully automated calorymetric method which is developed by *Erel.*[8,9] *Abdomen USG, abdomen tomography -if necessary-* and MRCP (magnetic resonance cholangiopancreatography) were done for all patients at the application.

The data collected were analyzed using the program SPSS 16. It was tested whether the data distribution was normal or not, by Smirnov-Kolmogorov test. The results that were obtained after definitive statistical analysis were expressed as mean ± standard deviation (interval: minimum-maximum) or numerically (percentage). While independent sample, t-test was used to compare parametric variables pertaining to two different groups, Mann-Whitney-U test was used to compare the non-parametric variables. One-way ANOVA test was used to compare the parametric variables pertaining to multi-groups. In case of p values less than 0.05, were considered statistically significant.

RESULTS

Ten of the 32 patients were male (31.3%) and 22 were female (68.8%). Mean age of the cases was 51.4 ± 19.4 years (20-85 years). Mean ages of female and male cases (56.7 ± 18.9 years and 49.1 ±19.5 years respectively) were statistically similar (p=0.308).

When the paraoxonase levels of the patients with systemic diseases and patients without

Table-I: Patients PON TAK TOS OSI Values.

	Admission	*48th hour*	*Recovery period (6th week)*
PON U/ml	176.5±108*	188.9±120.1**	198.3±96.8***
TAK mmol Troloks denk/L	1.9±0.8	1.7±0.4	1.9±0.3
TOS mikromol H2O2 denk/L	17.1±14.8	12.6±7.9	19.3±22.4
OSI Arbitrary unit)	1.0±0.9	0.8±0.4	0.9±0.9

*Difference between levels of paraoxonase at application and recovery period are statistically significant.
** Difference between levels of paraoxonase at 48th hour and recovery period are statistically significant.
*** Difference between levels of paraoxonase at application and 48th hour are not statistically significant.

systemic diseases were compared, no difference was detected in the arrival levels of paraoxonase, while differences were observed in paraoxonase-II (182.3 ± 38.5, 192 ± 28.2) and paraoxonase-III (158 ± 28.7, 230.9 ± 33.1) levels. However, this was not statistically significant.

According to Ranson criteria, the patients had a mean of 0.9 ± 0.9 points (interval: 0-5 points) as preliminary Ranson score. There was no statistically significant difference between male and female patients in terms of preliminary Ranson assessment (1.0 ± 0.8 points and 0.8 ± 0.9 points respectively, p=0.644). In the assessment based on the Ranson criteria looked at the 48th hour, it was observed that the same cases had 1.4 ± 1.4 points (interval: 0.6 points) as their mean. Likewise, there was no statistically significant difference between female and male patients according to the Ranson assessment after the treatment (1.2 ± 1.2 points vs. 1.9 ± 1.8 points respectively, p=0.297).

A statistically significant and positive correlation was observed between the ages of the cases and the levels of CRP (r=0.369, p=0.038). There was a significant, but negative correlation between the age and TOC 3 and OSI 3 values. (p=0.010 and p=0.006) There were positive correlations between the Ranson score and CRP at the admission of the patient, and between the 48th hour Ranson score and OSI 2 values, too. (p=0.025 and p=0.027 respectively)

There was a positive correlation between the Ranson score calculated after the clinic follow up and CRP concentrations. (r=0.690, p=0.001) A significant, but negative correlation was identified between the Ranson score calculated at the 48th hour and PON II values (p=0.030). CRP levels and TAC 1 levels were also directly and significantly correlated with each other (p=0.001).

There was a positive and significant correlation between the paraoxonase values and paraoxonase III values at the beginning of the disease (p=0.001). However, a positive and significant correlation was identified also between paraoxonase II and paraoxonase III values pertaining to the cases studied (p=0.001).

There was a positive and significant correlation between TAC 1 and TAC 3 values (r=0.502, p=0.029). Besides, there was a significant and positive correlation between TAC 2 and TAC 3 values. (r =0.570, p=0.011)

It was observed that TAC 3 values changed significantly according to the complications (p=0.029). According to that, compared to the cases in which there was no complication stemming from acute pancreatitis, TAC 3 values pertaining to the cases in which there were complications stemming from acute pancreatitis were higher significantly (1.9 ± 0.3 vs. 2.5 ± 0.1, p=0.009). (Table-I).

DISCUSSION

There are 11 criterias used in the Ranson scoring system. Five criterias are used to determine the degree of necrosis at admission. Score is correlated with mortality. Average scores are 1.6, 2.4 and 5.6 respectively in mild pancreatitis, severe pancreatitis and lethal pancreatitis.[22] In our study, average Ranson score was 2.3 in mild pancreatitis without complications and 4.3 in acute pancreatitis with complications. Limitations of the Ranson scoring are that it can only be completed after 48 hours. Due to the application difficulties in the other scoring systems and necessity of invasive monitoring used in acute pancreatitis, there are studies aiming to find new scoring systems.[23]

In one study, 143 patients with a diagnosis of acute pancreatitis with the Ranson scoring system grades a significant relationship between the developments of complications was noted.[24] In our study, a positive correlation was found between the incidence of complications and Ranson score. TAC 3 values were significantly changed by the developed complications. (p = 0.029).

In an experimental study by Franco-pons et al, acute pancreatitis was inducted in 36 rats. Serum paraoxonese levels of these rats were evaluated just after the induction and 18 h after the induction. They found a decrease in paraoxonase levels compared to the initial levels.[25] Also Unal et al.

found lower levels of PON in acute pancreatitis according to control group.[26] Many factors other than acute pancreatitis can affect alterations in paraoxonase levels. Feeding habits, vitamin use, smoking, obesity, anemia, diabetes, coronary artery disease, thyroid diseases and helicobacter pylori are among these factors. In our cases, there were no significant difference between PON values of admisson, 48th hour and 6 week, (p = 0.58). However, there was a positive correlation between the attack and disease-free period. A positive correlation between levels of paraoxonase with Ranson score is important. In our patients, there were positive correlations between PON levels and total cholesterol, HDL cholesterol. After evaluation of OSI, we found a significant negative correlation between CRP levels and recovery period OSI values in the patients. Existence of positive correlation between increasing CRP levels secondary to developed inflammation and OSI and decrease of OSI values after recovery period were expected results but lack of significant difference between the beginning and the 48th hour of hospitalization in the patients is a remarkable result. Previous studies enabled making global evaluations about oxidative stress level by using glutathione peroxidase and malondialdehyde level measurements.

In conclusion, our findings indicate that paraoxonase and OSI can be set as new parameters to predict the prognosis of acute pancreatitis.

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