



Role of serum Immunoglobulin E level in diagnosis of severity of cough variant asthma

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Abstract

Introduction: Cough variant asthma (CVA) is known by airway Hyper responsiveness and nonproductive chronic cough without wheezing for a minimum duration of 8 weeks. It is less common form of asthma. This study was conducted aiming to diagnose the role of serum Immunoglobulin E (IgE) in diagnosis of cough variant form of the disease.

Methods: In this cross sectional study, 80 patients with an age range of 5-14 years were included with clinical criteria for CVA who referred to pulmonology clinic of Tabriz Children Hospital, Tabriz, Iran. Serum IgE level was measured and severity of CVA based on Global Initiative for Asthma (GINA) classification was determined, finally the relationship between serum IgE level and severity of CVA was evaluated.

Results: In patients with CVA without history of allergic disease, mean serum titer of IgE was 138.2 ± 17.5 . Significant difference of serum IgE level in different severities of CVA was detected ($P = 0.001$).

Conclusion: Serum IgE level in patients with CVA is a reliable marker for diagnosis and evaluation of the severity of disease.

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Introduction

Cough is a prevalent complaint among individuals referring to the medical sites.¹ Chronic cough is defined as a cough that lasts more than 8 weeks.² Coughing may affect the quality of life (QOL).³ Asthma is a common chronic respiratory disease with significant morbidity. The incidence of asthma is higher among boys and families with a poor economic level.⁴ Children asthma is one of the most common causes of emergency referrals and school absence.⁵ In several studies carried out in different countries, an increasing incidence rate of asthma has been reported reaching about 50%. Causes of asthma are not completely clear, however combination of environmental exposure and

genetic predisposition have been considered of the causes.^{6,7}

Cough variant asthma (CVA) is a subtype of asthma in which cough is the predominant or sole symptom.⁸ CVA is known by airway Hyper responsiveness and dry chronic cough for a minimum of 8 weeks, which stops by bronchodilator.⁹ Unlike classic asthma, patients do not experience wheezing, shortness of breathing, and chest tightness.¹⁰ Fujimura et al. defined diagnostic criteria for CVA as follows:

1. Nonproductive cough more than 8 weeks
2. Absence of wheezing
3. Absence of postnasal discharge
4. Presence of airway hyperresponsiveness
5. Response to bronchodilator

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Table 1. Global Initiative for Asthma (GINA) classification for severity of cough variant asthma (CVA)

Classification	Symptoms/Diurnal	Symptoms/ Nocturnal	PEF or FEV 1 (%)	PEF variability (%)
STEP 1: Intermittent	< 1 time a week: asymptomatic normal PEF between attacks	≤ 2 times a month	≥ 80	< 20
STEP 2: Mild persistent	> 1 time a week but < 1 time a day: attacks may affect activity	> 2 times a month	≥ 80	20-30
STEP 3: Moderate persistent	Daily attacks affect activity	> 1 time a Week	60-80	> 30
STEP 4: Severe persistent	Continuous limited physical activity	Frequently	≤ 60	> 30

PEF: Peak expiratory Flow; EFR: Expiratory flow rate; FEV: Forced expiratory volume

6. Normal chest radiography

7. Probably normal spirometry finding

For diagnosis of CVA, existence of at least two of the above mentioned criteria and chronic cough are necessary.¹¹

According to Global Initiative for Asthma (GINA) classification, asthma has been divided into four categories based on daily or night symptom and spirometry values: Intermittent, mild persistent, moderate persistent, and severe persistent asthma (Table 1).¹²

Based on the knowledge of the researchers, no study has been conducted on the evaluation of serum IgE level and severity of CVA. Thus, this study was accomplished aiming to evaluate the relationship between serum IgE level and severity of CVA.

Methods

In this cross sectional study, 80 patients aged 5 to 14 years old with chronic cough more than 8 weeks and two diagnostic criteria for CVA (previously mentioned) were included. This study was performed from June 2016 to August 2017 on patients who referred to pulmonology clinic of Tabriz Children Hospital, Tabriz, Iran. 4 patients who had cough due to another reason such as cystic fibrosis, bronchiectasis, respiratory tract infection (RTI), which were diagnosed during the study or they couldn't do spirometry, were excluded.

Based on physical examination and spirometry values and clinical history, patients were divided into four groups based on severity of asthma: intermittent, mild

persistent, moderate persistent, and severe persistent asthma, and then the serum IgE level was measured among them.

The results were expressed as mean \pm standard deviation (SD). Statistical analysis were performed using the SPSS software (version 16, SPSS Inc., Chicago, IL, USA) and a P value of < 0.050 was considered to be statistically significant.

Results

Of 80 patients enrolled in this study, 4 (5.0%) patients who had cough but lacked CVA criteria or couldn't perform spirometry, were excluded. 28 (36.8%) and 48 (63.2%) of the patients were women and men, respectively. Mean age of the patients was 7.3 ± 0.3 years (5-14 years).

No statistically significant differences were obtained in age, sex, exposure to cigarette smoke, atopic status, and urban or rural and familial history of allergies among the patients.

The patients were divided in the aforementioned four groups as follows: 31 (40.8%), 25 (32.9%), 11 (14.5%), and 9 (11.8%) patients were included in intermittent, mild persistent, moderate persistent, and severe persistent asthma groups, respectively.

The mean of serum IgE level was obtained as 138.2 ± 17.5 (IU/ml). Serum IgE level in different severity of CVA was measured. The study showed significant differences between Serum IgE level and severity of CVA ($P = 0.001$) (Table 2).

Mean of serum IgE level among men and women was 156.0 ± 22.9 and 107.0 ± 26.6 (IU/ml), respectively, and no significant

difference was observed between the two groups ($P = 0.120$). This study indicated that in CVA, not only the serum Ig E level was high, but also it had different level in different severity of disease.

Table 2. Serum Immunoglobulin E (IgE) level in different level of cough variant asthma (CVA)

Severity CVA	Serum IgE level (mean \pm SD)	P
Intermittent	101.8 \pm 31.6	0.001
Mild persistent	104.5 \pm 23.7	
Moderate persistent	107.7 \pm 51.8	
Severe persistent	167.5 \pm 45.6	

CVA: Cough variant asthma; IgE: Immunoglobulin E; SD: Standard deviation

Discussion

Asthma is a chronic respiratory disease due to chronic inflammation and immune response causing reversible airway bronchospasm and air flow limitation. Cytokines and immunoglobulins play an essential role in pathogenesis of asthma.¹³

In this study, the serum IgE level was evaluated in patients with CVA based on severity of the disease. Mean serum IgE level was obtained as 138.0 ± 17.5 (IU/ml) and significant increase was observed with increasing severity of the disease.

Wang et al. reported that serum interleukins 4 and 5 (IL-4, IL-5) level in CVA were similar to classic asthma but serum IgE level was variable. In addition, serum IgE level in acute phase of CVA was higher than control phase and further studies was recommended.¹⁴

In another study, serum IgE, IL-4, and IL-13 levels were studied among patients with CVA and control group. They found that serum IgE, IL-4, and IL-13 level were significantly higher in CVA group.¹³ However, none of them has measured IgE level in different severity of CVA.

A study reported that nerve growth factor (NGF) and IL-4 in sputum and serum was higher than control group, which was

significantly decreased with treatment.¹²

IL-12, IL-4, IL-5, and transforming growth factor beta (TGFB) and IgE serum level in CVA were also measured in other studies and it was reported that these markers had a great role in pathogenesis of asthma and they decreased with treatment.^{4,5}

According to the present study and other similar studies, it can be asserted that IgE, IL, and other markers such as NGF increase in CVA, so they can be used for diagnosis and determination of severity of disease and response to treatment.

Limitations: The most important limitation of this study was sensitivity of laboratory diagnostic kits to IgE measurement.

Conclusion

Based on this study, serum IgE level can be used for diagnosis, classification and evaluation of response to treatment in CVA.

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Authors' Contribution

N. Bilan designed and supervised the study. H. Orang-Poor performed the data collection. A. Dastranji performed data analysis and drafting the article.

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Conflict of Interest

Authors have no conflict of interest.

Ethical Approval

This study was registered by the Medical Ethics Committee of Tabriz University of Medical Sciences (5/D/988080-1395/10/14).

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