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Acute Response of C - reactive protein to Single both Running test in Asthma patients

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ABSTRACT: A growing body of evidence supports an association of asthma with systemic inflammation. This study aimed to compare serum C - reactive protein (CRP) between adult men with asthma and healthy subjects and to assess acute response of this inflammatory cytokine to one exercise test in patients. For these purpose, 14 males aged 39 ± 2.2 years with mild to moderate asthma and 14 healthy subjects matched to age, sex and body weight were participated in this study. All participants were non-smoker and non-trained. Fasting blood samples were collected of all subjects in order to measure serum CRP. Then all subjects of asthma group were completed a single bout running test and blood samples were collected immediately after exercise. Student's t-tests for paired samples were performed to determine significance of change in CRP by exercise test in asthma subjects. Serum CRP levels in patients with asthma showed were significantly higher than those healthy group (p = 0.000). Compared to baseline, serum CRP concentration decreased significantly (p = 0.000) after exercise test in asthma patients. We concluded that short time exercise with moderate intensity can be improving inflammatory profile in asthma patients.

Keywords: Systemic Inflammation, Asthma, Exercise test

INTRODUCTION

Respiratory dysfunction is strongly associated with cardiovascular risk factors, arthrosclerosis, cardiovascular diseases, and mortality. However, respective mechanisms involved are still unknown. Asthma with allergic origin is a respiratory disease appearing with respiratory paths' robustness [1]. At the same time, scientific references contribute to a kind of reverse relationship between pulmonary function and systemic inflammation [2]. Systemic inflammation is a factor connecting between respiratory dysfunctions and cardiovascular diseases. An increase in cardiovascular risk factors is also seen in respiratory diseases like asthma. Respiratory function suppression is related to the systemic inflammation resulted from some plasma proteins [3,4].

In the meantime, as a cardiovascular risk factor, C - reactive protein (CRP) affects respiratory function among asthma patients through its inflammatory profile [3]. CRP is an inflammation-sensitive plasma protein. Its synthesis in lever is significantly regulated by IL-6 - another inflammatory cytokine [5]. In recent years, there have been relatively adequate evidences regarding the significant role of CRP measurement as an appropriate method for diagnosing inflammation in asthma patients [6, 7]. The difference between this inflammatory cytokine's levels is compared between atopic individuals or respiratory patients (like, asthma) and healthy individuals. Close relationship between CRP level changes and pulmonary capacities such as FEV1 have been reported by some studies before [8, 9, 10].

The relationship between CRP and respiratory function in asthma patients are to some extent similar to the relationship between respiratory function and other immunity system markers reported in other studies [11). Recent studies have reported a kind of close relationship between CRP increase and asthma [12, 13], respiratory dysfunctions [14, 15, 16, 17], and bronchi's hyper-response [10]. An increase in inflammatory mediators and decrease in anti-inflammatory cytokines in these patients have drawn researchers' attention to the identification of medicinal and non-medicinal treatment methods. That is, during two recent decades, extensive studies have been carried out to improve inflammatory profile in asthma patients and other respiratory diseases.

Among the recent non-medicinal external interventions, exercise and physical activity have been the main focus of health science researchers. On the other hand, similar to studies on other healthy or infected samples, opposing results are reported regarding the effect of exercise plans on inflammatory cytokines' levels (especially, CRP). That is, some studies have reported the useful effects [18, 19] yet some others the null effect of exercise plans on the inflammatory profile [20].

Rather, despite these paradoxical findings, few studies can be seen concerning the instant responses of inflammatory cytokines such as CRP (especially, on asthma patients). This study compares CRP serum levels between asthma patients and healthy individuals. It also measures the instant response of CRP as a cardiovascular risk factor or as an inflammatory cytokine in asthma patients in a relatively long term exercise session.

METHOD AND SUBJECTS

As previous mentioned, the main objective of present study was to determine acute response of serum CRP to one single bout running test in asthma patients. Patients was forty males with mild to moderate intensity of asthma aged 39 ± 2.2 year and body weight 90 ± 8.6 kg. Thirty healthy males were also participating in study to compare serum CRP with patients at baseline. After the nature of the study was explained in detail, informed consent was obtained from all participants.

All participants was non-trained and nonsmoker. Participants were included if they had not been involved in regular physical activity in the previous 6 months. A history of other chronic diseases such as type II diabetes, kidney or liver and cardiovascular disease was exclusion criteria.

Asthma diagnosis and its severity were determined by FEV1/FVC by special physician. Subjects were asked to refrain from tea, coffee, chocolates and caffeinated soft-drinks on the day of recording Spirometry. Subjects were instructed to take maximum inspiration and blow into the prevent pneumotach as rapidly, forcefully and completely as possible for a minimum of 6 seconds, followed by full and rapid inspiration to complete the flow volume loop. The best of the three trials was considered for data analysis.

Anthropometric measurements were performed in all study participants before breakfast, with the subject wearing light clothing without shoes. Standing height of the barefoot subjects was measured to the nearest 0.1 cm with the use of a wall-mounted stadiometer. Body weight was measured in duplicate in the morning following a 12h fast. Body mass index (BMI) was calculated by dividing body mass (kg) by height in meters squared (m^2). All of these measurements were conducted by the same researcher. Each of these measurements was conducted two times and the average was reported.

The subjects were advised to avoid any physical activity or exercise 48 hours before the blood sampling. A venous blood sample was collected from all the subjects who came after a 12h overnight fast. Blood samples were repeatedly collected in asthma patients immediately after exercise test. Exercise test involved 45 min running without slope at 70 % of maximal heart rate. Target heart rate was monitored by polar telemetry. Blood samples were dispensed into EDTA-coated tubes and centrifuged for 10 minutes in order to separate serum. Serum used to measuring IL-1β by ELISA method (Diagnostics Biochem Canada Inc High sensitivity C - reactive protein (Hs-CRP)). Intra and inter-assay coefficients of variation were 5.0 and 9.5%, respectively.

A. Statistical analysis

Statistical analysis was performed with the SPSS software version 16.0. The Kolmogorov-Smirnov test was applied to determine the variables with normal distribution. Independent student t test was used for between groups comparison at baseline. Student's t-tests for paired samples were performed to determine significance of changes in variables by exercise test in asthma subjects. Significance was accepted at $P < 0.05$.

RESULTS

The first aim of present study was to compare serum CRP between asthma patients and those with non-asthma subjects. Table 1 shows the descriptive anthropometric features of the study groups. Data of independent T test showed that serum CRP in asthma patients is significantly higher healthy subjects (2870 ± 2482 versus 1919 ± 811 pg/ml, $p < 0.05$). All Spirometrical markers in asthma patients were lower than normal group ($p < 0.05$).

Spirometrical characteristics of the study groups are also shown in Table 2.

Data by paired sample T test showed significant decrease in serum CRP after exercise test when compared with baseline (2870 ± 2482 to 1021 ± 913 pg/ml, $p = 0.003$), (Table 3 and Fig 1).

Table 1: Descriptive characteristics of anthropometrical markers of studied subjects (M ± SD).

group	**Age** (years)	**Weight** (kg)	**Height** (cm)	**BMI** (kg/m^2)	**AC** (%)	**HC** (pg/ml)	**AHO**
Asthma	39 ± 2.2	90 ± 8.6	174 ± 2.1	29.7±2.8	105 ± 11	106 ± 8	0.99 ± 0.6
Healthy	40 ± 3.1	88 ± 7.3	174 ± 3.1	29.07 ± 3.1	106 ± 6	108 ± 9	0.98 ± 0.06
BMI, body mass index; **BF,** Body fat percentage; **AC**, Abdominal circumference; **HC**, Hip circumference; **AHO**, abdominal to hip ratio							

Table 2: Descriptive characteristics of Spirometrical markers of studied subjects (M ± SD).

group	FVC	FEV1	FEV1/FVC	PEF	FEF (25% - 75%)	FEF (25%)	MVV
Asthma	82 ± 6.1	78 ± 5.4	66 ± 2.5	78 ± 14	64 ± 17	56 ± 12	33 ± 2
Healthy	84 ± 5.8	79 ± 6.3	67 ± 3.2	77 ± 11	65 ± 14	58 ± 9	34 ± 3.1

FVC, Forced vital capacity ; **FEV1**, Forced expiratory volume in 1 s ; **PEF**, Peak expiratory flow ; **FEF**, Forced expiratory flow 25%-75% ; **FEF**, Forced expiratory flow 75%; **MVV**, Maximal voluntary ventilation

Table 3: Data of Paired Samples Test of Serum CRP in response to exercise test

		Paired Differences				t	df	Sig. (2-tailed)
				95% Confidence Interv of the Difference				
		Mean	Std. Deviation	Lower	Upper			
Pair 1	C-Reactive protein (pre) - C-Reactive protein (post	387.643	403.960	154.403	620.882	3.591	13	.003

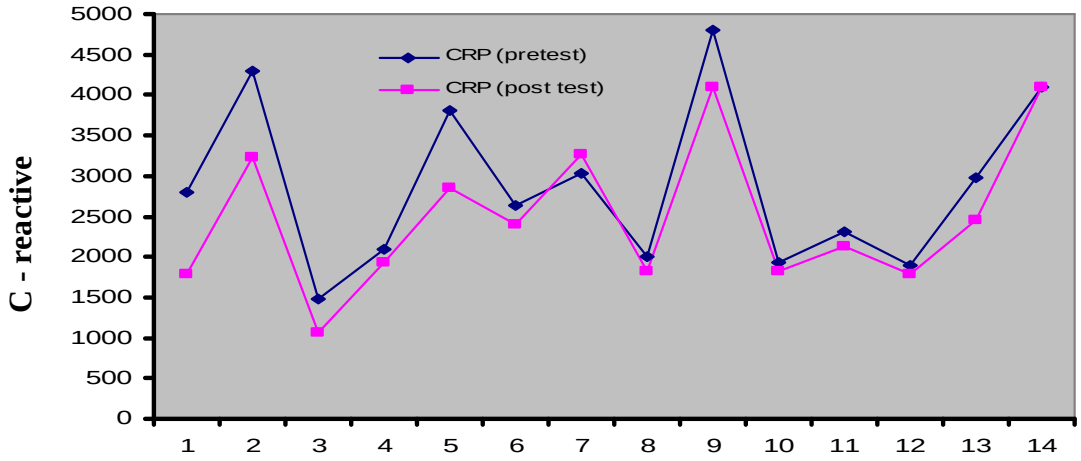

Fig 2: Serum CRP in response to exercise test in studied patients. Acute exercise resulted in significant decrease in serum CRP when compared with pretest.

DISCUSSION

The useful effects of exercises on inflammatory cytokines' levels in other healthy and infected samples have been frequently reported [21, 22]. Yet, some studies deny the effect of physical activity on pulmonary function and growth [23, 24]. However, results of the present study imply the advantageous effects of a single-session exercise (like, running with a relatively average rate) on anti-inflammatory aspects. That is, serum CRP levels significantly decrease to basic levels immediately after sport test.

Higher rest level of CRP in asthma patients (as compared to healthy individuals) is another finding of this study. These results support asthma as an inflammatory disease. The mutual relationship between these respiratory diseases and immunity system is reported in some recent studies [25, 26]. Namely, respective studies have frequently reported the relationship between respiratory paths' inflammation and (or) pulmonary function with systemic inflammation [27, 28].

Inflammatory processes in asthma are affected by a complex network of cytokines and growth factors secreted not only by inflammatory cells but also by other tissues such as epithelial cells, fibroblasts, and smooth muscles' cells. As a consequence, respiratory paths' mucus inflammation is followed by acute or chronic systemic inflammation in asthma patients [29].

However, concerning CRP (as an inflammatory cytokine), some studies deny any kind of relationship between CRP levels and spirometry indices such as blood FEV1 or IgE in asthma patients [30, 31]. Yet, most studies have reported a kind of close relationship between CRP level increase and asthma [12, 13] and respiratory dysfunctions [14, 15, 16, 17]. Several references have implied that adults suffering from asthma have higher CRP levels as compared to healthy individuals [13, 32]. On the other hand, some studies have also reported a reverse relationship between serum CRP levels and spirometry indices in asthma patients [6, 33]. If its levels are related to atopic levels, it will contribute to its effect on the role of overweight in allergic diseases and asthma. Although some studies have reported a negative relationship between respiratory function and inflammatory markers, few studies have reported the relationship between pulmonary function and CRP.

Most research reported the durable useful effects if physical activity on respective variables have exploited long term exercise plans. On the other hand, most of those studies explored the instant response of respective cytokines to a single exercise session have experienced no response or opposing responses [34, 35, 36]. Nevertheless, in the present study, a relatively long exercise session with a partially average intensity level led to the significant decrease of CRP in asthma patients immediately after cutting the test. Perhaps, this significant reduction of CRP can be attributed to the relatively average intensity of the exercise test. It is also possible that the CRP reduction is resulted from relatively high calorie consumption in response to sport test by the patients under study. This is because previous studies have implied that if sport test leads to negative energy balance in an individual, inflammatory profile will be improved [37, 38, 39].

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