Effect of Narrow Band Ultraviolet B Therapy versus Methotrexate on serum level of Interleukin ١٧and Interleukin ٢٣ in severe psoriasis patients

Thesis submitted for Partial Fulfillment of Master Degree in Dermatology, Venereology & Andrology

By

Mohamed Said Abd Elaziz Abd Elhameed

(M.B., B.Ch.)

Under supervision of

Prof. Dr. Tarek Mahmoud Elghandour

Professor of Dermatology, Venerology and Andrology
Faculty of Medicine
Ain-Shams University

Prof. Dr. Sahar El Sayed Ahmed

Assistant Professor of Dermatology, Venereology and Andrology
Faculty of Medicine
Ain Shams University

Dr. Dalia Gamal El Din Aly

Lecturer of Dermatology and Venereology
Medical Division
National Research Centre

Faculty of Medicine
Ain Shams University
٢٠١٢

بسم الله الرحمن الرحيم

قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ
الْحَكِيمُ

صدق الله العظيم

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%	Percent
ACT	Nuclear factor kappa-B activator ١
AICAR	٥-aminoimidazole-٤-carboxamide ribonucleotide
ALT	Aminotransferase
AP-١	Activator Protein-١
AP-١	Activator protein ١
APCs	Antigen-presenting cells
BB-UVB	Broad band ultaviolet B
CBC	Complete blood count
CCA-IMT	Common carotid arteries intima media thickness
CD٢	Cluster of differentiation ٢
DC	Dendritic cell
DHFR	Dihydrofolate reductase
dsRNA	Double-stranded RNA
EGF	Epidermal growth factor
EGF-R	Epidermal growth factor receptor
FA	Folic acid
FGF	Fibroblast growth factor
GM-CSF	granulocyte macrophage colony Stimulating Factor

HIDL	High intensity discharge lamps
HRP	Horseradish peroxidase
HS	Highly significant
IBD	Inflamatory bowel disease
ICAM	Intercellular adhesion molecule
IFN	Interferon
IKK	Inhibitor kappa kinase
IL	Interleukin
iNOS	Inducible nitric oxide synthase
Jak	Janus kinase
Jak٢	Janus kinase ٢
LFA-١	lymphocyte function associated antigen-١
LFA-٣	lymphocyte function associated antigen-٣
LTi	Lymphoid tissue inducer
MAPK	Mitogen-activated protein kinase
MED	Minimal erythema dose
mj	Millijole.
MMPs	Matrix metalloproteinases
MPD	Minimal phototoxic dose
MTX	Methotrexate
NB-UVB	Narrow band ultaviolot B
NF-κB	Nuclear factor kappa-light-chain-enhancer of activated B cells
ng	Nanogram

nm	Nanometer
NO	Nitric oxide
NS	Non significant
PAF	platelet activating factor
PASI	Psoriasis area and severity index
PC	Personal computer
PG	Prostaglandin
PI٣K	Phosphatidylinositol ٣-kinase
PLEVA	Pityriasis lichenoides et varioliformis acuta
PRP	Pityriasis rubra pilaris
PUVA	Psoralen ultraviolet A
RA	Rheumatoid arthritis
S	Significant
S١٠٠A٧	S١٠٠ calcium-binding protein A٧
SD	Standard deviation
SEF	Similar expression to FGF receptor
SEFIR	Similar expression to fibroblast growth factor genes and IL-١٧Rs
SPSS	Statistical package for Social Science
STAT-٣	Signal transducer and activator of transcription ٣
TAK١	Transforming growth factor-beta activated kinase ١
TGF	Transforming growth factor
TGF-β	Transforming growth factor-beta
TGF-β١	Transforming growth factor β١

Th	T helper
TILL	Toll/interleukin-١R-like loop
TIR	Toll-IL-١ receptor
TMB	Tetramethylbenzidine
TNF	Tumor necrosis factor
TRAF	Tumor necrosis factor receptor-associated factor
Tyk٢	Non-receptor tyrosine-protein kinase
UVA	Ultraviolet A
UVB	Ultraviolet B
UVC	Ultraviolet C
UVR	Ultraviolet radiation
VEGF	Vascular endothelial growth factor
α	Alpha
α -MSH	Neuropeptide alpha-melanocyte-stimulating hormone
β	Beta
γ	Gamma

Introduction

Psoriasis is a chronic inflammatory skin disease that affects ٢٪ to ٣٪ of the population worldwide and causes significant morbidity ***(Schon and Boehncke.,)***. Its etiology is unknown, but it is generally believed to be a complex autoimmune inflammatory disease with a genetic basis ***(Lowes et al., ٢٠٠٧)***.

It is well known that trauma, infections and drugs such as lithium, antimalarials, trimethoprim and sulfamethoxazole, as well as environmental, psychological and metabolic factors can trigger psoriasis ***(Dika et al., ٢٠٠٧)***.

A new population of IL-١٧-producing Th cells, accordingly named Th١٧, has been described and its involvement in autoimmune diseases has been shown ***(Weaver et al., ٢٠٠٧)***. The development and maintenance of Th١٧ cells have been linked to IL-٢٣, a key initiating cytokine in the development of autoimmunity ***(Kastelein et al., ٢٠٠٧)***. Th١٧cells differentiate from native CD٤+ T cells under the stimulation of IL-١, IL-٦, and transforming growth factor-β ***(Zaba et al., ٢٠٠٧)*** and their proliferation is driven by IL-٢٣ ***(Vanden-Eijnden et al.,)***. Th١٧ cells can produce IL-١٧, IL-٢٢, IL-٦, and TNF-α and are now considered responsible for many of the inflammatory autoimmune responses once attributed to Th١ cells ***(Huber et al., .)***.

The findings of elevated levels of IL-٢٣ and Th١٧-related cytokines in cutaneous lesions and in the serum of psoriatic patients, the association of IL٢٣R gene variants with psoriasis and the evidence of a functional role of Th١٧ cells in autoimmunity, provide the basis for a rising interest in the IL-٢٣/Th١٧ axis in psoriasis ***(Blauvelt, .)***.

Methotrexate is an effective therapy for patients with psoriasis. The presumed mode of action is the blockade of DNA synthesis, inhibiting cell proliferation in rapidly dividing tissues, including the hyperproliferative psoriatic epidermis and the gastrointestinal and germinative epithelium ***(Mcullough and Weinstein,*** ***).*** Methotrexate may also affect mononuclear cells in the skin, blood, or lymphatic tissues, leading to an immunosuppressive effect ***(Weinstein et al.,*** ***).***

The introduction of fluorescent bulbs with a limited spectrum of ٣١١–٣١٢nm (narrow-band (NB)-UVB) has marked an advance in phototherapy. When compared with conventional broad-band UVB therapy, treatment with NB-UVB has been found to have greater bioactivity ***(Walters*** **et al.,** ***).***

NB-UVB therapy reverses several pathologic alterations in psoriasis: the number of epidermal T lymphocytes and dendritic cells (DCs) decrease during phototherapy ***(Erkin et al., ٢٠٠٧).***

NB-UVB suppressed IL-١٧ and IL-٢٢ mRNAs, which strongly correlated with lesion resolution. Therefore, in addition to its known role in suppressing IFN-γ production, NB-UVB radiation therapy can also target the IL-١٧ pathway to resolve psoriatic inflammation ***(Johnson-Huang et al.,*** ***).***