Effect of Narrow Band Ultraviolet B on the Level of Interleukin-17 in Psoriasis Patients

Thesis

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List of Abbreviations

ACE	Angiotensin Converting Enzyme
APC	Antigen Presenting Cell
BAFF	B-cell Activating Factor
BD2	B Deficin 2
C/EBP	CCAAT/Enhancer Binding Protein
CBC	Complete Blood count
CCR	Chemotactic Cytokine Receptor
CD	Cluster of Differentiation
CD 4+	T helper cell
CD 8+	T suppressor cell
CPP	Chronic Plaque Psoriasis
DCs	Dendritic Cells
DNA	Deoxyribonucleic Acid
EAE	Experimental autoimmune encephalomyelitis
EP	Erythrodermic Psoriasis
FDA	Food and Drug Adminstration
G-CSF	Granulocyte-Colony Stimulating Factor
GM-CSF	Granulocyte Macrophage-Colony Stimulating Factor
GP	Guttate Psoriasis
GPP	Generalized Pustular Psoriasis
GWAS	Genome Wide Association Study
HIV	Human Immunodeficiency Virus
HLA	Human Leucocytic Antigen
IBD	Inflammatory Bowel Disease
ICAM 1	Intercellular Adhesion Molecule 1

List of Abbreviations (Cont.)

IFN-γ	Interferon-γ
IL	Interleukin
IL-1RI	Interleukin-1 Receptor I
IL-1RII	Interleukin-1 Receptor II
LC	Langerhan's Cell
LFA	Lymphocyte Function Associated Antigen
MED	Minimal Erythema Dose
MHC	Major Histocompatibility Complex
MMP	Matrix Metalloproteinase
MOP	Methoxypsoralen
MPD	Minimal Phototoxic Dose
NB-UVB	Narrow Band-Ultraviolet B
NF-κB	Nuclear Factor-κappa B
NK	Natural Killer
PASI	Psoriasis Area & Severity Index
PGE2	Prostaglandin E2
PPP	Palmoplantar Psoriasis
PSORS	Psoriasis susceptibility locus
PUVA	Psoralen-Ultraviolet A
RA	Rheumatoid Arthritis
SC	Subcutaneous
SEFIR	SEF/IL-17R
STAT	Signal Transducer and Activator of Transcription
SUP	Selective Ultraviolet Phototherapy
TCIs	Topical Calcineurin Inhibitors

List of Abbreviations (Cont.)

TCR	T Cell Receptor
TGF-α	Transforming Growth Factor-α
TGF-β	Transforming Growth Factor-β
Th1	T helper 1
Th2	T helper 2
TMP	Trimethylpsoralen
TNF-α	Tumor Necrosis Factor-α
TRAF6	Tumor necrosis factor Receptor-Associated Factor 6
UV	Ultraviolet
UVA	Ultraviolet A
UVB	Ultraviolet B
VEGF	Vascular Endothelial Growth Factor

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Introduction

Psoriasis is a complex inflammatory skin disease that affects 2.3% of the population worldwide. Although the initial events triggering a psoriatic lesion are still unknown, many environmental factors have been shown to play a role in psoriasis pathogenesis. External triggers such as physical trauma, infection, stress, drug and alcohol can trigger an initial episode of psoriasis in individuals who already have a genetic predisposition ***(Blauvet, 2007)***.

This trigger activates dendritic cells, such as Langerhan's cell (LC), inducing their migration to skin draining lymphocytes. Here, antigen specific T-cells are primed by migrated skin dendritic cells to differentiate into effector T-cells, then traffic to the skin, where they together induce the formation of a primary psoriatic plaque. During this step, some T-cell and dendritic cell start to infiltrate the epidermis, releasing proinflammatory cytokines which in turn stimulate keratinocyte proliferation ***(Ghoreschi et al., 2007)***.

Psoriasis can be considered as a T-cell mediated disease, with a complex role for a variety of cytokine interactions between keratinocytes and T-lymphocytes. Nearly forty years ago, T-cells were divided into helper, cytotoxic and suppressor cells types. Twenty years later, T-helper cells were further divided into Th1 and Th2 subsets. More recently Th1, Th2 paradigm has been updated including a new subset called Th17

cell. Although, such tidy categorization may be attractive in its simplicity, it has become apparent that the original Th1, Th2 paradigm is much more complicated than originally appreciated. For example, psoriasis was commonly considered to be a Th1 mediated disease, but now it is realized that such generalization was inaccurate and oversimplified ***(Steinman, 2008)***.

The identification of Th17 subset has now broadened our understanding of inflammatory process in human disease, which through the production of both IL-17 and IL-22, induction of chemokines and recruitment of other effector cells population might have essential function in psoriasis pathogenesis ***(Betteli et al., 2007)***.

Narrow band (NB-UVB) has been introduced for treatment of psoriasis and other inflammatory dermatoses. UVB irradiation inhibits cutaneous delayed-type hyper-sensitivity responses to haptens, and its therapeutic mechanism in psoriasis has been attributed to these immunosuppressive properties. Interestingly, irradiation of psoriatic skin lesions with standard UVB light causes rapid depletion of intraepidermal T-cells. As apoptosis is induced by in vitro UVB irradiation of T-cells, it has been proposed that UVB may have immunosuppressive effects in psoriasis through induction of apoptosis in disease-mediating T-cells ***(Ozawa et al., 1998)***.

Aim of the Work

The aim of this work is to study the effect of NB-UVB on the level of IL-17 in psoriasis patients.

Psoriasis

Definition:

Psoriasis is a chronic inflammatory skin disorder characterized by dermal hyperplasia. The key histological features of psoriatic skin are epidermal keratinocyte hyperproliferation, vascular proliferation and infiltration of Dentritic cells (DCs), macrophages, neutrophils and T-cells ***(Nestle et al., 2009)***.

Epidemiology:

Psoriasis affects both sexes equally. It can begin at any age, there are two peaks of onset, the first one from 16-22 years of age (early onset psoriasis) and the second from 57-60 years of age (late onset psoriasis) ***(Gelfand, 2005)***. Around one-third of people with psoriasis report a family history of the disease, and researchers have identified genetic loci associated with the condition. Studies of monozygotic twins suggest a 70% chance of a twin developing psoriasis if the other twin has psoriasis. The concordance is around 20% for dizygotic twins, these findings suggest both a genetic predisposition and an environmental response in developing psoriasis. Onset before age 40 usually indicates a greater genetic susceptibility and a more severe or recurrent course of psoriasis ***(Krueger and Ellis, 2005)***.

Psoriasis is more prevalent in Caucasian populations (estimated prevalence 1.5-3%), especially Northern European, with a reported peak prevalence between 3 and 4.8% in Norway ***(Farber and Nall, 1999)***.

The estimated prevalence of psoriasis is 0.4% in China, 0.3-1% in Japan, 0.8% in India and 1.2-1.4% in Mediterranean. It has never been reported in Latin American Indians. Psoriasis is also less common in Asian countries. Epidemiological studies carried out on West African and American Black populations have reported prevalence figures of 0.3-0.7% and 0.7% respectively ***(Christophers, 2001)***.

This shows that there is a significant inter-racial and geographical variation in the distribution of this disease and explains why there are no accurate figures of its general prevalence ***(Farber and Nall, 1999)***.

Etiology:

The etiology of psoriasis is not fully understood. There are two main hypotheses about the process that occurs in the development of the disease. The first considers psoriasis as primarily a disorder of excessive growth and reproduction of skin cells. The problem is simply seen as a fault of the epidermis and its keratinocytes. The second hypothesis sees the disease as being an immune-mediated disorder in which the excessive reproduction of skin cells is secondary to factors

produced by the immune system. T-cells (which normally help to protect the body against infection) become active, migrate to the dermis and trigger the release of cytokines (tumor necrosis factor-alpha [TNF-α], in particular) which cause inflammation and the rapid production of skin cells. It is not known what initiates the activation of the T-cells ***(Zenz et al., 2005)***.

Clinical Features:

Psoriasis varies in age and mode of onset, severity, course, duration and clinical morphology from one individual to another. There are many distinct clinical subtypes which often overlap: chronic plaque, guttate, generalised, palmoplantar, pustular and erythrodermic. Psoriasis can also involve the musculoskeletal system (psoriatic arthritis) and the nail apparatus ***(Lebwohl, 2003)***.

Chronic Plaque Psoriasis (CPP):

It is the classical form of psoriasis, which accounts for around 80% of diagnoses. It is characterized by well-demarcated erythematous plaques with adherent silvery-white scales, which preferentially affect elbows, knees, lumbosacral area, inter-gluteal cleft and scalp. Lesions often develop at sites of skin injury (Koebner phenomenon). Any kind of trauma to the skin can trigger this response, excoriation, burn, contact dermatitis, chemical irritation, infection and