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Evaluation of the serum pentraxin 3 levels in patients with stable asthma

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Abstract:

BACKGROUND AND AIM: Asthma is a chronic inflammatory airway disorder. Pentraxin 3 (PTX3) is a novel inflammatory indicator that plays a significant role in natural immunity. In our study, we aimed to identify the PTX3 levels and its relationship with disease severity in patients with asthma.

MATERIALS AND METHODS: Forty-two stable asthma patients with no comorbidity who had been previously diagnosed with asthma and were admitted to the outpatient clinic of chest diseases between December 2018 and June 2019 were included in the study together with 35 control subjects. The demographic data and the results of pulmonary function tests including the parameters of forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and FEV1/FVC of all cases were recorded. The serum PTX3 levels were measured by the ELISA method. The patients with asthma were classified into three groups as mild, moderate, and severe, according to the Global Initiative for Asthma.

RESULTS: Asthma and control groups were similar regarding age, gender, and body mass index. The FEV1 and FEV1/FVC values of the asthma group were lower compared to the controls. The PTX3 levels were significantly higher in the patient group with asthma compared to the control group ($P < 0.001$). The patients with mild, moderate, and severe asthma were similar regarding the PTX3 levels ($P = 0.551$). No correlation was found to be present between the PTX levels and the pulmonary function test parameters.

CONCLUSION: PTX3 is an indicator that has the capability of showing airway inflammation. However, it is inadequate to determine the severity of asthma.

Keywords:

Asthma, pentraxin 3, systemic inflammation

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Introduction

Asthma is a heterogeneous disorder characterized by chronic airway inflammation.[1] The most common symptoms of asthma are cough, shortness of breath, chest pain, and wheezing. Clinical symptoms and signs compatible with asthma should be present together with variable airway obstruction for diagnosing asthma. However, the incidence and severity of symptoms and the airway obstruction manifest variability in asthma. Even though such findings vary, inflammation is continuously present in asthma.[2]

For this reason, identification of markers that would show the airway inflammation more objectively is essential besides the clinical and functional characteristics for diagnosing asthma. Numerous markers have been investigated for the evaluation

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of inflammation in asthma. Eosinophils, eosinophilic cationic protein, IgE, and periostin have been the most prominent biomarkers among them.[3] Pentraxins (PTX) are peptides with short and long subgroups that play a role in natural immunity. Pentraxin 3 (PTX3) is a member of the long-PTX family. PTX3 is released from endothelial cells, fibroblasts, and inflammatory cells, such as macrophages and neutrophils.[4-10] It has been reported in conducted studies that PTX3 increased in cardiovascular and autoimmune disorders, sepsis, and cerebrovascular diseases.[4,11-16]

Regarding the respiratory system, it has been shown to increase in disorders such as chronic obstructive pulmonary disease (COPD), cystic fibrosis, acute lung injury, parapneumonic effusion, and lung carcinoma.[17-23] Very few studies related to PTX3 in adult patients with asthma are present, and the results of such studies are contradictory.[17,24-26] We aimed to investigate the relationship of PTX3 with inflammation in asthma and the presence of its correlation with disease severity.

Materials and Methods

Forty-two patients with asthma who were admitted to the outpatient clinic of chest diseases between December 2018 and June 2019 and had been diagnosed with asthma previously according to the criteria of the Global Initiative for Asthma (GINA) were included in the study.[2] Patients having diseases additional to asthma, those with exacerbation findings, and those having signs of active infection were excluded from the study. Thirty-five subjects who had neither respiratory nor other additional disorders and who did not manifest signs of active infection during admission were included as controls. The demographic characteristics of all participants in the patient and control groups such as age, gender, body mass index (BMI), and smoking status were recorded. The patients with asthma were divided into three groups as mild, moderate, and severe according to their minimal drug requirements during the last 3 months, as stated in the GINA guideline.[2] This study was approved by the local ethics committee (Protocol number: 2018/1386). The study was conducted in accordance with the principles of the Declaration of Helsinki. All participants signed informed consent forms.

Pulmonary function test

Spirometry was performed in the pulmonary function test laboratory at the seated position, following the criteria of the American Thoracic Society/European Respiratory Society, and using a Jaeger Master Scope spirometry device.[27] All tests were performed by a single technician certified for pulmonary function testing. Among spirometric parameters, the forced vital capacity (FVC), second forced expiratory volume in the first second (FEV1), and the FEV1/FVC ratio were used for assessment.

Measurements of serum pentraxin 3 levels

Blood samples were collected using standardized procedures and stored at −80°C. Serum PTX3 levels were determined via commercial human ELISA kits (Elabscience Biotechnology Co., Ltd. Building 4, Room 401, Guandong Science and Technology Industry Park, Wuhan, P.R.C.). Test results were calculated by Bioelisa Reader ElX800 using standard curve at 450 nm.

Statistical analysis

The data were analyzed using the SPSS software (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY, USA). The conformity of the variables with a normal distribution was determined using the Kolmogorov-Smirnov test. The continuous variables with a normal distribution were expressed as mean ± standard deviation, and those without a normal distribution were expressed as median (25–75 percentile). Categorical variables were expressed as numbers and percentages. Student's *t*-test, and when more than two independent variables were present, ANOVA were used for continuous variables showing a normal distribution. Mann–Whitney U-test, and when more than two independent variables were present, the Kruskal–Wallis test were used for continuous variables not showing a normal distribution. Pearson's Chi-square test and Fisher's exact test were used for the analysis of categorical variables. Pearson correlation analysis was used to analyze the relationships between the variables. $P < 0.05$ was considered statistically significant.

Results

Forty-two patients with asthma with a mean age of 47.19 ± 13.24 years and 35 control subjects with a mean age of 49.17 ± 15.90 years were included in the study. Thirty-three (78.6%) patients in the asthma group were female, and 9 (21.4%) were male, whereas 23 (65.7%) subjects were female, and 12 (34.3%) were male in the control group ($P = 0.207$). The BMI and smoking history of both the groups were similar. Among the pulmonary function test parameters, the FEV1 (percent predicted) value and the FEV1/FVC ratio were significantly lower in the asthma group compared to the control group ($P = 0.009$, and $P = 0.005$, respectively). The demographic data and the results of pulmonary function test parameters in the patient and control groups are presented in Table 1. The serum PTX3 levels in asthma patients (13.34 ± 3.36 ng/ml) were statistically significantly higher when compared to that of the control group (1.58 ± 0.61 ng/ml) ($P < 0.001$) [Figure 1]. When patients with asthma were classified according to GINA guidelines, six (14.3%) of the patients were determined to be in the mild group, 28 (66.6%) in the moderate

group and eight (19.1%) in the severe asthma group. No significant differences were present among the groups regarding age, gender, BMI, and smoking history. The results of the pulmonary function test parameters were similar among the three groups [Table 2]. PTX3 levels of the mild group (14.54 ± 4.57 ng/ml), the moderate group (12.97 ± 3.22 ng/ml), and the severe asthma group (13.75 ± 3.03 ng/ml) were statistically similar ($P = 0.551$) [Figure 2]. No correlation was present between the PTX3 levels and the results of pulmonary function test parameters [Table 3].

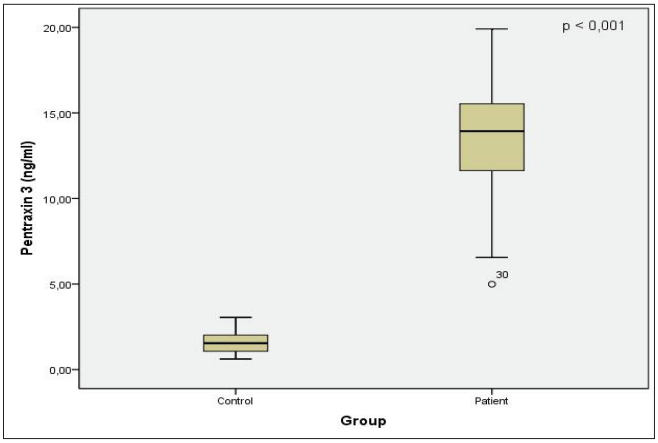

Figure 1: Comparison of pentraxin 3 levels between the patient and control groups

Discussion

In our study, the PTX3 levels were significantly higher in the asthma patients group when compared to the control group, and no correlation of PTX3 was determined with the severity of the disease.

In the literature, few studies related to the PTX3 levels in patients with asthma were published, and different results were reported in these studies. For example, in the study conducted by Gao *et al*., it was determined that no significant differences were present among the

Table 1: The demographic characteristics and pulmonary function test parameters of asthma and control groups

	Asthma (*n*=42)	Control (*n*=35)	*P*
Age (years)	47.19±13.24	49.17±15.90	0.553
Gender, *n* (%)			
Female	33 (78.6)	23 (65.7)	0.207
Male	9 (21.4)	12 (34.3)	
BMI	29.35±6.14	27.94±5.65	0.301
Smoking history, *n* (%)			
Smokers	7 (16.7)	6 (17.1)	0.947
Nonsmokers	30 (71.4)	24 (68.6)	
Ex-smokers	5 (11.9)	5 (14.3)	
Amount of smoking, packs/years	12.5 (10-25)	20 (10-30)	0.642
FVC, percent predicted	101.5 (93-113.25)	101 (93-111)	0.778
FEV1, percent predicted	88.83±20.51	101.2±19.62	0.009
FEV1/FVC	76.11±8.2	80.62±5.53	0.005

Variables are presented as, *n* (%), mean±SD, or median (25^{th} and 75^{th} interquartile range). BMI: Body mass index, FVC: Forced vital capacity, FEV1: Forced expiratory volume in one second, SD: Standard deviation

Table 2: Demographic and pulmonary function test parameters of the patients according to the asthma severity classification

	Mild asthma (*n*=6)	Moderate asthma (*n*=28)	Severe asthma (*n*=8)	*P*
Age (years)	39.83±15.38	48.32±13.95	48.75±7.22	0.347
Gender, *n* (%)				
Female	5 (83.3)	22 (78.6)	6 (75)	0.712
Male	1 (16.7)	6 (21.4)	2 (25)	
BMI	27.5±5.2	30.14±6.38	28±6.11	0.509
Smoking history, *n* (%)				
Smokers	1 (16.67)	3 (13.88)	3 (37.50)	0.649
Nonsmokers	4 (66.66)	22 (75)	4 (50)	
Ex-smokers	1 (16.67)	3 (11.12)	1 (12.50)	
Amount of smoking (package years)	21 (5-27)	10 (8.5-20.5)	22.5 (12.5-25)	0.577
FVC, percent predicted	99.5 (92-110)	102 (94-109.75)	92.5 (72.75-114)	0.204
FEV1, percent predicted	85.83±20.31	92.89±18.38	76.87±25.09	0.139
FEV1/FVC	76.16±12.17	77.32±7.46	71.87±6.85	0.259

Variables are presented as, *n* (%), mean±SD, or median (25^{th} and 75^{th} IQR). BMI: Body mass index, FVC: Forced vital capacity, FEV1: Forced expiratory volume in one second, SD: Standard deviation, IQR: Interquartile range

Table 3: Correlation analysis between the pentraxin 3 levels and pulmonary function test parameters

	Pentraxin 3 (ng/ml)	
	r	*P*
FVC (L)	0.118	0.174
FVC, percent predicted	0.249	0.111
FEV1 (L)	0.285	0.068
FEV1 (%)	0.053	0.737
FEV1/FVC	−0.208	0.186

FVC: Forced vital capacity, FEV1: Forced expiratory volume in one second

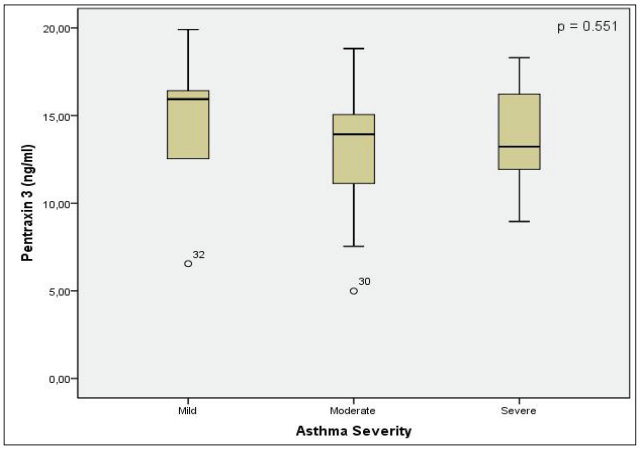

Figure 2: Distribution of the pentraxin 3 levels according to the asthma severity classification

eosinophilic asthma patients, noneosinophilic asthma patients, and the healthy controls.[25] In the same study, the sputum PTX3 levels of the noneosinophilic asthma patients were determined to be higher than the eosinophilic asthma patients and healthy controls. Schwingel *et al*., in their study, found that the sputum PTX3 levels were significantly higher in patients with COPD compared to patients with asthma and healthy controls and associated with the severity of COPD.[17] In that study, it was shown that the sputum PTX3 levels were found to be similar in asthma and control subjects. However, the number of patients was low, and their comorbidities were not mentioned.

In their study, Zhang *et al*. reported an increased PTX3 immunoreactivity in bronchial tissues of patients with allergic asthma compared to their control group and showed that PTX3 was mainly located in smooth muscle.[24] In a recent study, the asthma patient and control groups were reported as similar regarding the serum PTX3.[26] However, in that study, in addition to asthma, their patients had comorbidities such as hypertension, diabetes mellitus, and hypercholesterolemia. Apart from asthma in adulthood, PTX3 has also been investigated in children. Kim *et al*., in their study, determined that the sputum PTX3 levels of their pediatric patients with asthma were significantly higher than the control group.[28] In the study of Licari *et al*., it was determined that the serum PTX3 levels would be useful in showing low-grade inflammation in pediatric patients with asthma.[29]

In the studies published in the medical literature, the PTX3 levels were usually measured in the sputum. However, we have the opinion that, since asthma is a disorder accompanied by systemic inflammation, it is more important to show the markers of systemic inflammation in the serum. Even though different results were reported in the literature, the serum PTX3 levels were determined to be significantly higher in asthma patients compared to the control group in our study.

The levels of PTX3 have been reported to increase mainly in cardiovascular and cerebrovascular disorders, sepsis, etc.[4,11,13-16] Since patients with active infections and comorbidities had not been included in our study, it could be more reliably stated that the PTX levels increased in patients with asthma.

Few studies have been found to investigate the association between PTX3 and asthma severity, and different results were reported in those studies. Zhang *et al*.[24] and Licari *et al*.,[29] in their studies, reported that the PTX3 levels and asthma severity had no relationship. On the other hand, Kim *et al*. determined that a correlation was present between the severity of asthma and the PTX levels.[28] Moreover, in that study, a negative correlation was reported between the sputum PTX3 levels, FEV1, and FEV1/FVC. In our study, the PTX3 levels of patients with mild, moderate, and severe asthma grouped according to the asthma severity classification were similar. We have the opinion that this situation might have been related to the small number of patients in the mild and severe asthma groups in our study. In our study, no correlation was present between the serum PTX3 levels and pulmonary function test parameters.

Our study had various limitations. First of these was that the number of patients determined as mild and severe according to the asthma severity classification was insufficient for evaluating the relationship of the PTX3 levels with disease severity. The second limitation was that the patients with asthma included in our study were not classified according to different phenotypes.

Conclusion

The serum PTX3 is a novel marker that can be used as an indicator of airway inflammation in asthma; however, it seems to be inadequate in determining the severity of the disease. We have the opinion that this situation was related to the number of cases in our study. Therefore, we suggest that further studies with plenty of patients classified according to disease severity and phenotype are required.

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Nil.

Conflicts of interest
There are no conflicts of interest

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