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Cytokines concentrations in serum samples from allergic children—Multiple analysis to define biomarkers for better diagnosis of allergic inflammatory process

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ABSTRACT

Background: Allergic diseases can expand at any age as a result of complicated interaction of environmental and genetic factors. Through the years, studies have found that allergic diseases are primarily described by elevated Th2 pathway activation, leading to increased serum IgE levels, allergen reactivity, blood eosinophil counts and secreted interleukins.

Methods: A total of 20 patients with allergy and 20 matched controls participants were recruited for the study. A study was designed with the framework of an ongoing project at the Regional Children's Hospital in Olsztyn on the analysis of the immune profile of children with allergy and asthma. Diagnosis was conducted by medical specialists. Whole blood samples were collected and serum IL's and chemokin levels were made using ELISA kits.

Results: Results demonstrated that in comparison to the controls, the individuals with allergy showed significantly higher concentration of IL-1β, IL-4, IL-6, IL-8, IL-10, IL-13 and TNF-α. We also demonstrated significant correlations between the levels of cytokines which implies the presence of an interactive network between them. The results of ROC analysis indicated the 3-factors (IL-1β, IL-4, IL-8) could be additional, helpful biomarkers in better diagnosis of allergy.

Conclusions: In this study, serum levels of cytokine differed among children with allergy. However, the findings of this support the possibility of using an appropriate selection of serum cytokine for the diagnosis allergy and emphasize the need to standardize quantitative methods for serum analysis.

1. Introduction

Allergic conditions perform a spectrum of disorders, including: eczema, certain forms of asthma, food allergies, eosinophil esophagitis, insect and drug allergies. The time between 20–30 years, the prevalence of allergic disease has raised exponentially throughout the world and now affects approximately 1 in 5 people (Pawankar et al., 2013). Allergic diseases can expand at any age as a result of complicated interaction of environmental and genetic factors. Usually allergic disease, are correlated with one another, further illustrating the overlapping underlying mechanisms of pathogenesis and disease. Through the years, studies have found that allergic diseases are primarily described by elevated Th2 pathway activation, leading to increased serum IgE levels, allergen reactivity, and blood eosinophil counts (Zheng et al., 2011). Allergen-induced IgE synthesis can trigger eosinophils, basophils and mast cells to release cytokines for the differentiation of Th cells into Th2 cells to secrete interleukin-4 (IL-4), IL-5, IL-10 and IL-13 (Yssel and Groux, 2000). Numerous research in genetic contributed to the identification of large candidate genes in the pathogenesis of allergic inflammation and asthma. Many genes encode interleukins, which are produced by immune cells and mediating in the induction and the development of inflammatory responses.

Because the pathogenesis of allergic diseases, are complex process that may begin in the prenatal period, this is a time that the immune system could play an important role. A study was designed with the framework of an ongoing project at the Regional Children's Hospital in Olsztyn on the analysis of the immune profile of children with allergy and asthma. From these ongoing clinical studies and using data from the available published literature, a panel of cytokines were identified for serum measurements in children with allergic diseases. The

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Table 1
Characteristics of serum cytokines evaluated in this study.

Cytokine	Producing cells	Source	Receptors and receptors-bearing cells	Function
IL-1β	Produced by variety of cell types but vast majority of studies have focussed on its production within cells of the innate immune system:monocytes and macrophages	Monocytes, macrophage, endothelium, natural killer	IL-1RI; IL-1RII	IL-1 is principally an inflammatory cytokine. It apply to a group of cytokines with overlapping biologic properties (TNF-α, IL-6, IL-8, GM-CSF, PGE2 by macrophage). IL-1 with TNF and IL-6 share the capability to increase cell proliferation, co-stimulate T activation by enhancing production of cytokines like IL-2, and it's receptor, enhanced also B proliferation and muration. In addition, suppress or initiate gene expression for proteins and enhanced Natural Killer (NK) cytotoxity. IL-1 are ability to induce hypotension, sleep, anorexia, fever, bone resorption by osteoclasts and(acute phase proteins (APP). Pro-inflammatory activities by inducing chemokine and ICAM-1 and VCAM-1 on endothelium. Moreover, increases the synthesis of collagenases, resulting in the destruction of cartilage, stimulates the production of prostaglandins, leading to decrease in the pain threshold, encourage the release of pituitary hormones. In addition IL-1 has some host-defense properties (Feghali and Wright, 1997; Dinarello, 2002).
IL-4	Produced by activated lymphocytes (Th2), mast cells, basophils and NK.	Th2, Tc2, natural killer, mast cell	IL-2Rγ; IL-13Rα1	IL-4 has act many biological functions, including the differentiation of B cells into plasma cells as well as stimulation of activated B-cell and T-cell and mast cell (MC) proliferation, and also is a key regulator in adaptive humoral immunity. Up-regulates MHC klas II on B and macrophages, and CD23 on B cells; down regulates IL-12 production and thereby inhibits Th1 differentiation. IL-4 induces switch to IgG1 and IgE. IL-4 reduces the production of IFN-γ, IL-12, macrophages, Th1 cells, and dendritic cell and increases macrophage phagocytosis (Feghali and Wright, 1997; Braddock et al., 2018).
IL-6	IL-6 is secreted by T cells and macrophages to stimulate immune response.	Th2, monocyte, macrophage, bone narrow stroma	IL-6Rα chain (CD126), and the signal-transducing component gp130 (called CD130).	IL-6 is an critical mediator of fever and of the acute phase response. It is able of crossing the blood-brain barrier and beginning synthesis of Prostaglandin E2 (PGE2) in the hypothalamus, through developing the body's temperature set-point. In fatty tissue and also muscle, IL-6 prompt energy mobilization that leads to boost body temperature. IL-6 can be secreted by macrophages in response to specific microbial molecules, referred to a pathogen-associated molecular patterns (PAMPs). These are present on the cell surface and intracellular compartments and activate intracellular signaling cascades that give rise to inflammatory cytokine production. IL-6 is responsible for differentiation of myeloid stem cells and of B into plasma cells, induces APP, enhances T proliferation (Feghali and Wright, 1997; Ghasemi, 2018).
IL-8	Is a chemokine produced by macrophages and other cell types such as epithelial cells, airway smooth muscle cells and endothelial cells.	monocyte, macrophage, endothelium	CXCRI; CXCRII	IL-8, also known as *neutrophil chemotactic factor*, has two dominant functions. It cause chemotaxis in target cells, primarily neutrophils but also other granulocytes, causing them to migrate toward the site of infection. IL-8 also induces phagocytosis once they have arrived. IL-8 is also known to be a potent promoter of angiogenesis. In target cells, IL-8 induces a series of physiological responses required for migration and phagocytosis, such as increases in intracellular Ca^{2+}, exocytosis (e.g. histamine release). IL-8 is believed to play a role in the pathogenesis of bronchiolitis, a common respiratory tract disease caused by viral infection. mediates chemotaxis and activation of neutrophils (Feghali and Wright, 1997; Meniailo et al., 2018).

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