Original Paper

Evaluation of the Paraoxonase-1 Level in Patients with Acute Pancreatitis

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ABSTRACT: Background. This study, aimed to evaluate the role of paraoxonase-1 (PON-1), in the pathogenesis of acute pancreatitis (AP). PON-1 plays a significant role in antioxidant, anti-inflammatory and antiatherogenic responses and may help predict the severity of AP. Methods. A total of 50 patients with AP and 45 healthy volunteers were included in the study. AP was diagnosed when serum amylase and/or lipase values increased threefold and/or more than the upper limit of normal, together with a complaint of abdominal pain. Modified Atlanta and Ranson scoring were used for AP severity. Results. AP causes were biliary for 35 (70%) patients and idiopathic for 8 (16%) patients, AP developed in 6 (12%) patients after endoscopic retrograde pancreatography, and AP in 1 (2%) patient was a consequence hypertriglyceridemia. No difference in PON-1 level was found between the groups (PON-1=197.06±164.6 and 192.1±111.78, respectively, p=0.86). On the other hand, patients were stratified according to the modified Atlanta (177.5±166.8 for mild to moderate vs. 268.5±64.2 for severe, p<0.018) or Ranson (163.2±133.06 for mild vs. 208.8±158.0 for severe, p<0.016). PON-1 level was significantly higher in patients with severe AP compared to patients with mild and/or moderate disease. Conclusion. Although PON-1 level did not differ in patients with and without AP, PON-1 level increased significantly in parallel with the severity of AP. Thus, PON-1 can be a potential marker for the severity of the disease and can predict prognosis.

KEYWORDS: *Acute pancreatitis, paraoxonase-1, anti-inflammatory.*

Introduction

One of the most common reasons for hospitalizations for digestive system diseases is an inflammatory disorder identified as acute pancreatitis (AP) [1].

Since the pathophysiology of AP seems complicated, it has been suggested that a single factor causes pancreatic damage in nearly all cases.

Alcohol consumption and a diagnosis of gallstones blocking the pancreatic duct account for more than 80% of cases [2-4].

The most common classification for AP at present is the 2012 update of the Atlanta classification [5].

The absence of organ failure is the Atlanta classification's definition of mild disease.

Organ failure that manifests within the first 24 hours but resolves within 48 hours is considered moderate AP; organ failure that has persisted permanently is considered severe AP [5,6].

The Ranson criteria are one of the oldest scoring systems used to determine the severity of the disease.

For this scoring, patients with less than 3 points belong in the mild AP group, and patients with more than 3 points belong in the severe AP group [7].

Regardless of the underlying cause, premature activation of pancreatic proteolytic enzymes occurs, resulting in a series of changes that lead to cell damage and pancreatic self-digestion at times.

An inflammatory process begins with chemokines and inflammatory cytokines released from acinar cells, leading to activation of circulating macrophages and neutrophils.

A significant amount of cytotoxic substances and oxidants are secreted by the activated neutrophils, aggravating local pancreatic damage [2,8].

Oxidative stress then occurs due to an imbalance between free radicals and antioxidants [9,10].

Paraoxonase-1 (PON-1) is a calcium-dependent multifunctional enzyme with paraoxonase-1 (PON-1), Hcy-thiolactonase (HTase), aryl esterase (AREase), lactonase and paraoxonase (POase) activities.

PON-1 is mainly synthesized by the liver and associates with high-density lipoprotein in the bloodstream [11-13].

PON-1 attenuates oxidation of low-density lipoprotein, reduces foam cell formation by

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macrophages, and degrades homocysteine ethiolactone.

Therefore, PON-1 plays an important role in antiatherogenic responses and anti-inflammatory [14-16].

It plays a significant role in antiatherogenic, anti-inflammatory and antioxidant responses and may help predict AP severity.

PON-1 is important for antiatherogenic, anti-inflammatory, and antioxidant responses and could play a role in AP severity prediction.

The current research were designed at determining PON-1's role to the AP pathogenesis.

Material and Methods

This cross-sectional, prospective study was conducted on 50 patients who had been diagnosed with AP and were admitted to the emergency room, as well as 45 healthy volunteers.

The diagnosis of AP was accepted as a bigger than threefold increase in amylase and/or lipase values, in patients who presented with typical abdominal pain in the first 48-72h.

Pregnant women and patients with a history of malignant disease, organ failure, or organ transplantation were not included in the study.

The severity of the disease was assessed using the Ranson scoring indices indexes and the revised Atlanta classification.

Patients with a diagnosis of AP were divided into three groups, namely mild, moderate, and severe, in accordance with the revised Atlanta classification [5].

The parameters at the time of admission to hospital were used when calculating the Ranson score.

One point was given for each parameter.

Patients with a score of 3 and above were considered as having severe pancreatitis, while patients with a lower score were considered as suffered from mild pancreatitis [7].

Blood samples were taken within the first 48h of hospital admission.

After centrifugation (3500rpm, 10min-) serum samples were stored at-80°C.

PON-1 activity was performed according to the commercially available kit (Rel assay, Gaziantep, Turkey).

Basal PON-1 activity was calculated and stated in U/L.

Statistical Analysis

SPSS software version package program 22.0 (SPSS Inc., Chicago, Illinois, USA) was used to analyze the data.

To evaluate data based on categories, the Chi-Square test was used.

For continuous variables, the Mann-Whitney U test and Student's t test were used for parametric and nonparametric data, respectively.

The Pearson Correlation analysis was performed to assess the relationship between the PON-1 and variables such as age, gender, Atlanta score, and Ranson score.

Data is presented as mean±SD.

Statistical significance was defined as a value of $p < 0.05$.

The study was approved by the school of medicine at Harran University's ethics committee (HRU/ethical number: 09/03/2020-14381/05). All participants gave their informed consent.

Results

In the AP group, 22 (44%) patients were male, 28 (56%) were female, and the mean age was 54.0±18.2 years.

In the control group, 17 (37.8%) patients were male, 28 (62.2%) were female, and the mean age was 52.6±17.1 years.

Age and gender distribution in both groups were similar ($p>0.05$).

Biliary pancreatitis was found in 35 (70%) patients, idiopathic pancreatitis in 8 (16%) patients, pancreatitis after endoscopic retrograde pancreatography (ERCP) happened in 6 (12%) patients, and pancreatitis due to hypertriglyceridemia occurred in1 (2%) patient (Table 1).

Table 1. Cause of acute pancreatitis.

Etiological cause	N (%)
Biliary	35 (70%)
Idiopathic	8 (16%)
After endoscopic retrograde pancreatography	6 (12%)
Hypertriglyceridemia	1 (2%)

Table 2. Paraoxonase-1 (PON-1) levels of patient and control groups.

	AP group (n=50)	Control group (n=45)	p
PON-1	197.06±164.6	192.1±111.78	0.86

The mean PON-1 levels were 197.06±164.6 for the patient group with AP and 192.1±111.78 for the control group (p=0.86) (Table 2).

According to the Modified Atlanta Score, 41 (82%) patients had mild, 3 (6%) patients had moderate, and severe AP was diagnosed in 6 (12%) patients.

While PON-1 values were 177.5±166.8 for patients with mild and moderate AP, they were 268.5±64.2 for patients with severe AP, which was significantly higher for these latter patients (p<0.018) (Table 3).

Table 3. Paraoxonase-1 (PON-1) levels according to Atlanta and Ranson score severity.

	Atlanta score			Ranson score		
	Mild-to moderate	**Severe**	**p**	**Mild**	**Severe**	**p**
N (%)	41 (82%)	9 (18%)		37 (74%)	13 (26%)	
PON-1	177.5±166.8	268.5±64.2	0.018	163.2±133.06	208.8±158.0	0.016

On the other hand, according to the Ranson Score, 37 (74%) patients had mild AP and 13 (26%) patients had severe AP.

Table 3 shows that PON-1 levels were significantly higher in patients with severe AP (208.8±158) when compared to patients with mild AP (163.2±133.06, p<0.016).

No significant correlation was found between the PON-1 levels of the patients and age (r:-.082; p:0.572).

There was no significant correlation between Atlanta score and PON-1 level (r:-.240; p:0.094).

There was no significant relationship between Ranson score and PON-1 level (r:-.120; p:0.405).

When evaluated separately for both genders, it was found that there was no significant relationship between age, Atlanta and Ranson score and PON-1 levels.

Discussion

AP can have high morbidity and mortality when severe local and systemic complications occur.

One of the most common causes for gastrointestinal hospitalization is acute pancreatitis (AP), which is brought on by an abrupt increase in and severe pancreatic inflammation.

The disease has become more common over the past 20 years, increasing by more than 20%.

Although several studies addressed the pathogenesis of AP, its exact mechanism has not yet been determined [3,17].

The incidence of AP is at 34 cases per 100.000 people annually in the general population (95% (CI) 23-49), and there is no significant difference between genders [18].

In a study by Uyanikoglu A et al., 68% of the patients with AP in the Turkish population were female and 32% were male [10].

In our study, slightly more than half of the cases were women.

Gallstones and excessive alcohol consumption are the leading causes of AP, generally accounting for approximately 60%-80% of all cases, but these rates vary between populations [4].

In our study, the most common cause was biliary, followed by idiopathic and iatrogenic (post ERCP) causes.

This may be due to the lower rate of alcohol use in our region compared to western countries and the high amount of ERCP performed in our center.

PON-1 plays an important role in anti-inflammatory, antioxidant and antiatherogenic responses [14-16].

Various studies have shown that PON-1 polymorphisms may be associated with neurodegenerative diseases related with oxidation and inflammation, such as Alzheimer's [19].

In a study by Drehmer et al., PON-1 activity was low in patients with multiple sclerosis.

Hence, PON-1 became a sensitive marker for anthropometric and metabolic improvement in these patients [20].

It has also been shown that oxidation may have a role in AP [9,10].

In a study examining oxidative stress induced by smoking and inflammatory mechanisms, where membrane-associated antioxidants including PON-1 were evaluated, oxidation mechanisms were disrupted in AP [21].

PON-1 rs854560 allele frequencies did not differ between patients with chronic pancreatitis and healthy people.

However, in the subgroup analysis, the rs662 allele of PON-1 was found significantly more

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frequently in patients with idiopathic chronic pancreatitis [22].

In this study, we found that PON-1 levels did not increase in patients with AP, which may be due to the small number of cases analyzed.

More comprehensive studies on this subject are needed.

While the mortality rate in all AP cases is around 1%, this rate can reach up to 20%-30% in severe AP cases.

There is no single prognostic criterion to evaluate AP severity in the clinic.

Diagnosis of the disease and estimation of mortality are usually made using clinical data, imaging and biochemical analysis together.

It is obvious that more valid and useful parameters are needed for the diagnosis of the disease in the early stages and for the early detection of severe cases [23,24].

One this study, the increase in PON-1 levels with the severity of AP suggested that PON-1, as an inflammatory indicator, could predict the prognosis of the disease in patients with AP.

In conclusion, useful and susceptible markers showing whether the disease is severe or not in AP are important and essential for the care of the disease. PON-1 may be a potential marker to predict the disease severity.

Compliance with Ethical Standards

The study protocol was approved by the Ethics Committee of Clinical Research of Harran University.

The study was conducted in accordance with the principles of the Declaration of Helsinki.

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Conflict of interests

None to declare.

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