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Research Article

Urinary Bromotyrosine: Noninvasive Method to Evaluate Inflammation in Patients with Allergic Rhinitis -

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ABSTRACT

Background: The upper airway inflammation takes an important role in the pathophysiology of Allergic Rhinitis (AR) that is an IgE-mediated inflammatory disease and we have limited noninvasive methods to determine airway inflammation. The 3-Bromotyrosine (BrTyr) which is an indicator of eosinophil-catalysed protein oxidation shows inflammation level. Urinary levels of BrTyr could be used to evaluate inflammation in AR. This is the first study about evaluation of BrTyr levels in the urine of patients with AR.

Objective: We aimed to determine the benefit of urinary BrTyr measurement in evaluating inflammation in patients with AR.

Method: Thirty-six patients with allergic rhinitis and twenty-nine healthy volunteers were enrolled to this study. Urinary BrTyr levels were measured in all subjects.

Results: Urinary BrTyr levels were significantly higher in patients compared with control group ($p < 0.01$).

Conclusions: Urinary BrTyr level can be a noninvasive diagnostic test in patients with allergic rhinitis.

Keywords: Allergic rhinitis; Inflammation; Bromotyrosine; Urine

INTRODUCTION

Allergic Rhinitis (AR) is a type I allergic disease that is revealing through revelation of nasal mucosa to allergens [1]. When IgE mediated reaction starts, mast cells, eosinophils and basophils release histamine, leukotriene, platelet-activating factor, etc [2]. The most frequent diagnostic tests for AR are the percutaneous skin test and the allergen-specific Immunoglobulin E (IgE) antibody test [3,4]. Less frequent diagnostic tests involve nasal provocation test, intradermal skin test, nasal cytology (e.g., scraping, biopsy), and nasolaryngoscopy [5,6].

Asthma is an inflammatory disorder of the lower airway that is frequently coexist with AR. They are called as Allergic Airway Diseases (AADs) [1,2]. The airway inflammation takes an important role in AR and asthma. So the appraisal of inflammatory mechanisms could be beneficial in the assessment and control of patients with AADs [7,8]. Some published studies have shown that eosinophils generate hypobromous acid which encourage posttranslational alteration of tyrosine residues to produce 3-Bromotyrosine (BrTyr) [9,10]. There are investigations that present raise urinary BrTyr degrees in asthma patients [11,12] But there is not any study about the urine levels of BrTyr in patients with AR.

In this study, we determined the levels of urinary BrTyr levels in AR patients and compared with healthy volunteers. We hypothesized that the levels of BrTyr that is an airway inflammation marker would be higher in AR patients than in controls. The present results reveal that urinary BrTyr may be noninvasive diagnostic and prognostic marker in patients with AR such as asthma.

METHODS

Thirty-six newly diagnosed AR patients without asthma (age range 18-49 years (mean ± SD age, 34.6 ± 10.9)) who presented at the Otorhinolaryngology Department of Malatya Educational and Research Hospital between January 2018 and March 2019 were included in this prospective, observational study. Twenty-nine age and gender matched volunteer control participants (age range 18-51 years (mean ± SD age, 35.9 ± 11.8)) were chosen among healthy patients attending the same hospital during the same period. This study was approved by the Local Ethical Committee of Malatya Educational and Research Hospital, Turkey. Informed consent was obtained from all subjects.

At study entry, all subjects were examined in detail. Also routine blood and urine analyses, spirometry, sinus and chest X-rays were performed in all participants.

All participants with any clinical and laboratory evidence of inflammation, infection asthma, comorbid lung disease, cystic fibrosis, diabetes mellitus, any smoking history, those who had received hormone therapy and/or steroid therapy in the one month prior to the study or those who were taking any drugs that might affect inflammation parameters (including interleukins, non-steroidal anti-inflammatory drugs) were also excluded from the study.

Urine samples were taken from all subjects. The samples were inserted into 50 ml tubes and placed in to refrigerator at ±4°C. All urine samples were centrifugeted for 20 minutes at 1000×g and BrTyr level of supernatant was evaluated by an ELISA kits that obtained from Wuhan Fine Biological Technology Co.,Ltd (C6-323 Biolake, No.666Gaoxin AVE. Eastlake High-tech Development District, Wuhan, Hubei, China). The standard range of 3-BrY in this kit was 7.8-500ng/ml.

Statistical analyses were performed by using the SPSS software package, version 20.0 (SPSS Inc, Chicage, IL, USA) for Windows. Categorical variables are presented as percentages and continuous variables are presented as mean±SD. Statistical Analyses Comparisons of continuous variables between the two groups were measured with Wilcoxon rank-sum tests. Relationships between two continuous variables were evaluated with Spearman rank correlation coefficients. Categorical variables were assessed with likelihood ratio χ^2 tests (or two-tailed Fisher exact tests in the event that any of the expected frequencies was less than five). A value of $p < 0.01$ was defined as statistically significant.

Thirty-six patients with AR were included in the study (mean ±SD age, 34.6 ± 10.9; 25 (69.4%) males, 11 (30.6%) females). The control group included 29 healthy volunteers who were age and gender matched with the study group (mean ±SD age, 35.9 ± 11.8; 20 (69%) males, 9 (31%) females) (Supplemental table 1).

In AR group, urinary BrTyr levels did not differ between males and females, who had mean levels of BrTyr of 0.49 ± 0.12 ng/mg in males and 0.42 ± 0.11 ng/mg in females ($p = 0.173$). In control group, urinary BrTyr levels did not differ between males and females, who had mean levels of BrTyr of 0.07 ± 0.02 ng/mg in males and 0.09 ± 0.03 ng/mg in females ($p = 0.128$) (Supplemental figure 1). But mean urinary BrTyr levels of AR group significantly higher than control group ($p < 0.01$) (Supplemental table 2).

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DISCUSSION

AR and asthma are both chronic inflammatory diseases of respiratory tract and may have a mutual pathophysiology [1,2]. These inflammatory airway afflictions regularly coexist with other. In published literature, about 80% of asthma subjects documented to have AR and about 40% of AR patients reported to have asthma [7,8]. In guidelines, AR patients must be evaluated for asthma, and also patients with asthma should be assessed for AR [7]. The pathophysiologies of these diseases are unclear.

The variability in response to medications is assigned to distinct mechanisms inherent the respiratory tractus inflammation [11-14]. Biomarkers appropriate to the fundamental pathophysiological manage would be beneficial in private care of the patients with chronic inflammatory airway diseases [15,16].

Eosinophils are important cells and their products are important chase markers in respiratory tractus inflammation disorders such as asthma and AR [17].

Many biomarkers such as eosinophil products mentioned to be useful in determining the severity of inflammatory airway diseases and the response to treatment.

Most of the diagnostic tests require invasive procedures.

Eosinophil peroxidase is singular in transforming respiratory erupt produced hydrogen peroxide into hypobromous acid, a reactive brominating oxidant that modulates protein tyrosine residues forming BrTyr [10,18]. Thus BrTyr is a biochemical fingermark of eosinophil activation. BrTyr is a stable product that can be found in blood and urine.

Urinary BrTyr, a specific marker of reactive brominating oxidants formed by eosinophil-catalyzed oxidation, is known to increase in asthma [11].

Also we have found increase in urinary BrTyr levels in patients with AR that is a kind of airway inflammatory disease.

In conclusion, we suggest that the oxidative pathways invoked by eosinophil activation, as measured by urinary BrTyr, may be helpful to determine and follow AR patients. Further study is necessary to clarify how oxidative eosinophilic pathways effect pathophysiology of AR. Also noninvasive methods and parameters (urinary products etc) must be determined to diagnose and follow of AR patients (Supplemental tables 1,2) and (Supplemental figure 1).

CONFLICTS OF INTEREST STATEMENT

The authors whose names are listed in title page certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Table 1: Demographic distribution and comparison of patients.

		Groups			
		AR (n/%)	Control (n/%)	Total (n/%)	*p*
Gender	Male	25 / 69.4	20 / 69	45 / 69.2	0.197
	Female	11 / 30.6	9 / 31	20 / 30.8	
Age (Mean ± Standart Deviation)		34.6 ± 10.9	35.9 ± 11.8	66.9± 6.9	0.154

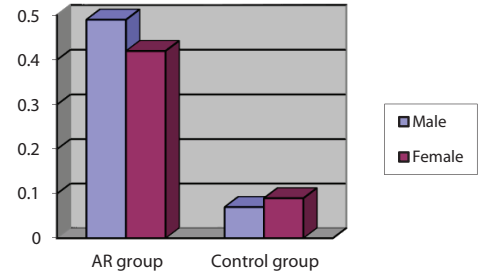

Figure 1: Urinary BrTyr levels of groups.

Table 2: Comparison of mean urinary BrTyr levels between groups.

	Groups						
	AR			Control			
	Male	Female	*p*	Male	Female	*p*	*p*
Urinary BrTyr (ng/mg)	0.49 ± 0.12	0.42 ± 0.11	0.173	0.07 ± 0.02	0.09 ± 0.03	0.128	
	0.47 ± 0.11			0.08 ± 0.02			<0.01

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