Evaluation of Serum 25 hydroxyvitamin D level in Vitiligo Patients Before and after Narrowband UVB

Thesis

Submitted for partial fulfillment of the master degree in Dermatology, Venereology and Andrology

by

Ahmed Sayed Mohamed Zidan

M.B, B.Ch.

Faculty of Medicine – Ain shams university

Under Supervision of

Prof. Nehal M Zu Elfakkar

Professor of Dermatology, Venereology and Andrology Faculty of Medicine – Ain shams university

Prof. Nermeen Samy Abdel Fattah

Professor of Dermatology, Venereology and Andrology

Faculty of Medicine – Ain shams university

Faculty of Medicine
Ain Shams University
2016

تقييم مستوى ٢٥ هيدركسي فيتامين دية مصل مرضي البهاق قبل وبعد التعرض للأشعة فوق البنفسجية "ب" ضيقة النطاق

رسالة

و التناسلية و توطئة للحصول على درجة الماجستير في الأمراض الجلدية

أمراض الذكورة مقدم من

الطبيب/ أحمد سيد محمد زيدان

بكالوريوس الطب و الجراحة كلية الطب – جامعة عين شمس

تحت إشراف

أ.د. نهال ذو الفقار

أستاذ الأمراض الجلدية و التناسلية و أمراض الذكورة كلية الطب - جامعة عين شمس

أ.د. نيرمين سامي عبدالفتاح

أستاذ الأمراض الجلدية و التناسلية و أمراض الذكورة كلية الطب - جامعة عين شمس

كلية الطب

جامعة عين شمس



سورة البقرة الآية: ٣٢



Acknowledgement

Thanks and praise to **God** first and foremost. I feel always indebted to **God**, the most kind and most merciful.

I would like to express my deepest thanks and respect to **Prof. Nehal M Zu Elfakkar**, Professor of Dermatology, Venereology and Andrology, Ain Shams University, for her valuable supervision, guidance and kind advice throughout this work.

Special thanks and deepest gratitude to **Prof.**Nermeen Samy Abdel Fattah, Professor of Dermatology, Venereology and Andrology, Ain Shams University, for her good support, continuous supervision and unlimited help during this



List Of Contents

Topic	Pages
List of abbreviations	I
List of tables	IV
List of figures	VI
Introduction	1
Aim of work	3
Review of literature	
Chapter 1: Vitiligo	4
• Chapter 2: Vitamin D	38
• Chapter 3: Narrowband UVB	64
Subject and Methods	81
Results	91
Discussion	707
Conclusion	112
Recommendation	113
Summary	114
References	116
Arabic summary	-

List of abbreviations

25(OH)D	25-hydroxy vitamin D
25-ohase	Vitamin D-25-hydroxylase
AA	Alopecia areata
AIDS	Acquired immunodeficiency syndrome
BB-UVB	Broadband ultraviolet B
BCC	Basal cell carcinoma
BSA	Body surface area
CD8+	Cluster of differentiation 8
CIs	Calcineurin inhibitors
CMV	Cytomegalo virus
COMT	Catechol-o-methyl transferase
CPD	Cyclobutane pyrimidine dimers
CSs	Corticosteroids
CYP	Cytochrome P450
DBP	Vitamin D binding protein
DC	Dendritic cell
EBV	Epstein-bar virus
EM	Electromagnetic spectrum
ET-1	Endothelin 1
FBXO11	F box only protein 11
FPHL	Female pattern hair loss
HE-NE	Helium-Neon laser
HF-NCSCs	Hair follicle-derived neural crest stem cells
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
IFN-γ	Interferon gamma
IgG	Immunoglobulin G
IL-1	Interleukin-1
IOM	Institute of medicine
KCs	Keratinocytes
KUVA	Khellin with ultraviolet A
LC	Langerhans cells

List of Abbreviations

MBEH	Mono-benzyl ether of hydroquinone
Mc1r	Melanocortin 1 receptor
MED	Minimal erythema dose
Melana /Mart-1	Melanoma antigen/ melanoma antigen recognized
Wielana /Wiart-1	by T cells 1
MITF-m	Microphthalmia associated transcription
1411 1 1 -111	factor-m
MM	Malignant melanoma
MOP	Methoxypsoralen
MV	Mixed vitiligo
NALP1	Nacht leucine-rich protein 1
NB-UVB	Narrowband ultraviolet B
NK	Natural killer cells
NLRP1	Nacht leucine-rich repeat and pyrin domains
NLKI 1	containing protein 1
Nm	Nanometers
NMSC	Non-melanoma skin cancer
NO	Nitric oxide
NSV	Non segmental vitiligo
OMP	Oral mini-pulse therapy
PG	Prostaglandins
PUVA	Psoralen with ultraviolet A
RDA	Recommended dietary allowances
SCC	Squamous cell carcinoma
SCF	Stem cell factor
SLE	Systemic Lupus erythrematosus
SV	Segmental vitiligo
SZA	Solar zenith angle
TE	Tellogen effluvium
TLR	Toll-like receptors
TNF-α	Tumour necrosis factor-alpha
TRP-1	Tyrosine related protein 1
TRP-2	Tyrosinase related protein 2
UVR	Ultraviolet radiation
VASI	Vitiligo area scoring index

List of Abbreviations

VDDR IIa	Vitamin D dependent rickets type IIa
VDR	Vitamin D-receptor
VGICC	Vitiligo global issues consensus conference
VIDA	Vitiligo disease activity score

List Of Tables

N0.	Title	Page
1	Typical Features of Segmental and Non segmental Vitiligo	22
2	Vitiligo disease activity score (VIDA)	31
3	List of depigmenting agents	36
4	NB-UVB radiation increment according to degree of erythema	71
5	Skin types/ initial NB-UVB dose according to skin type	72
6	Contraindications of NB-UVB	73
7	Description of personal and medical data among patients with vitiligo	92
8	25(OH)D levels among cases before treatment	92
9	25(OH)D levels among cases after treatment	93
10	Description of vitamin D levels before treatment, after treatment and change in Vitamin D data among cases	94
11	25(OH)D levels among control	95
12	Description of vitamin D among controls	96
13	Comparison between cases and controls as regard vitamin D	97
14	Comparison between cases and controls as regard vitamin D	98
15	Comparison between Vitamin D before and after treatment among cases	98
16	Comparison between Vitamin D before and after treatment among cases	99
17	ROC curve for discrimination between cases and controls using vitamin D level	100
18	Relation between personal data and Vitamin D level before treatment among cases	101
19	Relation between personal data and Vitamin D level after treatment among cases	103
20	Relation between personal data and Change in Vitamin D level after treatment among cases	104

List of Tables

N0.	Title	Page
21	Correlation between age and 25(OH)D before treatment and after treatment	104
22	Correlation between BSA and 25(OH)D before treatment and after treatment	105
23	Correlation between duration of vitiligo and levels of 25(OH)D before and after treatment	106
24	Multivariate regression to study independent factors affecting body surface area	106

List of Figures

N0.	Title	Page
1	Arguments for destruction of melanocytes by apoptosis	16
2	Inflammatory vitiligo. There is a figurate outline to the inflammatory border, which is sometimes misdiagnosed as tinea corporis	19
3	Vitiligo ponctué Confetti-like amelanotic macules	19
4	Sources of vitamin D	39
5	Sources, sites, and processing of vitamin D metabolites	42
6	Causes and consequences of vitamin D deficiency	61
7	Rule of nine	85
8	25(OH)D levels among cases before treatment	93
9	25(OH)D levels among cases after treatment	94
10	Level of 25(OH)D among controls	95
11	Comparison of 25(OH)D between cases before treatment and controls and between of level of 25(OH)D between cases after treatment and controls	97
12	Comparison of 25(OH)D between cases before treatment and cases after treatment	99
13	ROC curve for prediction of cases of vitiligo	100
14	Comparison of serum 25(OH)D level between male and female cases before treatment	102
15	Correlation between BSA and 25(OH)D before treatment and after treatment	105

Introduction

Vitiligo is an acquired depigmentary disorder characterized by the loss of functioning epidermal melanocytes and affects more than 0.5–1% of the worldwide population with devastating psychological and social consequences (*Feily et al.*, 2013). The exact pathologic mechanism has not been clarified yet; however, the autoimmune hypothesis is the most widely accepted explanation (*Shin et al.*, 2010).

Vitamin D3 can be obtained through the diet, but it is mainly biosynthesized from 7 dehydrocholesterol in the skin exposed to ultraviolet light (*Adorini and penna*, 2008). Vitamin D needs both 25 and 1 alpha hydroxylation to become active hormone 1,25(OH)D. It is estimated that approximately 3% of the human genome is regulated directly or indirectly by the vitamin D endocrine system (*Bouillon et al.*, 2008).

Vitamin D has been found immune-protective. It inhibits the maturation of Dendritic cells (DCs), regulates related cytokines to shift T helper 1 response to T helper 2 response. It inhibits T helper 17 cells, increases T regulatory cells to suppress auto-attack and maintain self-tolerance (*Ersoy-Evans*, 2010). Reduced vitamin D levels have been associated with many autoimmune diseases. Adequate supplementation may improve the prognosis (*Kriegel*, 2011).

Antroduction

A study was done on two groups of equally distributed vitiligo adult patients, Fitzpatrick skin photo types III-IV, 20 patients with systemic autoimmune diseases and 20 patients without autoimmune diseases with age, gender and skin phototype matched healthy controls. Patients had significant lower serum level of 25(OH)D level when they compared with the control. Patients with vitiligo and autoimmune diseases have lower serum 25(OH) D levels than vitiligo patients without autoimmune diseases but with no significant difference (*Hanan et al.*, 2013).

Various management options are available for vitiligo, however there is no single most effective treatment. Ultraviolet A phototherapy with topical or systemic psoralen has been the mainstay of treatment worldwide until the introduction of narrowband ultraviolet B, A landmark study by (Westerhof et al., 1997) compared NB-UVB and topical PUVA in patients with skin phototype III. 67% patients who received NB-UVB developed repigmentation compared to 46% in patients treated with topical PUVA. Similar results were observed (Bhatnagar et al., 1997) in comparing systemic PUVA with NB-UVB in patients with skin phototype IV and V. NB-UVB has advantages over PUVA: it is safe in pregnant women and children, there is less xerosis and erythema effects, and less perilesional hyperpigmentation. Post treatment eye protection is not required and the side effects psoralen like photosensitivity, nausea, vomiting, headache and cataracts can be avoided with NB-UVB.

Aim of the work

The aim of this work is to evaluate serum level of 25(OH)D in vitiligo patients before and after 3 months of narrowband UVB Phototherapy in comparison with age, sex and body mass index matched Controls.

Vitiligo

Vitiligo is a common acquired multifactorial and depigmenting cutaneous disorder characterized by asymptomatic, well circumscribed, milky or chalky white macules or patches (*Sehgal*, 2004). Histologically, it is characterized by the reduction of melanocytes until their complete loss in the basal and spinous layer of keratinocytes (*De Francesco et al.*, 2008).

Epidemiology

Vitiligo is the most prevalent pigmentary disorder that occurs worldwide with an incident rate between 0.1% and 2% (*Torello et al.*, 2008) irrespective to age, race (*Moretti et al.*, 2006) ethnic origin or skin color (*Whitton et al.*, 2008). The prevalence has been reported as high as 4% in some south Asian, Mexican and United States populations (*Sehgel and Srivastava*, 2007).

Vitiligo can develop at any age, but about 50% of cases appear before the age of 20 (*Halder and Nootheti*, 2003) and nearly 70-80% before the age of 30 years (*Herane*, 2003). *Barona et al.* (1995) found that in patients with unilateral vitiligo the mean age at onset was 16.3 years, compared to 24.8 years in patients with bilateral vitiligo.