



ARAŞTIRMA/RESEARCH

The role of neopterin in the diagnosis of patients with acute pancreatitis on admission to the emergency department

Acil servise başvuran akut pankreatit hastalarının tanısında neopterin rolü

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Abstract

Purpose: There are difficulties observed in the diagnosis of acute pancreatitis in emergency departments due to its different clinical properties and the insufficiencies in the methods of diagnosis. Since there is no specific biochemical indicator, the diagnosis is made usually late or with difficulty. Neopterin is an enzyme secreted from the macrophages and is an indicator of cellular immunity activation. The aim of this study was to determine the role of neopterin in the early diagnosis of acute pancreatitis .

Material and Methods: 39 patients, who had been hospitalized with the complaints of abdominal pain and diagnosed as acute pancreatitis via laboratory and screening methods, and 30 healthy controls were included in the study. Amylase, lipase, cholesterol and neopterin were measured in the patients' samples. The diagnoses were confirmed with abdominal ultrasound and computed tomography.

Results: The neopterin values in patients with acute pancreatitis were significantly higher than those of the control group.

Conclusion: Neopterin is an indicator which is elevated in certain inflammatory and autoimmune situations. We believe that it is important in the early diagnosis of acute pancreatitis. Further experimental and clinical studies should be conducted on the subject.

Key words: Acute pancreatitis, neopterin, emergency

Öz

Amaç: Akut pankreatit, değişken klinik özelliklere sahip olması ve tanı yöntemlerindeki yetersizlikler nedeniyle acil serviste bazen tanı güçlüğü yaşanmaktadır. Tanı koyduracak spesifik bir biyokimyasal belirteci olmadığından tanısı çoğu zaman zor ve geç konabilmektedir. Neopterin hücrel immünite aktivasyonunun bir göstergesi olup makrofajlardan salınan bir enzimdir. Çalışmamızda akut pankreatitin erken tanısında neopterin rolünün belirlenmesi amaçlandı.

Gereç ve Yöntem: Karın ağrısı şikayeti ile yatırılan laboratuvar ve görüntüleme yöntemleri ile akut pankreatit tanısı konulan 39 hasta ile sağlıklı 30 kontrol çalışmaya dahil edildi. Alınan numunelerden amilaz, lipaz, kolesterol ve neopterin çalışıldı. Hastaların tanıları abdominal ultrasonografi ve abdominal bilgisayarlı tomografi ile kesinleştirildi.

Bulgular: Akut pankreatit olan hastaların Neopterin değerleri sağlıklı gruba göre anlamlı yüksek olarak tespit edildi.

Sonuç: Neopterin birtakım inflamatuvar ve otoimmün durumlarda yükselen bir belirteçtir. Akut pankreatitin erken tanısında ve şiddetinin belirlenmesinde önemli olabileceğini düşünmekteyiz. Bu konuda daha ileri deneysel ve klinik çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Akut pankreatit, neopterin, acil

INTRODUCTION

Acute pancreatitis (AP) may be defined as a reversible inflammation of the pancreas with different degrees of involvement. This inflammatory condition may either be limited to the pancreas or

be spread to peripancreatic tissues and other organs systems¹. AP is a disease with quite a heterogeneous distribution which differs from mild edematous pancreatitis to severe necrotizing pancreatitis with 20% mortality. Yet, there are many controversial issues concerning its diagnosis and

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treatment². The clinical picture varies from the mild form that rapidly responds to treatment, to the severe form, which is accompanied by systemic findings, sepsis and multiple organ failure³. The disease is diagnosed via anamnesis, physical examination, serological indicators and radiological findings⁴. The disease may sometimes be difficult to diagnose in the emergency department, since the clinical picture of AP has changing characteristics and due to the factors that limit the methods of diagnosis. Yet, different parameters are used in the diagnosis and follow-up of AP. The levels of blood and urinary amylases, serum lipase, serum elastase-1, serum trypsin, serum phospholipase-A2, C-reactive protein, interleukin 6-8 and procalcitonin may be increased in acute pancreatitis⁵.

Neopterin (NP) is a sensitive indicator in the activation of cell-mediated immune reactions. Therefore, determination of the concentration of NP in various body fluids has a diagnostic value in different diseases including T lymphocytes and macrophages⁶. Although it is a molecule that has been investigated for more than 20 years in many different diseases, there is only a small number of studies on the relation of NP with Inflammatory Bowel Disease⁷.

In this study, we aimed to investigate the possible relationship of serum NP level in AP patients diagnosed in the emergency departments, with the early-stage of the disease and the severity of the disease using the current literature.

MATERIALS AND METHOD

This study was conducted between January 2012 and April 2012. The study was begun after having obtained approval from the ethics committee of Meram Medical Faculty. 39 patients with AP and 30 healthy controls were included in the study.

Patients with viral infections (eg. HIV, CMV), inflammatory diseases (sarcoidosis, celiac disease,

Table 1. Etiology of with acute pancreatitis patients

Etiology	The number of patients (n)	%
Biliary	23	57.9
Drug	3	7.5
Alcoholic	2	4.1
Hypercholesterolemia	1	2.5
Post ERCP	1	2.5
Postraumatic	1	2.5
Idiopathic	8	20.5

multiple sclerosis and aseptic meningoencephalitis), autoimmune diseases (rheumatoid arthritis, Crohn's disease, systemic lupus erythematosus, diabetes mellitus type I, ulcerative colitis, acute anterior uveitis, autoimmune thyroiditis) and malignant diseases (genital tumors, genito-urinary channel tumors, lung cancer, gastrointestinal carcinoma, pancreatic carcinoma, hematological neoplasms), which are known to interfere with neopterin levels, were excluded from the study.

The patients were diagnosed according to the clinical pictures, examinations, laboratory findings, ultrasound and abdominal tomography screenings. In order to analyze the levels of serum neopterin 3 ml blood samples of patients with AP were placed into Vacutainer tubes with gel. The samples were kept for 30 minutes for coagulation and centrifuged for 10 minutes at 3000 rpm. Serum samples were then pipetted into eppendorf tubes. The ELISA kit (E13396h Human Neopterin Elisa Kit China) was used for neopterin detection. The sensitive value of Nepterin was accepted as 0.156 ng/ml.

The data obtained from the patient and the control groups were analyzed using the SPSS (statistical package for social sciences) program. The non-parametric test Mann Whitney U and the Kruskal-Wallis Test were used in the analysis. A p value of <0.005 was considered as statistically significant.

RESULTS

39 patients with AP and 30 healthy controls were included in the study. Nineteen were female and 20 were male. The mean age was 57. The etiology in patients with AP included 23 cholelithiasis (57.9%), 2 alcohol use (4.1%), 3 drug-related AP (7.5%), 1 hypercholesterolemia (2.5%), 1 post-ERCP AP (2.5%), and 1 post-traumatic AP (2.5%). No etiological factor was present in the remaining 8 patients (Table 1).

The mean age of the control group was 28.5. They had no history of a disease. No complaints of abdominal pain or else were determined. They were randomized without gender consideration.

All the patients underwent panabdominal Ultrasonography and abdominal tomography. According to the results of these radiological screenings, edematous pancreatitis was determined in 35 of the patients, necrotizing pancreatitis was detected in 2, and pseudocyst was found in 2.

The neopterin values of the patients were compared according to the etiologies. No differences were observed between the neopterin values of patients with cholelithiasis, alcohol use, drug use, hypercholesterolemia, trauma- and ERCP-related AP ($p>0.005$). Likewise, no differences were observed between the neopterin values of the 3 different groups (edematous, necrotizing, pseudocyst) according to the radiological findings ($p>0.005$) (Table 2).

Table 2. Value of neopterin in edematous pancreatitis, others and control group

Groups	N	Minimum	Maximum	Mean	Std. Deviation
Edematous pancreatitis	35	0.79	26.13	3.99	4.95
Others (necrotizing and pseudocyst)	4	1.52	3.29	2.45	0.79
Control	30	0.10	0.20	0.15	0.029

The neopterin values in patients with AP were compared to that of the control group. The mean neopterin value of the patient groups was found to

be significantly higher than that of the control group ($p<0.005$) (Table 3,4).

Table 3. Comparison between the patient with edematous pancreatitis and control groups

Groups	N	Mean± Std. Deviation	P values
Edematous Pancreatitis	35	3.99±4.95	0.001
Control	30	0.15 ±0.03	

Table 4. Comparison between the patient with others and control groups

Groups	N	Mean± Std. Deviation	P values
Others	4	2.45±0.79	0.002
Control	30	0.15±0.03	

DISCUSSION

Acute pancreatitis is one of the diseases that should be considered in the distinctive diagnosis in cases admitted to emergency departments with abdominal pain. The clinical symptoms and findings may vary depending in particular on the age of the patient and the severity of the attack. The severity of the disease may vary from mild glandular oedema to dense necrosis and bleeding^{5,8,9}. The disease may sometimes be difficult to diagnose in emergency departments, since the clinical picture of acute pancreatitis has fluctuating characteristics and due to factors that limit the diagnosis methods. Nonetheless, different parameters are used in the diagnosis and follow-up of acute pancreatitis. The levels of blood and urinary amylases, serum lipase, serum elastase-1, serum trypsin, serum phospholipase-A2, C-reactive protein, interleukin 6-

8 and procalcitonin may be increased in acute pancreatitis. The increase in serum lipase level is more specific than the increase in amylase level^{1,5,10}. In our study, we evaluated the levels of neopterin, which is an indicator of inflammation.

NP is a molecule which is secreted from monocytes and macrophages by the induction of interferon-gamma. Its biological function has not been clearly demonstrated and it does not have a specific receptor. Its concentration is increased in several diseases with high monocyte/macrophage activity. It has been shown in abnormal concentrations in various clinical conditions. Measurement of NP from body fluids may provide information on the present situation of the cellular immune response and often helps predict the progression of the disease⁶. Increased levels of neopterin were detected in a study including patients with severe acute pancreatitis, and the levels of neopterin were

shown to be related to pancreatic necrosis and mortality¹¹.

In another study, the NP levels in severe pancreatitis were determined to increase faster than the NP levels in mild AP patients. The NP levels were demonstrated to reach extremely high values¹². The cellular immune response was stated to be important in acute pancreatitis in another study, and the levels of serum neopterin were shown to be important in demonstrating the severity of the disease¹³. Another study showed that the levels of neopterin were higher than normal in patients with acute pancreatitis or pancreas carcinoma¹⁴.

One study showed that the P values were higher than those of the control group in patients with pancreas adenocarcinoma and chronic pancreatitis. It was suggested in the same study that the use of NP values in the diagnosis of pancreatic diseases could be helpful¹⁵.

In our study, disregarding the severity of the disease, the neopterin levels of all the patients with AP were found to be elevated. These levels were demonstrated to be higher than that of the healthy group. It was also shown in our study that the high levels of NE were also correlated with the high levels of CRP, amylase and lipase. It was demonstrated in this study that the NE levels were increased in patients who diagnosed with acute pancreatitis in the emergency department. We believe that the NP levels can be more useful, in the diagnosis of AP. This role of NE in AP will be defined more clearly with further experimental and clinical studies.

REFERENCES

1. Carroll JK, Herrick B, Gipson T, Lee SP. Acute pancreatitis: diagnosis, prognosis, and treatment. *Am Fam Physician*. 2007;75:1513-20
2. Ming-Jun Xin, Hong Chen, Bin Luo, Jia-Bang Sun. Severe acute pancreatitis in the elderly: etiology and clinical characteristics. *World J Gastroenterol*. 2008;14:2517-21.
3. Maher MM, Lucey BC, Gervais DA, Mueller PR. Acute pancreatitis: the role of imaging and interventional radiology. *Cardiovasc Intervent Radiol*. 2004;27:208-25
4. Vlodov J, Tenner SM. Acute and chronic pancreatitis. *Prim Care*. 2001;28:607-28.
5. Koizumi M, Takada T, Kawarada Y, Hirata K, Mayumi T, Yoshida M et al. JPN Guidelines for the management of acute pancreatitis: diagnostic criteria for acute pancreatitis. *J Hepatobiliary Pancreat Surg*. 2006;13:25-32.
6. Hoffmann G, Wirlleitner B, Fuchs D. Potential role of immune system activation-associated production of neopterin derivatives in humans. *Inflamm Res*. 2003;52:313-21.
7. Forrest CM, Youd P, Kennedy A, Gould SR, Darlington LG, Stone TW. Purine, kynurenine, neopterin and lipid peroxidation levels in inflammatory bowel disease. *J Biomed Sci*. 2002;9:436-42.
8. Mitchell RM, Byrne MF, Baillie J. Pancreatitis. *Lancet*. 2003;361:1447-55.
9. Karaca E, Oktay C. The effect of prognostic criteria in patients with acute pancreatitis *Turkish Journal of Emergency Medicine*. 2008;8:18-25.
10. Vissers RJ, Abu-Laban RB. Acute and chronic pancreatitis. In *Emergency Medicine. A Comprehensive Study Guide*. 5th edition (Eds JE Tintinalli, GD Kelen, JS Stapczynski):588-592, New York, McGraw-Hill, 2000.
11. Kaufmann P, Tilz GP, Demel U, Wachter H, Kreijs GJ, Fuchs D. Neopterin plasma concentrations predict the course of severe acute pancreatitis. *Clin Chem Lab Med*. 1998;36:29-34.
12. Uomo G, Spada OA, Manes G, Feola B, Misso S, Cavallera A et al. Neopterin in acute pancreatitis. *Scand J Gastroenterol*. 1996;31:1032-6.
13. Mora A, Pérez-Mateo M, Viedma JA, Carballo F, Sánchez-Payá J, Liras G. Activation of cellular immune response in acute pancreatitis. *Gut*. 1997;40:794-7.
14. Piecuch J, Rudzki M, Orkisz W, Swietochowska E, Wielkoszynski T, Waniczek D et al. Neopterin—a potential factor for differentiation between pancreatic cancer and chronic pancreatitis. *Hepatogastroenterology*. 2008;55:258-61.
15. Talar-Wojnarowska R, Gasiórowska A, Olakowski M, Lekstan A, Lampe P, Malecka-Panas E. Clinical value of serum neopterin, tissue polypeptide-specific antigen and CA19-9 levels in differential diagnosis between pancreatic cancer and chronic pancreatitis. *Pancreatology*. 2010;10:689-94.