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Increased arterial stiffness in stable and severe asthma☆

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Pulmonary function;
Arterial stiffness;
High sensitivity C-reactive protein

Summary
Background: Systemic inflammation is related to disease progression in asthma. The brachial-ankle pulse wave velocity (baPWV) is a marker for early atherosclerotic changes. The aim of this study is to evaluate the baPWV levels in patients with stable and severe asthma.
Methods: We examined baPWV, high sensitivity C-reactive protein (CRP), lung function parameters, and arterial blood gas analysis in patients with asthma and control subjects. 85 stable asthma patients and 85 severe asthmatics were investigated. 85 control subjects matched for age, gender, body mass index (BMI) and smoking status were recruited.
Results: The patients with severe asthma had increased baPWV and CRP compared with the patients with stable asthma and control subjects. Furthermore, baPWV was elevated in stable asthma compared with control subjects. There was a negative correlation between baPWV and forced expiratory volume in 1 s (FEV_1), after adjusting age, gender, BMI and smoking status ($r = -0.414$, $p < 0.001$). Similarly, baPWV was negatively correlated with FEV_1/forced vital capacity (FVC) ($r = -0.431$, $p < 0.001$). Although there was no correlation between CRP and baPWV in patients with stable asthma, CRP was positively correlated with baPWV in patients with severe asthma ($r = 0.229$, $p = 0.039$).

☆ WX.S participated in data collection, data analysis and manuscript preparation. D.J participated in data collection and data analysis. Y.L participated in manuscript preparation and editing. RT.W participated in study design, data analysis and manuscript preparation. All authors read and approved the final manuscript.

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Conclusions: baPWV tends to increase as pathogenic condition aggravated in asthma. In addition, elevated baPWV correlates with impaired lung function. Our observation suggests that baPWV is useful for early detection of subclinical atherosclerosis in asthma.

Introduction

Asthma is an enormous public health problem in USA resulting in considerable burden and cost. Substantial evidence demonstrated asthma is a chronic inflammatory condition with activation of large numbers of immune and inflammatory cells within the airways. Recent studies reported that systemic inflammation is related to disease progression in asthma [1]. Some proinflammatory cytokines such as interleukin 6 (IL-6), tumor necrosis factor α (TNFα), and C reactive protein (CRP) are elevated in patients with asthma [1—3].

Elevated arterial stiffness, a marker of subclinical atherosclerosis, is associated with myocardial infarction, heart failure, stroke, renal disease, and elevated total mortality [4]. Pulse wave velocity (PWV) reflects the stiffness of central and peripheral muscular arteries and is widely used as an indicator of arterial stiffness and vascular damage. Brachial-ankle PWV (baPWV) measurement, a simple, noninvasive, and automated measurement method, is closely correlated with aortic PWV. Previous studies documented that increased baPWV is linked with metabolic syndrome, cardiovascular diseases, stroke, and renal disease, as well as elevated total mortality [5—8].

Mounting evidence revealed that the patients with asthma are at increased risks of hypertension, pulmonary embolism, coronary heart disease, heart failure, and all-cause mortality [9—12]. However, the changes of baPWV levels in asthma have not been clearly determined.

The purpose of the present study is to evaluate baPWV levels in stable and severe asthma.

Methods

Participants

The study enrolled 255 adults (aged >18 years, 114 men and 141 women) from June 2011 to June 2012. There were 170 patients with asthma and 85 controls without asthma. The severe asthma patients were included consecutively in the department of respiratory, the First Affiliated Hospital. The stable asthma patients and controls were recruited from the International Physical Examination and Healthy Center of the Second Affiliated Hospital. Control subjects were matched for age, gender, and body mass index (BMI), and smoking status. The study protocol was approved by the Ethics Committee of the First and Second Hospital of Harbin Medical University, China. Written informed consent was obtained from study participants.

Clinical examination

All the subjects underwent clinical examination which included anthropometric and blood pressure measurements. Body mass index (BMI) was calculated as weight (kg) divided by height (m^2). Blood pressure was determined using a mercury-gravity sphygmomanometer in a sitting position after a 15-min resting period. Systolic and diastolic blood pressures were measured twice on the same day and mean values were used in the analysis.

Biochemical measurements

Clinical data including smoking habits, medical history and medication use were recorded for each subject. The whole blood samples were drawn in EDTA-containing tubes after an 8-h overnight fasting and all samples were processed within 30 min after blood collection with an autoanalyzer (Sysmex XE-2100, Kobe, Japan). High sensitivity C-reactive protein (CRP) was measured by the nephelometric method (Dade Behring, Marburg, Germany). An arterial blood sample was assayed with a blood gas analyzer (GEM premier 3000, MA, USA) while the subjects were breathing room air for at least 30 min. Forced expiratory volume in one second (FEV_1) was determined with a spirometer (Jaeger, Wurzburg, Germany) according to the American Thoracic Society criteria. Spirometric measurements were analyzed three times and the best result was used in our study. The inter- and intra-assays coefficients of variation (CVs) of all these assays were below 5%.

Measurement of baPWV

BaPWV was measured using an automatic device (model MB3000, M&B Electronic Instruments, Beijing, China). The baPWV was automatically calculated according to the formula (L/PTT). L is the difference between the length from the heart to ankle and the length from the heart to brachium. PTT was the pulse transit time between the brachial and tibial arterial waveforms. All measurements were conducted by a single examiner who was blinded to the clinical data. The method was validated in a previous report [13].

Diagnosis and exclusion criteria

Stable and severe asthma was defined according to Global Initiative Strategy for Asthma Management (GINA) guidelines. Exclusion criteria were chronic lung disease other than asthma, coronary heart disease, systemic inflammatory diseases, heart failure, renal failure, and medical treatment with statins, angiotensin converting enzyme inhibitors, and systemic glucocorticoids during the previous 8 weeks.

Statistical analysis

Data were expressed as means $\pm$ SD or median (interquartile range) for continuous variables or percentage for