

Clinical and Histological evaluation of Vitiligo patients treated by Narrow band-UVB (311nm) Phototherapy

Thesis

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List of abbreviations

AA	Arachidonic Acid
AIDS	Acquired Immunodeficiency Syndrome
AOx	Antioxidant
APC	Antigen Presenting Cell
APECED	Autoimmune Polyendocrinopathy Candidiasis-Ectodermal Dystrophy
BB-UVB	Broad Band Ultraviolet B radiation
BCC	Basal Cell Carcinoma
bFGF	basic Fibroblast Growth Factor
CMV	Cytomegalovirus
CPD	Cyclobutane Pyrimidine Dimers
CTCL	Cutaneous T-cell Lymphoma
CUA	Cis Urocanic Acid
DLN	Draining Lymph Node
EBV	Epstein-Barr Virus
ECP	Extracorporeal Photochemotherapy
EM	Electromagnetic spectrum
ET-1	Endothelin-1
GM-CSF	Granulocyte-Macrophage- Colony Stimulating Factor
gp100	Glycoprotein 100 melanocyte antigen
GSH	Glutathione
GVHD	Graft Versus Host Disease
HIDL	High intensity discharge lamps
HIV	Human Immunodeficiency Virus
IFN	Interferon
IL-1α	Interlukin-1 alpha
IPD	Immediate Pigment Darkening
IS	Immune Suppression
K	Keratinocyte
LC	Langerhans Cell
LTC-4	Leukotrienes C4
M	Macrophages
MAO	Monoamine Oxidase
MC1R	Melanocortin 1 Receptor
MCTD	Mixed Connective Tissue Disease
MED	Minimal Erythematous Dose
Melan A/ MART-1	melanocyte differentiating antigens
MHC class II	major histocompatibility complex class II
MMPs	Metalloproteinases
MOP	Methoxypsoralen
MP	Matrix Proteins
MSH	Melanocyte Stimulating Hormone
N	Neutrophils
NB- UVB	Narrow Band Ultraviolet B radiation
NE	Norepinephrine

NHP	Natural Health Product
NMSC	Non Melanoma Skin Cancer
NO	Nitric Oxide
PAF	Platelet activating factor
PDT	Photodynamic Therapy
PGE2	Prostaglandin E2
PMLE	Polymorphic Light Eruption
PPD	Persistent Pigment Darkening
PRP	Pityriasis Rubra Pilaris
PUVA	Psoralen combined with Ultraviolet A radiation
PUVAsol	Solar PUVA instead of artificial PUVA (using solar irradiation instead of an artificial UVA source)
RER	Rough Endoplasmic Reticulum
RNS	Reactive nitrogen species
ROS	Reactive oxygen species
SBC	Sunburn Cell
SC	Stratum Corneum
SCC	Squamous Cell Carcinoma
SCF	Stem Cell Factor
SLE	Systemic Lupus Erythematosus
T	Tyrosinase
TGF	Transforming Growth Factor
Th1 cells	T helper 1 cells
TL-01 lamp	NB-UVB lamp
TMP	Trimethylpsoralen
TNF-α	Tumor Necrosis Factor- α
TRP-1, TRP-2	Tryptophan-1, Tryptophan -2 autoantigens
UCA	Urocanic Acid
UVC	Ultraviolet C irradiation
UVR	Ultraviolet Radiation
VASI	Vitiligo Area Scoring Index

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Introduction

Vitiligo is a common, acquired, multifactorial and depigmenting cutaneous disorder, characterized by asymptomatic, well circumscribed, milky or chalky white macule(s) or patch(s) (*Sehgal, 2004*). Vitiligo occurs worldwide with an overall prevalence of 1%. Adults and children of both sexes are equally affected. The proportions of patients with positive family history vary from one part of the world to another (*Behl et al., 2003*).

Histologically, vitiligo is characterized by the reduction of the melanocytes until their complete loss and by the disappearance of the melanin granules in the basal and spinous layer keratinocytes (*De Francesco et al., 2008*). Etiopathogenesis of vitiligo is believed to involve a combination of autoimmune, genetic and environmental factors. In addition, the neural, self destructive and biochemical hypothesis have also been proposed (*Forschner et al., 2007*). Vitiligo is progressive disease associated with remissions and exacerbations correlating with triggering events such as emotional stress (*Behl et al., 2003*).

Vitiligo may show morphological variations in the form of trichrome, quadrichrome, pentachrome, blue and inflammatory vitiligo. Also it can be classified into segmental, generalized or universal (*Sehgal and Srivastava, 2007*), it may be associated with premature graying of hair, halo nevus, alopecia areata (*Khandpur and Reddy, 2001*), and other autoimmune diseases such as diabetes mellitus (*Kim et al., 2002*).

Numerous treatment modalities have been used to treat vitiligo, such as corticosteroids (systemic, topical and intralesional), topical immunomodulators, skin grafts and psoralen combined with ultraviolet A (PUVA) (*Nordland et al., 1993*). Among the most recent advances in treating vitiligo have been narrow band ultraviolet B (NB-UVB)

phototherapy, targeted ultraviolet B phototherapy and excimer laser (*Majid, 2010*).

Phototherapy with NB-UVB (311nm) for treating vitiligo was first reported in **1997** by *Westerhof and Nieuweboer-krobotova*. Subsequently, several studies confirmed the effectiveness of the therapy in different skin phototypes. The efficacy and safety observed with NB-UVB have helped it to replace PUVA as the treatment of choice in generalized vitiligo. The exact mechanism of action of NB-UVB in vitiligo is unknown (*Parsad et al., 2010*).

NB-UVB radiation probably acts in the upregulation of the melanogenesis and melanocytes migration. In **1995**, *Imokawa* and others found that endothelin-1 (ET-1) is probably a major UVB-associated melanogenic stimulator in UVB-induced pigmentation, and that UVB light stimulates the secretion of interleukin-1 α (IL-1 α) by keratinocytes, so as to increase endothelin-1 gene expression in an autocrine fashion.

The predominant type of repigmentation after NB-UVB is perifollicular. Therefore, it is at least theoretically justified to believe that it has some relation to the melanocyte reserve in the outer root sheath. A two-step effect of NB-UVB has been proposed, both of them may occur simultaneously. Firstly, there is immunomodulation (local as well as systemic), leading to down-regulation of immune attack against the melanocytes. Subsequently, the melanocytes are stimulated to migrate to the epidermis and synthesize melanin (*Parasad et al., 2010*).

Phototherapy was given three times per week on non-consecutive days (*Stinco et al., 2009*). Clinical experience with NB-UVB in vitiligo has generally been for a short duration, and there is currently no established safe limit for its maximum duration of use in treatment of this condition (*Parsad et al., 2010*). So, if no improvement is seen within 6 months, NB-UVB therapy should be discontinued (*Gawkrodger et al., 2008*).