

Hanaa Mohammed

بسم الله الرحمن الرحيم

مركز الشبكات وتكنولوجيا المعلومات قسم التوثيق الإلكتروني





Safaa Mahmoud



جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها على هذه الأقراص المدمجة قد أعدت دون أية تغيرات







A comparative study on the efficacy and safety of using Azathioprine alone, combining it with Narrow Band (UVB) and to oral minipulse Steroids plus NB-UVB in stabilizing active non-segmental vitiligo

Thesis

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

Presented by

Nourhan Alaa Eldin Abd El-Hafez

(M.B., B.Ch) Ain Shams University

Supervised by

Prof. Dr. Marwa Mohamed Abd El-Raheem Abdallah

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

Dr. Rania Mahmoud El-husseiny

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

> Faculty of Medicine Ain Shams University 2022



سورة البقرة الآية: ٣٢



First and foremost thanks to ALLAH, the Most Merciful.

I'd like to express my respectful thanks and profound gratitude to **Prof. Dr. Marwa Mohamed Abd El-Raheem Abdallah,** Professor of Dermatology, Venereology and Andrology Faculty of Medicine, Ain-Shams University for her 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 **Dr. Rania Mahmoud Elhusseiny,** Associate Professor of Dermatology, Venereology and Andrology Faculty of Medicine, Ain-Shams University, for her kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.

Nourhan Alaa Eldin

List of Contents

Title	Page

List of Abbreviations		
List	of TablesIII	
List	of FiguresVI	
Intro	duction1	
Aim	of the Work3	
Revi	ew of Literature	
Cha	pter (1): Vitiligo4	
0	Classification5	
0	Pathogenesis9	
0	Diagnosis17	
0	Treatment	
Cha	pter (2): Steroids38	
0	Mechanism of action40	
0	Indications41	
0	Contraindications42	
0	Side effects43	
Cha	pter (3): Azathioprine45	
0	Mechanism of action47	
0	Adverse effects48	
0	Indications50	
0	Contraindications51	
Cha	pter (4): Narrow Band UVB Phototherapy54	
0	Mechanism of action57	
0	Contraindications60	
0	Adverse effects62	

∠List of Contents

Patients and Methods	66
Results	72
Discussion	119
Conclusion	125
Recommendations	126
Summary	127
References	130
Arabic Summary	١١

&List of Abbreviations

Tist of Abbreviations

ACE	:	Angiotensin converting enzyme
AZA	:	Azathioprine.
BBUVB	:	Broad Band UVB.
bFGF	:	Basic fibroblast growth factor
CS	:	Corticosteroids.
DAMP	:	Damage associated molecular pattern.
FDA	:	Food and drug administration.
FMS	••	Fontana-Masson stain.
Gp100	••	Glycoprotein 100.
HF-NCSCS	••	Hair Follicle-Derived Neural Crest Stem Cells
HGF		Hepatocyte growth Factor
HSP70i		Heat shock protein 70i.
IBD	:	inflammatory bowel disease
ICAM-1		Intercellular adhesion molecule- 1.
IFN	:	Interferon
LRR	:	Leucine-rich repeats.
MART-1	:	Melanoma antigen recognized by T1 cells
MC1R	:	Melanocortin 1 receptor
NBUVB	:	Narrow band ultraviolet B rays
NSV	:	Non segmental vitiligo.
OMP	:	Oral minipulse steroids.
PAMP	:	Pathogen associated molecular pattern.
PRR	:	Pattern recognition receptor.
PUVA	:	Psoralen plus UVA.
RNS		Reactive nitrogen species.
ROS	:	Reactive oxygen species.
SCC	:	Squamous cell carcinoma

&List of Abbreviations

SLE	:	Systemic lupus erythermatosus
TCI	••	Topical Calcineurin Inhibitors
TCS	••	Topical corticosteroids.
TNF	••	Tumor necrosis factor.
TPMT	••	Thiopurine methyl transeferase
TRP	••	Tyrosinase-related protein.
UV	••	Ultraviolet.
UVR	:	Ultra violet radiation
VASI	••	Vitiligo area scoring index.
VES	:	Vitiligo extent score.
VES PLUS	:	Vitiligo extent score plus.
VIDA VES score	:	Vitiligo disease activity score.

List of Tables

Classification of vitiligo	. 8
Differential diagnoses for vitiligo	22
List of depigmented agents	36
Steroids classification	39
Contraindications of NB-UVB	60
Demographic data and clinical characteristics of studied patients.	73
The baseline VES, VES PLUS and VIDA score (before treatment) among group A cases	74
Description of VES, VES PLUS and VIDA score among group A cases at week 4 of treatment	75
Description of VES, VES PLUS and VIDA score among group A cases at week 8 of treatment:	76
Description of VES, VES PLUS and VIDA score among group A cases at week 12 of treatment	77
Description of the change in VES and VES PLUS among group A cases from before to 3 months after treatment:	78
Comparison between Baseline and follow up VES among group A cases	79
Comparison between Baseline and follow up VES plus among group A cases	80
Description of baseline VES, VES PLUS and VIDA score among group B cases	81
Description of VES, VES PLUS and VIDA among group B cases at week 4 of treatment	82
Description of VES, VES PLUS and VIDA among group B cases at week 8 of treatment	83
Description of VES, VES PLUS and VIDA score among group B cases at week 12 of treatment	84
	List of depigmented agents Steroids classification

■ List of Tables

Table (18):	Description of the change in VES and VES PLUS cases between before and after 3 months of treatment among group B
Table (19):	Comparison between Baseline and follow up VES among group B cases
Table (20):	Comparison between Baseline and follow up VES plus among group B cases
Table (21):	Description of baseline VES, VES PLUS and VIDA score among group C cases
Table (22):	Description of VES, VES PLUS and VIDA score among group C cases at week 4 of treatment
Table (23):	Description of VES, VES PLUS and VIDA score among group C cases at week 8 of treatment
Table (24):	Description of VES, VES PLUS and VIDA score among group C cases at week 12 of treatment
Table (25):	Description of the change in VES and VES PLUS among group C cases
Table (26):	Comparison between Baseline and follow up VES among group C cases
Table (27):	Comparison between Baseline and follow up VES PLUS among group C cases
Table (28):	Comparison between the 3 study groups as regard baseline VES, VES PLUS and VIDA score
Table (29):	Comparison between the 3 study groups as regards VES, VES PLUS and VIDA score at week 4 of treatment
Table (30):	Comparison between the 3 groups as regard VES, VES PLUS and VIDA score at week 8 of treatment
Table (31):	Comparison between the 3 groups as regard VES, VES PLUS and VIDA at week 12 of treatment 101
Table (32):	Comparison between the three groups as regards the change in VES and VES plus between baseline and at week 12 of treatment

■ List of Tables

Table (33):	Comparison between 3 groups as regards cessation of activity and Onset of activity cessation after treatment
Table (34):	Comparison between 3 groups as regards stoppage of vitiligo activity
Table (35):	Comparison between the 3 groups as regard the percentage of repigmentation after treatment 107
Table (36):	Comparison between the three groups as regards side effects
Table (37):	Correlation between each of patient's age, disease duration and age of first onset with change in VES and VES plus
Table (38):	Relation between patient's gender and family history of vitiligo with change in VES plus after 3 months of treatment
Table (39):	Relation between Cessation of vitiligo activity and onset of cessation with patient's age
Table (40):	Relation between Cessation of vitiligo activity and the onset of cessation with disease duration
Table (41):	Relation between Cessation of vitiligo activity and onset of cessation with Age of first disease onset 113
Table (42):	Relation between Cessation of vitiligo activity, onset of cessation with patient's gender
Table (43):	Relation between Cessation of vitiligo activity and onset of cessation with Family history of vitiligo 113

List of Figures

Figure (1):	Non-segmental Vitiligo
Figure (2):	Segmental Vitiligo
Figure (3):	Vitiligo pathogenesis: The flare-up,
	stabilisation, and repigmentation phases 10
Figure (4):	Pathogenesis of non-segmental vitiligo
Figure (5):	Vitiligo lesions better evidenced under Wood's
	lamp than under visible light 18
Figure (6):	Dermoscopy of vitiligo
Figure (7):	Histopathology of Vitiligo showing the absence
	of melanocytes in basal layer of the epidermis
	(H&E, X400)
Figure (8):	Histopathology of normal and vitiligus skin by
	FMS
Figure (9):	VES score
Figure (10):	Added perifollicular scale in the VESplus 25
Figure (11):	Treatment guidelines of vitiligo
Figure (12):	The whole process of azathioprine synthesis 46
Figure (13):	Metabolic pathway for azathioprine (AZA) 48
Figure (14):	Types of UVR 57
Figure (15):	Comparison between the 3 study groups as
	regard baseline VES and VES PLUS96
Figure (16):	Comparison between the 3 groups as regard
	after 1 month VES and VES PLUS98
Figure (17):	Comparison between the 3 study groups as
	regard VES and VES PLUS after 2 months of
	treatment
Figure (18):	Comparison between the 3 groups as regard
	VES and VES PLUS after 3 months of
	treatment
Figure (19):	Comparison between the three groups as regard
	the change in VES and VES plus between
	before and after 3 months of treatment 104
Figure (20):	Comparison between 3 groups as regards
	stoppage of vitiligo activity

Z List of Figures

Figure (21):	Comparison between the three groups as
	regards occurrence of repigmentation 108
Figure (22):	Comparison between the three groups as
	regards percentage of repigmentation 108
Figure (23):	Comparison between the three groups as regard
	side effects
Figure (24):	Both hands of a male patient 49-year-old with
8 \	active non-segmental vitilgo of 10 years
	duration before and after 3 months of treatment
	(OMP +NBUVB)(Group A)
Figure (25):	The back of the same patient before and after 3
1 igui (20).	months of treatment (OMP +NBUVB)(Group A) 115
Figure (26):	The back of a female patient 40- year-old with
	active non-segmental vitiligo since 1 year before
	and after 3 months of treatment (AZA +
	NBUVB)(Group B) 116
Figure (27):	The chest of afemale patient 35-year-old with
_ -g (_ · · / ·	active non-segmental vitiligo since 2 years
	before and after 3 months of treatment (AZA +
	NBUVB)(Group B)
Figure (28):	A female patient 39-year-old with active non-
11guit (20).	segmental vitiligo since 1 year before and after 3
	months of treatment (AZA alone) (Group C) 118
Figure (20).	A female patient 40-year-old with active non-
Figure (29):	- · · · · · · · · · · · · · · · · · · ·
	segmental vitiligo since 1 year befor and after 3
	months of treatment (AZA alone) (Group C) 118

Introduction

Ditiligo is an idiopathic, acquired, circumscribed, hypomelanotic skin disorder, characterized by milky white patches of different sizes and shapes. It is due to loss of functional melanocytes resulting in the absence of pigment production of the skin and mucosal surfaces (*Taieb and Picardo*, 2010).

The most common form of vitiligo, non-segmental vitiligo or vitiligo vulgaris, is symmetrical and may be localized to certain areas. It may also spread to involve the entire body surface. In contrast, segmental vitiligo only affects one side of the body and usually has limited progression. The two types of vitiligo may co-exist, in which case response to treatment in the segmented areas is usually poor (*Picardo and Taieb*, 2010; Ezzedine et al. 2012).

The immune system has a great role in the pathogenesis of all non-segmental vitiligo, including focal, generalized and universal types. Therefore, the available therapeutic modalities are directed toward suppression or regulation of these immunological changes (*Radmanesh and Saedi*, 2006).

Topical corticosteroids (TCS) are used as first-line therapy as monotherapy (e.g. in localized vitiligo), or in combination with phototherapy or other topical agents (e.g. in generalized vitiligo). Systemic corticosteroids halt disease progression and induce repigmentation when used at the onset or early stages of disease, in some cases resulting in complete