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Is atherosklerosis developing risk in patients with asthma?

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Abstract

Asthma is an inflammatory disease of the airways and is characterized by attacks of bronchospasm. Atherosclerosis develops as a result of a series of systemic inflammatory processes that begin with arterial endothelial dysfunction. Arteries tend to dilate in hypoxemic conditions Flow-Mediated Dilation (FMD) is a non-invasive, low-cost, straightforward and effective method that was described some 20 years ago, showing endothelial function and therefore a predisposition to atherosclerosis, according to the reflex vasodilation response of the artery after occlusion. In this study, we aimed to evaluate the susceptibility of these patients to atherosclerosis by performing the FMD test in controlled and uncontrolled asthma groups. We included 61 asthma patients in this study and 30 healthy people enrolled thi study as control group. Thirty-two of the patients were uncontrolled, did not receive regular treatment and were not followed up regularly, whereas 29 patients were full symptom control. Pulmonary function tests were performed on all subjects who met the inclusion criteria of the study and gave informed consent. After the pulmonary function test, the right brachial artery diameters of all cases were measured from intima to intima by Doppler USG. FEV1 values were 67.28±9.89% in in patients with uncontrolled astma, and 79±7 in symptom free group of astma patients. The initial brachial artery diameter was 4.40±0.33 and The measurement made after 5 minutes was 4.69±0.296 ($p<0.001$) in patients with uncontrolled astmatic patents. The difference between these two measurements was 0.29±0.16. FMD tet results in Symptom free patients values were 4.45±03 and 4.81±0.4 respectively ($p<0.001$). Initial and after measurements difference between symptom free and uncontrolled patients were 0.36±0.16 and 0.29±0.11 $p<0.01$. There was not statistically significant difference between symptom free patients and healthy group. We have shown that vascular disfunction in symptomatic astma patients with FMD test. Atherosclerosis developing might be higher in asthma patients and this patients should be encourage to regular medicine usage.

Keywords: Asthma, athheorsclerosis, flow-mediated dilation, FEV1, symptoms

Introduction

Asthma is an inflammatory disease of the airways and is characterized by attacks of bronchospasm [1]. In current studies, it has been reported that patients with asthma are prone to systemic inflammation as well as inflammation, known to develop in the respiratory tract. Systemic inflammation biomarkers such as CRP, TNF-alpha, and IL-6 are found to be high in asthmatic patients [2-5].

In the 2021 report published by the global initiative for asthma (GINA), asthma diagnostic questions asked to the person and their scoring were made. In the same report, patients with controlled and uncontrolled asthma were described in detail according to, and in compliance with, treatment protocols. According to the report; patients whose symptoms and risk of future severe asthma attacks are controlled, defined as patients with controlled asthma. Patients that's outside of this category defined as patients with uncontrolled asthma. We used the criteria published in this report when selecting our asthma patients and distinguishing between controlled and uncontrolled asthma patients [6].

Atherosclerosis develops as a result of a series of systemic inflammatory processes that begin with arterial endothelial dysfunction. Although fatty plaques accumulating under the endothelium in atherosclerosis contribute significantly to the endothelial dysfunction process, the event is a systemic inflammatory process. Atherosclerosis adversely affects many vital organs such as the heart, the brain, the kidneys and causes life-threatening clinical reflections such as heart attacks, cerebral hemorrhages, hypertension and kidney failure [7-9].

Flow-Mediated Dilation (FMD) is a non-invasive, low-cost, straightforward and effective method that was described some 20 years ago, showing endothelial damage and therefore a predisposition to atherosclerosis, according to the reflex

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vasodilation response of the artery after occlusion [10,11]. In this study, we aimed to evaluate the susceptibility of these patients to atherosclerosis by performing the FMD test in controlled and uncontrolled asthma groups.

Material and Methods

Patient selection

We included 61 asthma patients (female/male ratio: 33/28) and 30 healthy people in this study. Thirty-two of which were uncontrolled, did not receive regular treatment and were not followed up regularly, whereas 29 patients were full symptom free. We performed the internationally accepted asthma control score test (6) on all cases. Smokers people, patients who chronic disease, hyperlipidemia and diabetes were excluded from the study. Informed written consent to the study protocol was obtained from all subjects and ethic comity approwed

Pulmonary function test (PFT) measurement

Pulmonary function tests were performed on all subjects who met the inclusion criteria of the study and gave informed consent. The Pulmonary Function test M.E.C. PFT Systems Pocket-Spiro model 2016-year tests were carried out with a handheld portable device. Values were obtained in accordance with the acceptability criteria in the ATS/ERS guideline and were recorded: the PFT results of all cases included in the study were thus obtained. The cases were rested for 10 minutes at normal room temperature and light, prior to the pulmonary function test

Doppler USG measurement

Flow-Mediated Dilation (FMD): After the pulmonary function test, the right brachial artery diameters of all cases were measured from intima to intima by Doppler USG, with the Mindray brand DP-10 model portable ultrasound device, in a comfortable seat at normal room temperature and light. The cuff, attached to the right arm, was inflated to a pressure of at least 50mmHg above the pressure that would close the brachial artery. After a period of 5 minutes, the cuff was opened and distal blood flow was ensured, and 1 minute after this step, the brachial artery diameter was again recorded. It was measured from intima to intima with the same Doppler USG.

Statistical analysis

The SPPS 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) statistical package program was used to evaluate the data.

Results

The age of the participants in the study was 60.62±14.92 years.. FEV1% values are 67±9 and 79±7 in uncontrolled and symptom free groups respectively. The initial brachial artery diameter was 4.40±0.33. The measurement were performed after 5 minutes was 4.69±0.29 ($p<0.001$). Symptom free groups values were 4.45±0.3 vs 4.81±0.4mm in respect ($p<0.001$), initial diameters and last diameters in FMD test results were 0.29±0.16 vs 0.36±0.16 milimeters ($p<0.01$). There was also a statistically significant difference between uncontrolled patients and symptom free groups (Table-I).

Table 1. FMD test result in asthma patients groups and healthy people

	Uncontrolled asthma n:32	Symptom free group: n:29	Healthy group n:30
Initial brachial diameter (mm)	4.40±0.33 *	4.45±03 **	4.48±0.9
Five minutes after diamter	4.69±0.296*	4.81±0.4 **	4.82±0,4
FEV1 %	67±9	79±7	81±6
Difference	0.29±0.11***	0.36±0.16 ***	
***p<0.001, **p<0.001 ***p<0.01**			

Discussion

Asthma is a disease characterized by localized inflammation of the respiratory tract [1]. Studies have shown that inflammation in asthma patients is not only localized, but also that these patients are prone to systemic inflammation [12-14]. Konior-Rozlachowska A. et al., in their experimental studies in guinea pigs, determined that allergic asthma and atherosclerosis are inflammatory diseases characterized by similar inflammatory cell clusters in the circulation in addition to mast cells in the airway and vessel wall, and that they are all inflammatory diseases exhibiting the grooves of both pathologies associated with systemic inflammation, as well as local inflammation [15]. Although inflammatory mediators have been extensively studied in the pathogenesis of asthma, research on endothelial functions is limited. Whereas inflammatory mediators must cross the endothelium to reach and damage the airways and lung parenchyma, recent studies have shown that the endothelium does not function normally in patients with COPD [16,17]. Where angiogenesis has been proven to be increased in asthma patients, studies on endothelial dysfunction are much more infrequent. Endothelial dysfunction may play an important role in the pathogenesis of asthma, as it is known to develop at the end of a series of inflammatory processes that begin with endothelial dysfunction in atherosclerosis, which is a systemic vascular disease [18-23]. The common denominator of endothelial dysfunction in asthma and atherosclerosis thus prompted us to investigate the tendency of asthma patients to atherosclerosis.

The non-invasive and practical method of showing endothelial damage is FMD. It is characterized by the opening of the brachial artery after a period of occlusion, and the vasodilation of the brachial artery as a reflex, as a result of NO secreted from the damaged endothelium (20). Although the FMD method received some criticism at the time it was initially described, it is reliable and accepted in terms of showing endothelial damage, if applied correctly. There is evidently a need for studies to develop a guideline that is accepted by everyone for the FMD method and in order to standardize the procedure.

We applied the FMD method to detect the tendency to atherosclerosis in asthma patients and the difference in FMD measurements of all our asthma cases was statistically significant. This was valuable in terms of demonstrating endothelial dysfunction in asthma patients and indicates that asthma patients are prone to atherosclerosis, and that endothelial dysfunction plays an important role in the pathogenesis of asthma. Vasculogenesis has been proven in the pathogenesis of asthma [24], but studies on endothelial dysfunction are necessary and we think that our study will provide

some incentive. Developing treatments for endothelial damage in asthma patients will create a new dimension in asthma treatment.

When we compared our asthma cases as controlled and uncontrolled groups, we found that the uncontrolled group had a statistically significant higher susceptibility to atherosclerosis. In other words, if asthma is not treated and gets progressively worse, atherosclerosis becomes more and more severe. This appears to be related to increased endothelial dysfunction in patients with uncontrolled asthma. The increase in endothelial dysfunction also increases the endothelial dysfunction in the systemic vascular bed and triggers the susceptibility to atherosclerosis.

Conclusion

We think that the potential for developing atherosclerosis is high in asthma patients as a result of endothelial dysfunction, and our study offers a broader perspective in the approach to patients with asthma, including atherosclerosis. Therefore, we believe that in the process of evaluating a patient with asthma, atherosclerosis should not only be considered, but that in addition to asthma treatment, the life expectancy and quality of life of these patients would increase with preventive measures and treatments for atherosclerosis. Studies aimed at preventing or treating endothelial damage will contribute significantly to the treatment of asthma and atherosclerosis, and our results support such studies in the future.

Limitations

The most important limitation of our study is that; we could not show endothelial damage in both the pulmonary vascular bed and the systemic vascular bed with biochemical markers and morphological imaging methods, in asthma patients.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical approval
Alanya Alaaddin Keykubat Unicersity clinical research ethic committee decisiom number: 17-01 decision date: 10.11.2021

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