The Role of Interleukines in Asthmatic Patients

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Abstract

Background: Asthma is a chronic inflammatory disease of the airways because body exposure to foreign materials that stimulate immune response characterized by secretion of cytokines from inflammatory cells.

Objective: Diagnosis of asthma to detect about IgE, IL1B, IL2, IL8, IL10, IL12 in patients clinically suspected.

Patients and Methods: 50 blood samples out patients were collected in a labeled 5 ml tubes, aged (26 years to 58 years) were tested by Enzyme Linked Immuno Sorbent Assay to detect IgE, IL1B, IL2, IL8, IL10, and IL12 were carried in Al-Hussein Hospital in Kerbala, during the period from May to August 2010.

Results: 50 patients were evaluated for asthma and correlation between IL1B, IL2, IL8, IL10, IL12 values (20, 76, 62, 44, 76)% respectively and IgE value (50%). Increasing values of IL2, IL8, IL10, IL12 (36, 26, 24, 32)% respectively at ages (37-47) years were led to decreased IgE value (10%) and IL2, IL8 values were (24, 22)% respectively compared with IgE (10%).

Conclusions: Importance studying factors (IL1B, IL2, IL8, IL10, IL12) in diagnosis of Asthmatic patients after clinically diagnosis.

دور الأيضاضيات عند مرضى الربى
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الخلاصة

الخلفية: الربى مرض التهابي مزمن يصيب الجهاز التنفسي نتيجة تعرض المريض للمواد الغريبة المحفزة للاستجابة المناعية. تم تشخيص الربى في المرضى المشكوك بهم سريرياً باستخدام الفحوصات المصلية.

المريض وطريقة العمل: تم تجميع 50 نموذج دم من المراجعين بعد تخصيصهم من قبل الطبيب المختص. وتم وضعهم في أنابيب اختبار سعة 5 مل. بامعة تراوحت بين (26-58) سنة باستخدام اختبار ELISA للكشف عن IgE, IL1B, IL2, IL8, IL10, IL12.

وتقدم 50 مريض بالربى وتظهر النتائج في المقابل التالية:

النتائج: تم تقييم 50 مريض بالربى. فاقترح النتائج في التالي:

نسبة ارتفاع IgE (50%): 20, 76, 62, 44, 76% (IgE).

نسبة ارتفاع IL1B, IL2, IL8, IL10, IL12 (20, 24, 23, 26, 21)% عند الاعمار (37-48) سنة ذات ارتفاع قيمة IgE (10%) عند الاعمار (48-58) سنة ذات ارتفاع قيمة IgE (22%)

الاستنتاجات: أهمية دراسة الأيضاضيات (12) في تشخيص مرضى الربى بعد تشخيصهم سريرياً.

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Introduction

Asthma is one of the few chronic diseases in the developed world that is increasing in prevalence, despite better understanding of its pathogenesis and improved treatments (1).

It is one of the most common disorders encountered in clinical medicine in both children and adults(2). interleukin (IL) A general term for numerous cytokines synthesized by leukocytes. Includes multiple secreted proteins that facilitate inflammation exchange among leukocytes and activate signaling that regulates hematopoietic cell growth, differentiation, and function.

Cytokines are extracellular signalling proteins and are produced by different cell types involved in cell-to-cell interactions, having an effect on closely adjacent cells. Cytokines play an integral role in the coordination and persistence of the chronic allergic inflammatory process in asthma. They act on target cells to cause a wide array of cellular functions, including activation, proliferation, chemotaxis, immunomodulation, release of other cytokines or mediators, growth and cell differentiation, and apoptosis. Classification of cytokines with regard to airways disease is best considered functionally, such as proinflammatory cytokines, T-cell derived cytokines, chemotactrant cytokines (chemokines) for eosinophils, neutrophils, monocytes/macrophages and T cells, anti-inflammatory cytokines and growth factors(3).

IL-1β is an important growth factor for Th2 cells in response to antigen primed antigen presenting cells but not for Th1 cells(4).

IL-1β induces airway neutrophilia and increases airways responsiveness selectively to bradykinin in the rat.297 IL-1α can induce eosinophil accumulation in rat skin, an effect blocked by an anti-IL-8 antibody(5).

Levels of IL-2 are increased in bronchoalveolar lavage fluid of patients with symptomatic asthma(6).

IL-2 is secreted by antigen activated T cells following activation, accompanied later by an upregulation of high affinity IL-2 receptors on the same cells. Binding of IL-2 to IL-2R induces proliferation of T cells, secretion of cytokines, and enhanced expression of receptors for other growth factors such as insulin. The IL-2 receptor complex is then removed from the T cell surface by internalisation. IL-2 can also be produced by eosinophils, and by airway epithelial cells(7,8).

The major groups of cytokines are lymphokines, proinflammatory cytokine, inhibitory cytokines and growth factors. Patho-physiology of asthma is still poorly understood and its cause remains unknown(9).

Cytokines play an important role in modulating inflammatory responses and, as a result, airway tone, and an important role of IL-10, downstream of the inflammatory cascade, in regulating the tone of the airways after allergic sensitization and challenge. IL-10 is a regulatory cytokine that has been suggested for treatment of asthma because of its immunosuppressive and anti-inflammatory properties(10).

IL-10 inhibits the late response and the influx of eosinophils and lymphocytes after allergen challenge in the Brown-Norway rat(11).

Given its anti-inflammatory properties and these effects in animal models of allergic inflammation, IL-10 may have beneficial effects in asthma(12).

However, no such studies have been performed yet. Administration of IL-10 to normal volunteers induced a fall in circulating CD2, CD3, CD4, and CD8 lymphocytes with suppression of mitogen induced T cell proliferation and reduction of TNF-α and IL-1α production from whole blood stimulated with endotoxin ex vivo(13).
The aim of this study was to investigate the major role of (IL 1B, IL 2, IL 8, IL 10, IL 12) in asthmatic patients and its correlation with IgE.

Methods
Blood samples were taken from 50 asthmatic patients, whose age range 26–58 years, the samples were collected during May to August 2010 at Al-Hussein hospital. All of them had atopic rhinitis, and 7 normal individuals as control. The blood was spun at 3,000 rpm and the serum separated. The sera were stored at -20°C till testing. 50 Serum specimens were tested by EIA (DRG.USA) to detect IgE and EASIA to detect IL1β, IL2, IL 8, IL 10, IL 12 (Biosource, Belgium) according to manufacturer’s instructions.

Statistical analysis
The data were analyzed were analyzed by using Dencan statistics at Probability values were considered to be significant at ≤0.01 (14).

Results and Discussion
Table 1 was revealed that correlation between IL 1B, IL 2, IL 8, IL 10, IL 12 values (20,76,62,44,76)% respectively and IgE value (50)%. A central mediator in atopic asthma is IgE antibody, which is produced by sensitized allergen-specific B cells. Allergens are antigens that elicit hypersensitivity or allergic reactions and that by themselves can increase IgE levels in the serum in susceptible subjects subsequent to stimulation. B cells, by presenting the allergen fragments in conjunction with the major histocompatibility complex (MHC), can activate specific Th2 helper cells to produce numerous cytokines, leading to further B-cell activation and antibody release (15). Chemical respiratory allergy is also an important occupational health problem, but there are currently available no validated methods for hazard identification, partly because of the fact that the relevant cellular and molecular mechanisms of sensitization of the respiratory tract have been unclear, with particular controversy regarding an obligatory role for IgE (16).

Table 2 was revealed Increasing values of IL2, IL 8, IL 10, IL 12 (36, 26, 24, 32)% respectively at ages (37-47) years were led to decreased IgE value (10%), and IL 2, IL 8 values were (24, 22)% respectively comparison with IgE (10%). While at ages 48-58 years that increased IL 2, IL 8 values were (24, 22)%

IL1 plays a significant role in regulation of hematopoiesis (17). IL-2 levels are increased in bronchoalveolar lavage fluid from patients with symptomatic asthma (18). IL 8 induced an immunoglobulin (IgE)-mediated response in human lung Samples (19).

IL-10 is a potent antiinflammatory cytokine which inhibits the synthesis of many inflammatory proteins, including cytokines, and inflammatory enzymes that are over-expressed in asthma (20). Major action of IL-12 is to induce the development of Th1 cells, while suppressing Th2 cells. It is likely that IL-12 plays a critical role in determining the balance between Th1 and Th2 cells, thereby inhibiting IgE synthesis and allergic inflammation. This effect of IL-12 on Th2 responses and allergic inflammation has suggested that it might be a useful candidate for asthma (21).

Our study was revealed significant value compared with healthy persons at p ≥ 0.01.

In other study was indicated that increase of IL1β at asthmatic patients is mainly cell associated (22).
This study agreement with that study was indicated IL-12 promote Th1 response and inhibit Th2 response, inhibit IgE synthesis(23)(24).

IL-8 mediates the recruitment and activation of neutrophils in inflamed tissue (25).

IL-8 can be detected in synovial fluid from patients with various inflammatory rheumatic diseases (26).

The recent discovery that rodent mast cells secrete cytokines as a result of an IgE-dependent stimulus is a major advance. Produce lower amounts of IL-12, which decreases Th2 type inflammation by stimulating Th1 cell differentiation and inhibition of IgE-synthesis(27).

Whereas airway eosinophilia and total serum IgE levels are increased in sensitized IL-10 knockout mice (28)(29).

IL-10 is a regulatory cytokine that has been suggested for treatment of asthma because of its immunosuppressive and anti-inflammatory properties(30).

IL-12 may play an important part in inhibiting inappropriate IgE synthesis and allergic inflammation as a result of allergen exposure(31).

The present study found statistically significant difference between the mean values of serum IL1B,IL 2,IL 8,IL 10 and IgE.

**Conclusion**

The present results confirmed a significant correlation between serum levels of IL1B,IL 2,IL 8,IL 10 and IgE and the severity of asthma. The complex interactions between IL1B,IL 2,IL 8,IL 10 and IgE in asthmatic patients need further investigations. Further studies are needed to evaluate correlation between cytokines and acute and chronic phases of asthma.

**References**


Table 1. Comparison between Values of IgE, IL1β, IL 2, IL 8, IL 10, IL 12 in healthy and patients.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>IgE 5-100 IU/ml</th>
<th>IL1β 0-17 pg/ml</th>
<th>IL2 0-0.1 IU/ml</th>
<th>IL 8 0-1.1 pg/ml</th>
<th>IL 10 0-3.3 pg/ml</th>
<th>IL 12 0-3 pg/ml</th>
</tr>
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<tbody>
<tr>
<td>Total</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Healthy(mean)</td>
<td>10.50</td>
<td>1.50</td>
<td>0.5</td>
<td>0.8</td>
<td>0.10</td>
<td>0.60</td>
</tr>
<tr>
<td>Patients(mean)</td>
<td>187.37</td>
<td>10</td>
<td>38</td>
<td>31</td>
<td>22</td>
<td>38</td>
</tr>
<tr>
<td>Percentage</td>
<td>(50%)</td>
<td>(20%)</td>
<td>(76%)</td>
<td>(62%)</td>
<td>(44%)</td>
<td>(76%)</td>
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Table 2. Correlation between IgE, IL1β, IL 2, IL 8, IL 10, IL 12 and ages.

<table>
<thead>
<tr>
<th>Age groups(years)</th>
<th>No</th>
<th>IgE</th>
<th>IL1β</th>
<th>IL 2</th>
<th>IL 8</th>
<th>IL 10</th>
<th>IL 12</th>
</tr>
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<tbody>
<tr>
<td>26-36</td>
<td>8</td>
<td>4(8%)</td>
<td>1(2%)</td>
<td>7(14%)</td>
<td>5(10%)</td>
<td>3(6%)</td>
<td>6(12%)</td>
</tr>
<tr>
<td>37-47</td>
<td>25</td>
<td>5(10%)</td>
<td>5(10%)</td>
<td>18(36%)</td>
<td>13(26%)</td>
<td>12(24%)</td>
<td>16(32%)</td>
</tr>
<tr>
<td>48-58</td>
<td>17</td>
<td>5(10%)</td>
<td>7(14%)</td>
<td>12(24%)</td>
<td>11(22%)</td>
<td>6(12%)</td>
<td>6(12%)</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>24(48%)</td>
<td>13(26%)</td>
<td>37(74%)</td>
<td>29(58%)</td>
<td>21(42%)</td>
<td>28(56%)</td>
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