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,IL 1B,IL 2IL 8,,IL10 ,and 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 Linkined Immuno Sorbant Assay to detect IgE,IL 1B,IL 2IL 8,,IL10 ,and IL12 were carried in Al-Hussein Hospital in Kerbala ,during the period from May to Augest 2010.

Results:50 patients were evaluated for asthma and correlation between IL 1B,IL 2,IL 8,IL 10 ,IL 12 values (20,76,62,44,76)% respectively and IgE value (50)%.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 comparion with IgE(10%).

Conclusions: Importance studying factors(IL 1B,IL 2,IL 8,IL 10 ,IL 12) in diagnosis of Asthmatic patients after clinically diagnosis .

دور الابيضاضيات عند مرضى الربو

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الخلاصة

الخلفية: الربو مرض التهابي مزمن يصيب المجاري التنفسية نتيجة تعرض المريض للمواد الغريبة المحفزة للاستجابة المناعية يتميز بافراز الابيضاضيات من الخلايا الالتهابية.

الهدف :تم تشخيص الربو في المرضى المشكوك بهم سريريا باستخدام الفحوصات المصلية.

المرضى وطرائق العمل:تم جمع 50 نموذج دم من المراجعين بعد تشخيصهم من قبل الطبيب المختص وتم وضعها في انابيب اختبار سعة 5 مل باعمار تتراوحت بين (26- 58)سنة باستخدام اختبار ELISA للكشف عن(IgE,IL 12 ,IL 10 ,IL 8 ,IL 2 ,IL 1B)وقد تم انجازها في مستشفى الحسين (ع) التعليمي للفترة من مايس الى آب 2010 .

النتائج: تم تقييم 50 مريض بالربو أ ظهرت النتائج قيم المعايير التالية على التوالي:
% (20,76,62,44,76)12 ,IL 10 ,IL 8 ,IL 2 ,IL 1B , مقارنة مع قيمة IgE(50%) ازدياد قيم IL2,IL (8 ,IL 10 ,IL 12) عند الاعمار (37-47) سنة كانت على التوالي (32،24،26،36)% ادت الى انخفاض قيمة IgE(10%) في حين كانت قيم (IL 2،IL 8) عند الاعمار (48-58) سنة كانت على التوالي (22،24)% مقارنة مع قيمة IgE(10%).

الاستنتاجات:أهمية دراسة الابيضاضيات (IL 12, IL 10 ,IL 8 ,IL 2 ,IL 1B) في تشخيص مرضى الربو بعد تشخيصهم سريريا.

Introduction

Asthma is one of the few chronic diseases in the de-veloped 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, chemoattractant 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-1â 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-á and IL-1â 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 Augest 2010 at Al-Hussein hospital . All of 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, Belghium) according to manufacturer's instructions.

Statical 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 Discusion

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 comparion 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 bron-choalveolar lavage fluid from patients with symptomatic asthma (18)

IL 8 induced an immunoglobulin (Ig)E-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 Th**1** cells, while suppressing Th**2** cells. It is likely that IL-12 plays a critical role in determining the balance between Th**1** and Th**2** cells, thereby inhibiting IgE synthesis and allergic inflammation. This effect of IL-12 on Th**2** 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 Th**1** response and inhibit Th**2** 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.

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Table.1 ,Comparsion between Values of IgE,IL1B,IL 2,IL 8,IL 10,IL 12 in healthy and patients .

Parameters	IgE 5-100 IU/ml	IL1β 0-17 pg/ml	IL2 0-0.1 IU/ml	IL 8 0-1.1 pg/ml	IL 10 0-3.3 pg/ml	IL 12 0-3 pg/ml
Total	50	50	50	50	50	50
Healthy(mean)	10.50	1.50	0.5	0.8	0.10	0.60
Patients(mean)	187.37	10	38	31	22	38
Percentage	(50%)	(20%)	(76%)	(62%)	(44%)	(76%)

Table .2,Correlation between IgE,IL1B,IL 2,IL 8,IL 10 ,IL 12 and ages.

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