Evaluation of Microneedling With or Without Topical 5-fluorouracil in Treatment of Stable Non-segmental Vitiligo

Thesis

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List of Abbreviations

Abb.	Full term
5-FU	5-Fluorouracil
5-FUH2	5-Fluoro dihydrouracil
AKs	Actinic keratoses
BB-UVB	Broad Band Ultraviolet B
BCC	Basal cell carcinomas
BSA	Body surface area
CL	Cardiolipin
CRC	Colorectal cancer
CTLA4	Cytotoxic T lymphocytic antigen 4
DNA	Deoxyribonucleic acid
DOPA	Dihydro phenylalanine
DPD	Dihydro pyrimidine dehydrogenase.
DRS	Diffuse reflectance spectroscopy
dTMP	Deoxythymidine mono-phosphate
dUMP	Deoxyuridine mono-phosphate
Ecad	E-cadherin
ECG	Electrocardiography
ER	Endoplasmic reticulum
ER-YAG	Erbium: yttrium-aluminum-garnet
FdUMP	Fluorode oxyuridine monophosphate
FdUTP	Fluorodeoxyuridine triphosphate
FUTP	Fluorouridine triphosphate
GTP	Guanisine triphosphate
H2O2	Hydrogen peroxide
HLA-DR	Human leukocyte antigen- DR [HLA-DR]
HMB45	Melanoma monoclonal antibody
HPV	Human papillomavirus
ID	Intradermal injection
IFN-γ	Interferon gamma
IL	Interleukin

List of Abbreviations Cont...

Abb.	Full term
KA	Keratoacanthoma
KP	Koebner phenomenon
KUVA	Khellin and ultraviolet A
LTC4	Leukotriene C4
LTD4	Leukotriene D4
MART	Melanoma Antigen Recognized by T cells
MBEH	Monobenzyl ether of hydroquinone
MCHR	Melanin-concentrating hormone receptor
MITF	Melanocyte inducing transcription factor
MKTP	Melanocyte keratinocyte transplantation
MOP	Methoxypsoralen
MP	Methoxyphenol
NBUVB	Narrow Band Ultraviolet B
NCECS	Non cultural epidermal cell suspension
NGF	Nerve growth factors
NMSC	Nonmelanoma skin cancer
NPY	Neuropeptide Y
NSV	Non segmental vitiligo
PASI	Psoriasis Area and Severity Index
PG	Punch grafting
PUVA	Psoralen and ultraviolet A
QSR	Q-switched ruby laser
RCM	Reflectance confocal microscopy
RNA	Ribonucleic acid
ROS	Reactive oxygen species
SBEG	Suction blister epidermal grafting
SCC	Squamous cell carcinoma
STDS	Sexual transmitted diseases
SV	Segmental vitiligo

List of Abbreviations Cont...

Abb.	Full term
T reg	Regulatory T cells
TFH	Follicular Helper T cell
TGF-β	Transforming growth factor B
Th	T helper cells
TH	Tyrosine hydroxylase
TNF	Tumor necrosis factor
TRP	Tyrosine related protein
TS	Thymidylate synthetase
UTP	Uridine triphosphate
UVA	Ultraviolet A
UVB	Ultraviolet B
UVR	Ultraviolet radiation
VASI	Vitiligo Area Scoring Index
VESTA	Vitiligo Extent Score for a Target Area
VETF	Vitiligo European Task Force
VETI	Vitiligo Extent Tensity Index
VIDA	Vitiligo disease activity score

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ABSTRACT

Background: This study will evaluate the effect of microneedling of vitiligo lesion with and without topical 5 fluorouracil. Vitiligo is an acquired pigmentary disorder of unknown etiology, affecting approximately 1 % of the world population, without predilection for race or sex. It is characterized by white macules and patches, whose size increases over time, due to the loss of melanocytes. Vitiligo can appear at any time, and it significantly impairs the patients' quality-of-life

Objective: To compare the efficacy of microneedling followed by 5-FU with microneedling alone in the treatment of stable non-segmental vitiligo.

Patients and Methods: This interventional study was held in Dermatology, Andrology & STDs department, Faculty of Medicine, Ain Shams University during the period from January till November 2019. Fifty patients with stable non-segmental vitiligo were included in the study.

Results: Regarding the efficacy of treatment with microneedling only vs microneedling with 5-FU in our study, there is statistically significant difference between the two sides according to treatment response, needling with 5-FU side showed response in 76% of cases, while needling side alone showed (0%) response. The degree of improvement among our patients in microneedling with 5-FU side, we detect different grades of repigmentation as 12 patients of the studied participants (24%) showed no repigmentation, 23 patients (46%) showed mild grade (<25% repigmentation), 15 patients (30%) showed moderate grade (25–50% repigmentation) and no one of the studied participants experienced either good grade (50–75% repigmentation) either excellent grade (more than

75% repigmentation). Our study showed no relation between repigmentation response and both demographic and clinical data of the patients as (age, gender, family history, duration of disease, VASI severity score and Fitzpatrick skin phototype). On the other hand, we found statistically significant difference with better repigmentation after microneedling with 5FU on certain sites of vitiligo. We noticed that lesions on the trunk and extremities showed better results while the acral parts showed no response. Observing side effects after treatment, we noticed that, there is statistically significant difference in side effects incidence between two sides. Side treated with microneedling and 5-FU experienced more frequent side effects as compared with the side treated with microneedling only, these side effects included, slight to moderate pain and burning sensation during procedure that was tolerated and disappeared within few minutes to hours and minimal erythema in the first few days post procedure.

Conclusion: On the basis of the current study, we can conclude that microneedling followed by topical 5% 5-FU of vitiligo lesion is safe and tolerable method of treatment of vitiligo. It can induce repigmentation in vitiligo lesion but it could not be considered as effective method of treatment. We need to combined it with other treatment modalities to improve the outcome. However, long follow-up of the patients is needed.

Keywords: 5-Flourouracil, vitiligo, microneedling

INTRODUCTION

Vitiligo, the most common depigmented disorder, is an acquired disease characterized by progressive loss of melanocytes. Vitiligo occurs worldwide with an estimated prevalence of 0.5-1% in most populations and no sexual predominance. In 50% of cases, lesions develop before the age of 20 years and a familial susceptibility has been described ***(Lotti et al., 2019).***

Clinically, vitiligo characterized by patchy depigmentation, the disease is frequently associated with cosmetic disfigurement and considerable psychological distress. The primary pathophysiological causes for the loss of functioning melanocytes include genetic predisposition, autoimmune mechanisms and oxidative stress ***(Bleuel & Eberlein, 2018).***

Several treatment modalities are available and new ones are being developed. Treatments for vitiligo include topical agents, phototherapy-photochemotherapy, as well as systemic and surgical options. Topical agents, such as steroids and calcineurin inhibitors, are preferred particularly for restricted lesions, while phototherapy-photochemotherapy is preferred for patients with diffuse involvement. Mini-pulse systemic steroid treatment is used for patients with rapidly progressive disease ***(Relke & Gooderham, 2019).***

Surgical are proposed as a therapeutic option in patients with segmental vitiligo, in which lesions tend to be stable, focal and medical therapies fail to induce repigmentation ***(Dillon et al., 2017).***

5-Flourouracil (5-FU) is an antimetabolite analogue of the naturally occurring pyrimidine uracil. It is metabolized via the same metabolic pathways as uracil. Due to its antimitotic activity, it is easy to understand that topical 5-FU is a useful therapy for the treatment of many dermatological disorders characterized by a high mitotic rate (e.g., nonmelanoma skin cancers, actinic keratosis, benign tumours, nail psoriasis, and porokeratosis) ***(Sachs et al., 2009; Desai et al., 2012).***

Clinically, localized hyperpigmentations have been reported during systemic treatment of various cancers by 5-FU. Usually, these hyperpigmented lesions are located on the normally pigmented extremities (hands and feet) and tongue. It has been postulated that these hyperpigmentations could be considered as postinflammatory hyperpigmentations on sites submitted to repeated friction **(*Chan & Lin, 2010).***

Microneedling-assisted drug delivery (MADD) involves the use of microneedles to generate microchannels through which a drug can diffuse to enhance the transdermal delivary, other techniques include curettage, dermabrasion, pressure waves, vacuum, and radiofrequency, by using these modalities many of medications have been successfully delivered