Levels of Serum - Activated Oxidation Protein Products (AOPP) in Patients With Asthma

Astım'lı Hastalarda Serum Aktif Oksidasyon Protein Ürünleri (AOPP Düzeyleri)

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ABSTRACT

Aim: This study aims to compare the levels of serum activated oxidation protein products (AOPP) between patients with asthma and healthy controls and to investigate a possible relationship between AOPP levels and disease duration and laboratory results.

Material and Method: Total of 54 subjects including 34 asthma patients and 20 healthy controls who were admitted to Kırıkkale Yüksek Ihtisas Hospital Chest Disease Policlinic and Yenimahalle State Hospital Chest Disease Outpatient Clinic were included. The levels of serum AOPP were compared between the groups. A statistically significant relationship between AOPP levels and comorbidities (hypertension, diabetes, etc), leukocyte counts, sedimentation rates, C-reactive protein levels, and hemoglobin levels were investigated.

Results: There was no statistically significant difference in serum AOPP levels between the patient group and controls (75.61 ± 32.22 μM and 73.23 ± 20.87 μM). No statistically significant relationship was observed between serum AOPP levels and duration of asthma, the presence of comorbidities, leukocyte counts, sedimentation rates, C - reactive protein, and hemoglobin levels among the patients with asthma and healthy controls.

Conclusion: We conclude that further large-scale controlled studies are required to establish the definite role of serum AOPP levels, a novel indicator of oxidative stress, in patients with asthma.

Keywords: Asthma, activated oxidation protein products, inflammation, clinical importance

Özet

Amaç:: Bu çalışmanın amacı astımlı ve sağlıklı control grubu bireyler arasında serum aktif oksidasyon protein ürünlerini (AOPP) karşılaştırmak ve AOPP düzeyleri ve hastalık süresi ve laboratuar parametreleri arasındaki muhtemel ilişkileri incelemektir.

Yöntem ve Gereçler: Çalışmaya Kırıkkale Yüksek İhtisas Hastanesi Göğüs Hastalıkları Polikliniğine ve Yenimahalle Semt Devlet Hastanesi Göğüs Hastalıkları Polikliniğine gelen toplam 54 astımlı hasta ve 20 sağlıklı kontrol grubu birey alındı. Serum AOPP düzeyleri gruplar arasında karşılaştırıldı. Serum AOPP düzeyleri ve komorbiditeler (hipertansiyon, diyabet vs), lökosit miktarı, sedimentasyon oranı, C-reaktif protein ve hemoglobin düzeyleri arasında istatistiksel olarak ilişki araştırıldı.

Bulgular: AOPÜ düzeyleri açısından hasta ve kontrol grubu arasında istatistiksel olarak önemli fark yoktu (75.61 ± 32.22 μM and 73.23 ± 20.87 μM). Astımlı hasta ve sağlıklı kontrol grubu bireyler arasında serum AOPÜ düzeyleri ile astım süresi, komorbidite varlığı, lökosit miktarı, sedimentasyon oranı, C-reaktif protein ve hemoglobin düzeyleri arasında istatistiksel olarak önemli ilişki yoktu.

Sonuç: Astımlı hastalarda oksidatif stresin yeni bir göstergesi olan serum AOPP düzeylerinin kesin rolünün saptanması için daha geniş kapsamlı kontrollü çalışmalara ihtiyaç olduğu görüşündeyiz.

Anahtar Kelimeler: Astım, aktif oksidasyon protein ürünleri, inflamasyon, klinik önemi.

Introduction

Free oxygen radicals (FOR) have been reported to play roles in tissue injury and the etiopathogenesis of several diseases in recent years. Inflammatory cells, mediators, oxidative stress, and oxidation proteins have been demonstrated to contribute in the pathogenesis of asthma, which is a chronic inflammatory disease of the airway (1-6). The anti-oxidative capacity becomes inadequate in the case of excessive production of free oxygen radicals in the lungs, resulting in oxidative injury. Eosinophils, alveolar macrophages, and neutrophils secrete abundant FOR in patients with asthma. Free oxygen radicals cause smooth muscle contraction in the airways, tissue injury, bronchiolar hypersensitivity, and release histamine and other mediators (4-8). Asthma is a disease characterized with the inflammation of chronic airways (7). FOR might play a role in the pathogenesis of asthma because they are secreted by the inflammatory cells (6-8).

The objective of this study was to compare serum activated oxidation protein product (AOPP) levels in patients with asthma and healthy controls, and determine the relationship between serum AOPP levels and the duration of asthma, and laboratory results (leukocyte count, sedimentation rate, and C - reactive protein (CRP)).

Materials and Method

Participants: 34 patients with asthma (25 females, 9 males; mean age: 49.38 ± 14.68 years) and 20 healthy controls (11 females, 9 males; mean age: 35.9 ± 9.94 years) presenting to the Thoracic Medicine Outpatients' Clinic of Kırıkkale Specialty Hospital were included in the study.

Procedures: The diagnosis of asthma was established based on the Global Initiative for Asthma (GINA) guidelines (9). Pulmonary function test, physical examination and postero-anterior X rays radiography of all subjects were performed. Pulmonary function tests (PFT) were performed with flow sensitive spirometer according to American Thoracic Society (ATS) guidelines (10).

Exclusion criteria were: asthma exacerbation, other respiratuary diseases such as chronic obstructive pulmonary disease, interstisial lung disease, obstructive sleep apnea, acut infections and uncontrolled comorbidities such as malignansy, severe hepatic failure.

Blood samples were drawn from patients to determine serum AOPP levels before therapy was initiated. The duration of time after the establishment of asthma diagnosis, concomitant diseases (hypertension, diabetes, etc.), leukocyte count, sedimentation rate, CRP, and hemoglobin levels were also recorded. Serum AOPP levels were determined with the ELISA method as instructed by the manufacturer.

Serum AOPP levels were compared between patients and controls. The relationship between serum AOPP levels and the duration of time after the establishment of diagnosis, concomitant diseases (hypertension, diabetes, etc.) leukocyte count, sedimentation rate, CRP, and hemoglobin levels was statistically determined. Serum AOPP levels were examined by the instructions of the manufacturer.

Ethical consideration: The study protocol was approved by

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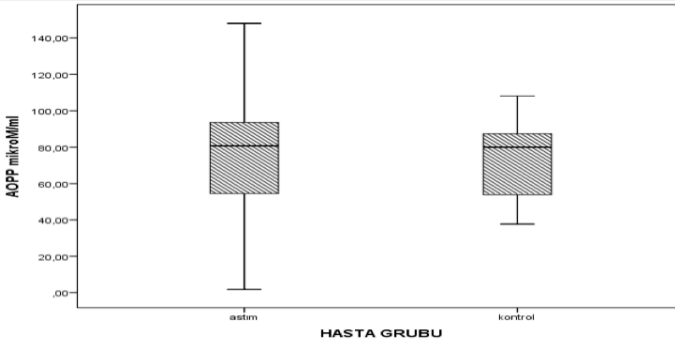

Figure: Serum AOPP levels of patients with asthma and controls are demonstrated.

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	AOPP mikroM/ml	
	r values	p values
Duration of asthma	-0,140	0,429
Diabetes mellitus	-0,135	0,446
Hypertension	-0,087	0,625
Leucocyte	0,076	0,669
Sedimentation	-0,030	0,865
CRP	-0,256	0,143
Haemoglobin	-0,103	0,561

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The groups (patients and controls) introduced themselves before applying the questionnaire, giving information on the subject and duration of the procedure. The subjects were informed that they were included in the study on voluntary basis.

Statistical Analysis

The statistical analysis was performed using Windows SPSS 15 software.

Data analysis was performed with the help of SPSS for Windows 15 program. For the variables whose descriptive statistical distribution is normal, mean ± standard deviation is found and for the variables whose descriptive statistical

distribution is not normal, median (min. – max) is found; and nominal variables are displayed as number of case and (%). Significantly difference in terms of means is tested with " t test " and significantly difference in terms of median is tested with " Mann Whitney test ". Nominal variables were tested with Pearson Chi – Square and Fisher Exact test. While searching the correlation between continuous variables, Spearman correlation test was used if the distribution was not normal; however Pearson correlation test was used if the distribution was normal. A P value of $<= 0.05$ was considered statistically significant.

Results

No significant difference was determined between patients with asthma and healthy controls in terms of sex and mean age. No statistically significant difference was determined between patients with asthma and the control group in terms of mean serum AOPP levels (75.61 ± 32.22 µM and 73.23 ± 20.87 µM, respectively) (Figure). No statistically significant relationship was determined between serum AOPP levels and duration of asthma, concomitant diseases, leukocyte count, sedimentation rate, CRP, and hemoglobin levels in patients with asthma (Table)

Table The correlation between serum AOPP level and clinical and laboratory findings.

Statistical significance $p<0.05$

AOPP: Activated oxidation protein product

CRP: C - reactive protein

Discussion

Oxidative stress is the disequilibrium between the cellular free radical production and the body's anti-oxidative defense (3). Oxidative stress is also defined as the damage caused by reactive oxygen species (ROS) on cells, tissues and organs. Intracellular and extracellular circumstances resulting in the chemical or metabolic formation of ROS are termed oxidative stress (1, 3). Most ROS are endogens and secreted during the energy production in mitochondria. Free radicals and reactive non-radical types are found at low levels in cells and tissues. The secretion and clearance of free oxygen radicals maintain balance by various anti - oxidative compounds and enzymes. AOPP are recently defined markers of oxidative stress. AOPP were first found in patients with chronic renal failure by Witko - Sarsat et al. in 1996 (2, 3).

Oxidative stress has been reported to participate in the pathogenesis of several diseases including atherosclerosis, chronic obstructive lung disease (COPD), and rheumatoid arthritis (3, 8).

It is associated with levels of free oxygen radicals, malondialdehyde (MDA), and AOPP. It has been reported that free oxygen radicals increase the transcription of inflammatory genes. Lipid peroxidation of membrane lipids is also an important mechanism in the formation of tissue injury secondary to free oxygen radicals. In patients with asthma, FOR activity has been reported to be increased and anti-oxidative capacity has been reported to be either increased or decreased (6,7,8,11).

Tekin et al. (8) reported that super oxide dismutase (SOD) activity decreased in patients with asthma compared to controls. Kurusawa et al. (12) reported that SOD levels are higher in patients with asthma compared to healthy individuals. Moreover, Mihmanli et al. (11) reported that oxidative and anti - oxidative substances increased in asthmatic cases compared to controls. Serum catalase enzyme was a marker of the anti-oxidative system and MDA was a marker of the oxidative system in the latter study. Malondialdehyde (MDA) and catalase levels were higher in patients compared to controls.

Markers of oxidative stress and inflammation were investigated in patients with exacerbation of chronic obstructive lung disease (COPD) in the study of Stanojkoviç et al. (13) MDA, AOPP and total oxidative capacity measured at the time of hospitalization and discharge were significantly higher in patients with asthma compared to controls and admission values. Serum AOPP levels at hospital admission and discharge were found to be significantly higher in patients compared to controls. Serum superoxide dismutase level, a marker of anti - oxidative capacity, was significantly lower in patients compared to controls at both admission and discharge. Serum AOPP concentration was comparable with MDA concentration. A significant relationship was determined between the CRP level as a marker of inflammation and the markers of oxidative stress.

Although levels of serum AOPP, a novel marker of oxidative stress, were mildly elevated in patients with asthma compared to controls, no statistically significant relationship was determined between the two groups.

Consequently, we believe, further controlled studies with greater sample sizes should be performed to determine the importance of serum AOPP levels as a novel marker of oxidative stress.

REFERENCES

1. Sırmatel F, Duygu F, Celik H, Selek Ş, Sırmatel Ö, Gürsoy B, Eriş FN. Kronik viral hepatit olgularında total oksidatif seviye ve total antioksidan kapasitenin değerlendirilmesi. Klimik Dergisi 2009; 22: 92-96 (Article in Turkish).
2. Liu H, Han T, Tian J, Zhu ZY, Liu Y, Li Y, Xiao SX, Li Y, Feng YY. Monitoring oxidative stress in acute - on - chronic liver failure by advanced oxidation protein products. Hepatol Res. 2012; 42: 171-180.
3. Ozenirler S, Erkan G, Gülbahar O, Bostankolu Ö, Demirel ÖÖ, Bilgihan A, Akyol G. Serum levels of advanced oxidation protein products, malonyldialdehyde, and total radical trapping antioxidant parameter in patients with chronic hepatitis C. Turk J Gastroenterol. 2011; 22: 47-53.
4. Bateman ED. Severity and control of severe asthma. JAllergy Clin Immunol 2006; 117: 519-521.
5. Taylor DR, Bateman ED, Boulet LP, Boushey HA, Busse WW, Casale TB, Chanez P, Enright PL, Gibson PG, de Jongste JC, et al. A new perspective on concepts of asthma severity and control. Eur Respir J 2008; 32: 545-554.
6. Vural H, Uzun K, Erel U. Antioxidant status and lipid peroxidation in asthma. Solunum Hastalıkları 1999; 10: 77-83.
7. Türk Toraks Derneği Ulusal Astım Tanı ve Tedavi Rehberi. Toraks Derg 2000; Ek 1.
8. Tekin D, Sin BA, Mungan D, Misirligil Z, Yavuzer S. The antioxidative defense in asthma. J Asthma. 2000; 37: 59-63.
9. Global Initiative for Asthma (GINA). GIobal strategy for asthma managemement and prevention. Revised 2012. http://www.ginasthma.org/. Accessed 1/28/14.
10. Standardization of spirometry. Statement of the American Thoracic Society. Am Rev Respir Dis 1987;136:1285-1298.
11. Mihmanlı A, Guneylioğlu D, Ozseker F, Arslan S, Özgel M, Akkaya E. Astımlı Hastalarda Serbest Oksijen Radikalleri ve Antioksidanların Aktiviteleri. Toraks Dergisi 2003; 4: 264-268.
12. Kurosawa M, Kobayashi H, Nakano M. Cu-Zn superoxide dismutase activities in platelets from stable bronchial asthmatic patients.Int Arch Allergy Immunol. 1993; 101: 61-65.
13. Stanojkovic I, Stevuljevic JK, Milenkovis B, Spasic S, Vujic T, Stefanovic A, Llic A, Ivanisevic J. Pulmonary Function, oxidative stres and inflammatory markers in severe COPD exacerbation. Respiratory Medicine 2011, 105; 31-37.

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