The effect of PUVA and NB UVB phototherapy on serum Osteopontin in psoriatic patients

Thesis

Submitted for Partial Fulfillment of Master Degree in Dermatology, Andrology and Venereology

Presented by

Eman El Sherbiny El Sayed

M.B.B.Ch

Faculty of Medicine, Cairo University

Supervised by

Prof. Dr. Saleh Mohammed El Shiemy

Professor of Dermatology, Venereology and Andrology

Faculty of Medicine, Ain Shams University

Prof. Dr. Mona Mohammed El Fangary

Professor of Dermatology, Venereology and Andrology

Faculty of Medicine

Misr University for Science and Technology

Faculty of Medicine

Ain Shams University

2019

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to ALLAH, the Most Kind and Most Merciful.

I'd like to express my respectful thanks and profound gratitude to ***Prof. Dr. Saleh Mohammed El Shiemy,*** *Professor of Dermatology, Venereology and Andrology - Faculty of Medicine- Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to ***Prof. Dr. Mona Mohammed El Fangary,*** *Professor of Dermatology, Venereology and Andrology, Faculty of Medicine, MUST University, for her kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I would like to express my hearty thanks to all my family for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients participated in this study.

Eman El Sherbiny El Sayed

List of Contents

List of Tables

List of Figures

List of Figures

List of Abbreviations

Abb.	Full term
AMP	*Antimicrobial peptide*
APCs	*Antigen-presenting cells*
BMI	*Body mass index*
BSA	*Body surface area*
CAD	*Coronary artery disease*
CCL20	*CC chemokine ligand 20*
cGRP	*Calcitonin gene-related peptide*
CLA	*Cutaneous lymphocyte antigen*
CRP	*C-reactive protein*
CTCL	*Cutaneous T-cell lymphoma*
DCs	*Dendritic cells*
DM	*Diabetes mellitus*
dWAT	*Dermal white adipose tissue*
ECM	*Extracellular matrix*
ELISA	*Enzyme linked immunosorobent assay*
GM-CSF	*Granulocyte-macrophage colony stimulating factor*
HBD	*Heparin binding domains*
HBD	*Human β-defensin*
HBD3	*Human B defensing 3*
HDL	*High-density lipoprotein*
HLA	*Human leukocyte antigen*
HSPG	*Heparin sulfate proteoglycans*
IFN	*Inteferon-α*
IFN-γ	*Interferon*
IL	*Interleukin*
ILCs	*Innate lymphoid cells*
iNOS	*Inducible nitric oxide synthase*
iOPN	*Intracellular iOPN*

List of Abbreviations (Cont...)

Abb.	Full term
IRF7	*Interferon regulatory factor 7*
KCs	*Keratinocytes*
LCE3B	*Late cornified envelope 3B*
LCE3C1	*Late cornified envelope 3C1*
LCs	*Langerhans cells*
LDL	*Low-density lipoprotein*
LFA-1	*Lymphocyte function-associated antigen-1*
Mas	*Monoadducts*
mDCs	*Myeloid dendritic cells*
MED	*Minimal erythema dose*
MHC I	*Major histocompatibility complex class I molecules*
MHC II	*Major histocompatibility complex class II molecules*
MI	*Myocardial infarction*
MMPs	*Metalloproteinases*
NK	*Natural killer*
OPN	*Osteopontin*
ox-LDL	*Oxidized LDL*
PASI	*Psoriasis area and severity index*
pDCs	*Plasmacytoid dendritic cells*
PRL	*Prolactin*
PSORS1	*Psoriasis susceptibility 1*
PSORS9	*Psoriasis susceptibility 9*
RGD	*Arginine-glycine-aspartic acid binding sequence*
SD	*Standard deviation*
SMC	*Smooth muscle cells*
sOPN	*Secreted OPN*

List of Abbreviations (Cont...)

Abb.	Full term
SP	*Substance P*
SVVYGLR	*Serine, valine, valine, tyrosine, glycine, leucine, arginine*
sWAT	*Subcutaneous white adipose tissue*
TGF-β	*Tumor growth factor*
Th	*T helper*
TLR	*Toll-like receptor*
TNF-α	*Tumor necrosis factor*
TNF-α	*Tumor necrosis factor alpha*
Treg	*T regulatory cell*
UV	*Ultra violet*
VIP	*Vasoactive --intestinal peptide*
VLDL	*Very low-density lipoprotein*
WC	*Waist circumference*

INTRODUCTION

Psoriasis is a chronic inflammatory disease that occurs in about 0.1% - 3% of the population ***(Park and Lee, 2010)***. It is characterized by an immune-related pathogenesis, a genetic background which may be triggered by several environmental factors including smoking and infections ***(Mercuri and Naldi, 2010)*** leading to a T cell-mediated cytokine production that drives hyper proliferation and abnormal differentiation of keratinocytes ***(Park and Lee, 2010)*.**

Osteopontin (OPN) is a multifunctional glycophosphoprotein secreted by many cell types, including osteoblasts, lymphocytes, macrophages, epithelial cells and vascular smooth muscle cells. It has been implicated in numerous physiologic and pathologic events including cell survival, cell mediated immunity and inflammation ***(Chen et al., 2009).***

It has been demonstrated that OPN modulates inflammatory processes involved in psoriasis, which is the most prevalent T-cell mediated inflammatory disease in humans through its action as chemotactic factor, supporting the adhesion and modulating the function of T cells and monocytes/macrophages ***(Bummino et al., 2009).***

Osteopontin acts as a mediator involved mainly in inflammation and tissue remodeling, yet it has become apparent that it may exert important cardiovascular effect as well. High

circulating OPN levels have been reported in several inflammatory diseases, including multiple sclerosis, lupus erythematosis, rheumatoid arthritis and in psoriasis ***(Chen et al., 2009).***

Management of psoriasis includes topical therapy, ultraviolet light (phototherapy), systemic agents and biological treatments. Phototherapy is an essential therapeutic option for patients with psoriasis and has been used for more than 75 years. The most commonly used types of phototherapy are photochemotherapy using psoralen ultraviolet A (PUVA) and Narrow band ultraviolet B (NB-UVB) therapy ***(Jensen et al., 2010).***

AIM OF THE WORK

Estimation of serum OPN level in patients with psoriasis vulgaris and evaluation of the effect of PUVA and NB UVB phototherapy on serum OPN level after treatment.

Chapter 1

PSORIASIS

Psoriasis is a chronic, immune-mediated inflammatory skin disease that is associated with multiple comorbidities. It affects 2% of the Western population, with varying prevalence among different ethnic groups ***(Reich, 2012).***

I- Epidemiology of Psoriasis:

a) *Incidence:*

Psoriasis represents a significant public heath challenge, affecting approximately 125 million people globally. Prevalence estimates within adult populations range from 0.91% in the U.S.A. to 8.5% in Norway ***(Griffths et al., 2017***).

b) *Age & sex:*

Psoriasis can begin at any age. Late - onset psoriasis (diagnosed > 40 years of age) shows little difference in distribution between males and females. However, early onset psoriasis showed clear differences with females being more likely to be diagnosed with psoriasis at an earlier age ***(Springate et al., 2017).***

Psoriasis that starts in childhood has high family incidence and the earlier the onset, the worse the prognosis ***(Romiti et al., 2009)***. Studies with twins have shown affection of monozygotic twins up to 70% probability that the other will

be affected, too and only a 20% probability for dizygotic twins ***(Witte and Sabat, 2015).***

II- Diagnosis of Psoriasis:

The diagnosis of psoriasis is primarily clinical and a skin biopsy is usually not necessary for classic presentations of the disease. It's characterized clinically by erythematous scaly lesions and pathologically by hyperproliferation of epidermal keratinocytes with resulting hyperkeratosis, infiltration of lymphocytes, and angiogenesis ***(Mercuri and Naldi, 2010).***

Clinical Variants:

Chronic plaque psoriasis is the most common variant of psoriasis vulgaris. The characteristic lesions are sharply demarcated, scaly, erythematous plaques. The plaques may be pruritic and/or painful. They can be ovoid, round, or irregular in morphology and are often symmetrically distributed. When the xerotic scale is removed with scraping, points of fine bleeding may be seen (Auspitz sign). Lesions may develop at sites of trauma or injury, known as the Koebner phenomenon. The plaques are predominantly located on the elbows, knees, lower back, umbilicus, hands and feet but can occur anywhere on the body ***(Whan et al., 2017).***

Guttate psoriasis appears particularly in children and young adults after acute streptococcal infections. Lesions are rounded or slightely oval varing from 2mm-1cm in diameter &