

ESTIMATION OF INTERLEUKIN-6 LEVEL IN PSORIASIS PATIENTS

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INTRODUCTION

The main inducer cytokines are Interferon α (IFN- α), Tumor Necrosis Factor-Alpha (TNF- α) and Interleukin 1 (IL1) which are secreted by T helper (Th1) lymphocytes, while the main suppressor cytokines are Tumor Growth Factor Beta (TGF β) Interleukin 4 (IL4), Interleukin 10 (IL10) and Interleukin 6 (IL6) secreted by T helper 2 lymphocytes (1).

Psoriasis is a common genetically determined inflammatory and proliferative disease of the skin. This condition has a cytokine profile mainly of TNF- α , IL1 and INF- γ , which represent cytokines released from Th1 cells change in this cytokine pattern (2). Since Interleukin 6 (IL6) is shown to have many biologic activities relevant to the pathogenesis of psoriasis, the role of this cytokine in psoriasis has invited attention. IL6 is a multifunctional inflammatory cytokine that is produced by monocytes, keratinocytes, endothelial cells and fibroblasts in normal skin. The epidermal hyperplasia of psoriasis may be partially explained by an overproduction of this cytokine.

The aim of this study is to evaluate the levels of cytokine IL6 in patients with psoriasis and to demonstrate the possible correlation of this level with the clinical picture.

METHODS AND MATERIALS

This study includes 38 patients with psoriasis. They were selected from patients attending the outpatient clinics of Dermatology Department of Al Ain hospital. There were 25 males and 13 females with an average age of 27 years. All patients were subjected to full history and clinical examination, taking into consideration the morphology and distribution of skin lesions. Disease was classified into mild (24), moderate (9) and severe (5) according to PASI score.

Ten healthy individuals were included in this study as control group, consisting of 7 males and 3 females. 10 ml blood was taken from each patient and control, coagulated, separated by centrifuging and then frozen at -20°C. ELISA kit (Biosource Europe S.A Belgium) with minimum detectable limit 2 pg/ml (Car # KAC 1261) was used to measure the serum level of IL6. Quantitative data were summarized as means and standard error. Group means were compared by student t-test. Pearson correlation coefficient was calculated to measure the divergence and strength of linear association between quantitative data. Spearman correlation coefficient was used when several (repeated) data exist. A 0.5% probability level ($P < 0.05$) was considered statistically significant.

RESULTS

This study included 38 patients with psoriasis. They were 25 males, 13 females with an average age of 27.8 ± 2.4 years range (8-60). PASI scores were 6.6 ± 1.1 for mild cases (24 patients), 22.48 ± 1.4 for moderate cases (9 patients) and 44.36 ± 6.2 for severe cases (5 patients). The serum levels of interleukin-6 (IL6) in psoriasis in comparison with control were significantly different (table 1 and 2). IL6 in severe cases were significantly higher than mild and moderate cases.

	Mild cases	Moderate	Severe
Age			
Sex : -	2:1	3:1	1:3
Duration	5.1 ± 0.8	7.4 ± 1.4	7.9 ± 3.1
PASI score	6.6 ± 1.1	22.48 ± 1.4	44.36 ± 6.2

	IL6	p
Control	6.6 ± 0.9	
Mild	47.3 ± 1.2	< 0.001
Moderate	56.4 ± 2.2	< 0.001
Severe	79.9 ± 5.1	< 0.001

Table 1 and 2: Severity and clinical characteristics of the patients.

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DISCUSSION

Psoriasis is a common skin disorder characterised by thickened, scaly plaques formed of hyperplastic keratinocytes. Earlier thought to be a primary disorder of cell proliferation, it is now recognised as a T cell mediated inflammatory process wherein keratinocyte multiplication is a secondary phenomenon (3).

Stimulation and sustenance of keratinocyte proliferation is performed by elaboration of an intercellular network of small proteins, the cytokines, which act in an autocrine and paracrine fashion to mediate their effects.

Cytokines are low molecular weight glycoproteins secreted by leucocytes and other cells that regulate immune responses and other cell proliferative processes. The cytokine network is an elaborate interplay of various chemicals acting on their target cells in a stimulatory or inhibitory manner to achieve a final result such as tissue repair, cell growth, differentiation or proliferation. These molecules act by binding to their specific cell membrane receptors causing a cascade of chemical reactions leading to induction or inhibition of genes forming proteins. Cytokines are formed transiently in an orderly and regulated manner. Cytokines have multiple overlapping actions, which may be synergistic or antagonistic to each other. This may be related to the expression of cell-surface receptors. Many cytokines have multiple actions and effects on different pathologic processes. Interleukins are group of cytokines, which currently number upto 27 (4).

The immunohistological study of psoriatic plaques reveals the collection of T lymphocytes, both helper (Th) and suppressor (Tc), with the latter predominating. The helper subset (CD4) is for induction and maintenance of disease, while the suppressor (CD8) cells are the main effector cells. Depending on the cytokines elaborated, T cell responses can be categorised into type 1 and type 2, with psoriasis being a type 1 disease showing mainly IL2, INF- α and TNF- α , while Atopic dermatitis is the prototype type 2 response disorder, with formation of IL4, IL5, IL6, IL9 and others. Th1 cytokines activate cytotoxic, inflammatory and DTH responses, while Th2 cells help regulate antibody formation and allergic responses. Th1 cytokines suppress the effects of Th2, and vice versa. Thus, Th1/Th2 balance is crucial in determining the type of response and course of disease. Cytokines expressed by psoriatic lesions include IL1, IL2, IL6, IL8, TNF- γ INF- α and various growth factors (5).

IL6 is a major mediator of host response to injury or infection. IL6 is mainly produced by T and B lymphocytes, as well as fibroblasts and macrophages. It is

also constitutively expressed by epidermal cells (6). Its principal target cells are B cells and liver hepatocytes. It induces B cell differentiation, forming antibodies, and release of acute phase proteins from hepatocytes. IL6 induces release of IL2 and IL2R from T cells, maturation of megakaryocytes and osteoclast formation. IL1 increases and IL10 inhibits synthesis of IL6.

IL6 has both stimulatory and suppressive effects on cell proliferation and differentiation. It causes keratinocyte proliferation (mitogenic effect) and increased TNF- γ production by these cells. IL6 production can be upgraded by UV radiation, as well as by IL1, INF- γ , TNF- α and certain viruses, and suppressed by dexamethasone (7).

IL6 levels are increased in suction blister fluid from lesional psoriatic skin (8). Unstimulated keratinocytes usually produce minimal levels of IL6 (9). Increased lesional IL6 production and increased serum IL6 is seen in patients with psoriasis (10). There is an increased expression of IL6 from psoriatic keratinocytes, and it stimulates keratinocyte proliferation in culture (11). Treatment reduces IL6 levels in the lesions. It is notable that dermal fibroblasts express increased levels of IL6, compared to epidermal cells.

IL6 is released upon tissue injury, inflammation, bacterial and viral infections, all factors that are either present or implicated in psoriasis. IL6 and IL8 enhance activation, proliferation and chemotaxis of T cells, thus having a pro-inflammatory role. They are responsible for the accumulation of T cells within the psoriatic lesion (12).

It can thus be said that IL6 is one of the important factors in the pathogenesis of psoriasis, which acts by activating T cells in the plaque to produce pro-inflammatory cytokines and other mediators and by increasing chemotaxis of T cells into the lesional skin, thereby maintaining the inflammation.

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**BETA-BLOCKER THERAPY BENEFICIAL
FOR PEANUT ALLERGY PATIENTS WITH HEART DISEASE;
CLEANING AGENTS SUCCESSFUL IN ELIMINATING PEANUT ALLERGEN,
FROM THE JOURNAL OF ALLERGY & CLINICAL IMMUNOLOGY**

MILWAUKEE — New research shows that beta-blocker therapy should still improve the survival rate in patients who suffer from peanut allergies and have heart disease, according a study featured in the May 2004 Journal of Allergy & Clinical Immunology (JACI). The JACI is the peer-reviewed scientific journal of the American Academy of Allergy, Asthma & Immunology (AAAAI).

In heart disease patients, treatment with beta-blockers lowers the risk of subsequent heart attacks. For peanut allergy sufferers, epinephrine is the recommended treatment for severe allergic reactions. However, epinephrine may be ineffective in those patients taking beta-blockers for their heart disease.

John A. Tenbrook, Jr., MD, and colleagues from Tufts-New England Medical center in Boston and National Jewish Medical and Research Center in Denver, used a computer simulation to capture the risks of death from heart disease and from anaphylaxis for a population of 10,000 patients with heart disease and peanut allergy. They found that for peanut allergic patients who are post heart attack or who have had congestive heart failure, the heart disease benefit of beta-blockers outweighs the increased likelihood of dying from anaphylaxis.

As the prevalence of peanut allergy increases in the United States, more patients may be faced with the choice of discontinuing their beta-blocker therapy. However, findings from the JACI study provide a framework to aid clinicians and patients in the decision making process.

Common household cleaning agents successful in eliminating peanut allergen. Peanut allergen is relatively easily cleaned from hands and tabletops with common household cleaning agents and does not appear to be widely distributed in schools, according to a study featured in the May 2004 Journal of Allergy and Clinical Immunology (JACI).

Tamara T. Perry, MD, and colleagues from Johns Hopkins School of Medicine examined several factors: peanut allergen on surfaces in schools, the presence of residual peanut protein after using cleaning products, and airborne peanut protein when people were eating several forms of peanut.

Researchers found that there is a relatively low risk of exposure to peanut allergen when tables contaminated with small quantities of peanut butter are carefully cleaned with most common household cleaning products or water. Common household cleaning agents, except dishwashing liquid, easily removed peanut allergen from tabletops. Also, large amounts of peanut butter were removed from hands using liquid soap, bar soap or commercial wipes. However, researchers noted that plain water and antibacterial hand sanitizer did leave detectable peanut allergen on the hands. These cleaning methods are less than ideal and may result in contamination of other objects.

The study's findings provide a better understanding of the extent and likelihood of potential exposure to peanut allergen in various settings. Researchers conclude that there is relatively low risk of exposure to significant concentrations of the major peanut allergen when surfaces and hands are cleaned with common household cleaning agents and that school cafeteria tables and desks are not likely to be source of significant exposure for more peanut allergic patients.

The AAAAI is the largest professional medical specialty organization in the United States representing allergists, asthma specialists, clinical immunologists, allied health professionals and others with a special interest in the research and treatment of allergic disease. Allergy/immunology specialists are pediatric or internal medicine physicians who have elected an additional two years of training to become specialized in the treatment of asthma, allergy and immunologic disease. Established in 1943, the AAAAI has nearly 6,000 members in the United States, Canada and 60 other countries. The AAAAI serves as an advocate to the public by providing educational information through its Web site at www.aaaai.org or the toll-free physician referral and information line at 1-800-822-2762.