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Study of Effect of NB-UVB on Serum and Tissue CXCL9 in Vitiligenous Patients

Thesis

Submitted for Partial Fulfillment of Master Degree in

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By

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قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

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Ebtihal Hassan Mahmoud

ABSTRACT

Study of Effect of NB-UVB on Serum and Tissue levels of CXCL9 in Vitiligenous Patients

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Background: CXCL 9 is a chemokine of Th1 which plays a significant role in the development of vitiligo. NB-UVB is an effective modality for treatment of vitiligo.

Objective: To finding whether NB-UVB can affect serum and tissue CXCL9 level or not.

Patients and Methods: The present study included 20 patients suffering from non-segmental vitiligo and 20 age- and sex- matched healthy controls, their age ranged from 18 to 65 years old, they were recruited from the outpatient clinic of Dermatology and Andrology Department in Ain Shams University Hospital during the period from May 2019 till December 2019.

Results: We evaluated disease severity by assessment of body surface area (BSA) of vitiligo disease in patients with calculation of VES score before NB-UVB and to evaluate patient improvement after treatment with NB-UVB we recalculated VES score after NB-UVB and calculated VES plus score. There was significant decrease in the surface area of the disease after treatment with NB-UVB than before.

Conclusion: The present study provides clinical data to support the role of CXCL9 in vitiligo particularly during the activity of the disease. Also our findings draw our attention to CXCL9 not only as a marker of disease activity, but also potentially as a marker of treatment response. So, targeting the IFN-γ-chemokine axis might be an effective treatment strategy.

Keywords: Vitiligo, chemokine, NB-UVB

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List of Abbreviations

Abb.	Full term
BB-UVB	*Broadband UVB*
bFGF	*Basic fibroblast growth factor*
CNS	*Central nervous system*
CTLs	*Cytotoxic Lymphocytes*
DAMPs	*Damage-associated molecular patterns*
Epi	*Epinephrine*
ET-1	*Endothelin-1*
GM-CSF	*Granulocyte-monocyte colony stimulating factor*
GSH-Px	*Glutathione peroxidase activity*
GWA	*Genome-wide association*
HSP	*Heat-shock proteins*
ICAM-1	*Intercellular adhesion molecule-1*
IFN-γ	*Interferon gamma*
LFA-1	*Lymphocyte function-associated antigen-1*
MBEH	*Mono Benzyl Ether of Hydroquinone*
MDA	*Malonyldialdehyde*
MHC	*Major histocompatibility complex*
MIG	*Monokine induced by gamma interferon*
MMP-1	*Matrix metalloproteinase-1*
MP	*Methoxyl Phenol*
NB-UVB	*Narrowband UVB*
NE	*Norepinephrine*
NK	*Natural Killer*
NPs	*Neuropeptides*
NPY	*Neuropeptide Y*
NSV	*Non-segmental vitiligo*
POMC	*Pro-opiomelanocortin*
PUVA	*Psolaren ultraviolet-A*

List of Abbreviations (Cont...)

Abb.	Full term
ROS	*Reactive oxygen species*
SCF	*Stem cell factor*
SV	*Segmental vitiligo*
TAMs	*Tumor-associated macrophages*
TGF-β	*Transforming growth factor β*
TNF-α	*Tumor necrosis factor alpha*
Topical 5-FU	*Topical 5-Fluorouracil*
Tregs	*T regulatory cells*
UCA	*Urocanic acid*
UV	*Ultraviolet*
UVB	*Ultraviolet B*
VGICC	*Vitiligo Global Issues Consensus Conference*

INTRODUCTION

Vitiligo is a common pigmentation disease that affects 1–2% of the global population. The two sexes are equally affected, with no differences in rates of occurrence according to skin type or race. The main manifestation of vitiligo is skin depigmentation, which significantly influences appearance and brings enormous psychological stress for patients ***(Grimes and Miller, 2018).***

Vitiligo is classified into two main types: segmental (SV) and non-segmental (NSV). Most cases are NSV, meaning they affect both sides. About 10% of cases are SV, meaning they mostly involve one side of the body ***(Ezzedine et al., 2015).***

The exact cause of vitiligo is unknown. It is believed to be due to genetic susceptibility that is triggered by an environmental factor results in an autoimmune disease. This results in the destruction of skin pigment cells ***(Ezzedine et al., 2015).*** That's why higher frequencies of circulating autoantibodies have been observed in patients with vitiligo ***(Ingordo et al., 2014).***

Chemokines play an important role in regulating the homing of immune cells ***(Vazirinejad et al., 2014).*** In particular, the recruitment and retention of T cells into specific tissues is thought to be mediated by local chemokine and chemokine receptor proteins at the T-cell surface. More and

more research indicates that an imbalance in the T-helper (Th) cell system, with a dominant Th1 pattern, favours the development of vitiligo ***(Dwivedi et al., 2013).***

Depigmentation is accompanied by the expression of type 1 cytokines, such as interferon (IFN)−γ and tumour necrosis factor (TNF)−α ***(Dwivedi et al., 2013).***

IFN-γ is the most important cytokine, that is associated with the Th1 immune response ***(Annunziato et al., 2014).*** IFN-γ induce the release of chemokine which is called CXCL9 ***(Lacotte et al., 2009).***

CXCL9 binds to its specific receptor, chemokine (C-X-C motif) receptor (CXCR)3, and regulates immune responses by recruitment and activation of T cells, monocytes, and natural killer cells. CXCR3 is expressed not only by immune cells but also by endothelial cells, mesangial cells, thyrocytes and other epithelial cells ***(Antonelli et al., 2014).***

CXCL9 has been detected in inflammatory processes and autoimmunity. Studies revealed that the expression of serum CXCL9 was significantly elevated in patients with both progressive and stable vitiligo compared with healthy controls. Also levels of serum CXCL9 was significantly higher in patients in the progressive stage than in those in the stable stage, suggesting a mechanistic role of this chemokine in vitiligo ***(Wang et al., 2016).*** Other studies revealed that serum