Pulsed Dye Laser in the Treatment of Psoriatic Nails: A Controlled Study

Thesis

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By

Nehad Youssef Mosaad Youssef
M.B.B.Ch
Faculty of Medicine -Ain Shams University

Under Supervision of

Prof. Dr. Hanan Mohamed Ahmed Saleh
Professor of Dermatology, Venereology and Andrology
Faculty of Medicine -Ain Shams University

Associate Prof. Dr. Mahmoud Abd Elrahim Abdallah
Associate Professor of Dermatology, Venereology and Andrology
Faculty of Medicine -Ain Shams University

Faculty of Medicine
Ain Shams University

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List of abbreviations

Abbreviation	Full term
α	Alpha
β	Beta
γ	Gamma
A.A	Arachidonic acid
Ag	Antigen
AMPs	Antimicrobial peptides
AP	Activator protein
APC	Antigen presenting cell
BCC	Basal cell carcinoma
BSA	Body surface area
CCL / CXCL	Chemokine
CCR / CXCR	Chemokine receptor
CD	Cluster of differentiation
CLA	Cutaneous lymphocyte associated antigen
CTACK	Cutaneous T-cell Attracting Chemokine
DC	Dendritic cell
DNA	Deoxyribonucleic acid
DLSO	Distal and distal-lateral subungual onychomycosis
DPN	Dermatosis papulosa nigra
EGF-R	Epidermal growth factor receptor
EMA	European Medicines Agency
FU	Fluorouracil
GM-CSF	Granulocyte macrophage colony stimulating factor
HBD	Human b-defensin
HEV	High endothelial venule
HIV	Human immune deficiency virus
HLA	Human leukocyte antigen
H-pylori	Helicobacter pylori
HSP	Heat shock protein
ICAM	Intercellular adhesion molecule
IFN	Interferon
Ig	Immunoglobulin
IGF	Insulin like growth factor
IL	Interleukin
ILVEN	Inflammatory linear verrucous epidermal nevus

iNOS	Inducible nitric oxide synthase
IPL	Intense pulsed light
KGF	Keratinocyte growth factor
LFA	Lymphocyte function associated antigen
MC	Molluscum contagiosum
MHC	Major histocompatibility complex
MIP	Macrophage inflammatory protein
mRNA	Messenger ribonucleic acid
NAPSI	Nail psoriasis severity index
NFκβ	Nuclear factor kappa beta
NGF	Nerve growth factor
NK	Natural killer cell
P acnes	Propioni-bacterium acnes
PASI	Psoriasis area and severity index
PDL	Pulsed dye laser
PDT	Photodynamic therapy
PNF	Proximal nail fold
PPP	Palmoplanter pustulosis
PSORS	Psoriasis susceptibility
PUVA	UVA + oral psoralen (Photo-chemotherapy)
PWS	Port-wine stain
SD	Standard deviation
SLPI	Secretory leukocyte protease inhibitor
STAT	Signal Transducer and Activator of Transcription
TCM	Central memory T cell
TCR	T cell receptor
TE	Effector T cell
TEM	Effector memory T cell
Tgase	Transglutaminase
TGF	Transforming growth factor
Th	Helper T cell
TLR	Toll-like receptor
TNF	Tumour necrosis factor
Treg	Regulatory T cell
UV	Ultraviolet
VCAM	Vascular cell adhesion molecule
VEGF	Vascular endothelial growth factor
VIP	Vasoactive intestinal peptide
VLA	Very late antigen
VV	Verruca vulgaris

Introduction

Psoriasis is a chronic, inflammatory, immune-mediated skin disease characterized by epidermal proliferation; also, the psoriatic papillary dermis shows excessive microvasculature and T-cell expansion. The superficial dermal microvascular bed displays morphological changes during the early phase of psoriatic plaque formation, predominantly elongation and tortuosity of the dermal capillary loops and an increase in capillary volume ***(Hern et al., 2001).*** This expanded superficial microvasculature may be important in facilitating the access of activated T cells into the skin and in maintaining the psoriatic plaques. Also, there is evidence that the dermal angiogenesis is directly related to epidermal hyperplasia ***(Hern et al., 2001*** *and* ***Hern et al., 2005).*** Selectively thermolysing the abnormal psoriatic blood vessels could be beneficial for the treatment of psoriasis as they seem to have an important role in the formation and sustainability of clinical lesions ***(Karsai et al., 2007).***

Psoriasis has variable clinical presentations; it may involve the skin, joints, and nails, either alone or in combination. Nail psoriasis affects up to 50% of patients with cutaneous psoriasis ***(Rich and Scher, 2003).***

Nail affection as the only clinical feature of psoriasis is

rare; however, the lifetime incidence of nail involvement in psoriasis patients is estimated to be 80% to 90% ***(Gregoriou et al., 2008).*** Nail psoriasis can involve the nail bed and / or the nail matrix, the clinical findings of psoriatic nail matrix affection include pitting (the most common manifestation) as well as crumbling, red spots in lunula and leukonychia; whereas, nail bed affection manifests as nail bed discoloration, onycholysis, subungual hyperkeratosis, abnormalities of the nail plate, and splinter haemorrhages ***(Jiaravuthisan et al., 2007).*** Nail psoriasis has a significant adverse effect on patients' quality of life; over 50% of patients with nail psoriasis considered their condition an embarrassing cosmetic handicap that interfered with their job and they also reported pain as a symptom ***(Rich et al., 2008).***

Although there are several available treatment options for psoriasis, the options for nail psoriasis are limited, and nail psoriasis tends to be persistent and refractory to therapy, thus making its management challenging and distressing for patients and physicians. The management of nail psoriasis can be topical treatments such as corticosteroids, calcipotriol, anthralin, tazarotene, fluorouracil, and cyclosporine; intralesional corticosteroid injections; phototherapy; photochemotherapy or systemic therapies such as cyclosporine, methotrexate and etretinate. However, the inconsistent results of a number of

studies for psoriatic nails make it difficult to have well-founded conclusions ***(Gregoriou et al., 2008*** *and* ***Radtke et al., 2013).*** The biologics have shown efficacy in treating refractory nail psoriasis especially infliximab which seems to be the most effective option with the strongest evidence; however, long-term safety data regarding the use of this class of therapy still needs more exploration ***(Dehesa and Tosti, 2012*** *and* ***Langley et al., 2012).***

Pulsed Dye Laser (PDL) has been broadly used for treating cutaneous ectatic vascular disorders such as: port wine stains, hemangiomas and telangiectasias ***(Smit et al., 2005).*** PDL has been used for treating psoriasis because of the highly vascular nature of psoriatic lesions ***(Tournas et al., 2004*** *and* ***Zabielinski et al., 2012).*** Several studies have shown the PDL efficacy in treatment of resistant plaque psoriasis and it has been recommended as an alternative approach to control the disease ***(Hern et al., 2001****;* ***Hern et al., 2005*** *and* ***Erceg et al., 2006).*** PDL waves are well absorbed by oxyhemoglobin leading to microvessel damage and destruction ***(Garden et al., 1986).*** PDL has been also proven to decrease the number of cytotoxic T cells in the epidermis and helper T cells in the dermis ***(Bovenschen et al., 2007).*** The most frequently chosen wavelengths for PDL therapeutic use are 585 and 595 nm, which can effectively reach the nail bed through the nail plate ***(Karsai et al., 2007*** *and* ***Oram***

et al., 2010).

Several studies were done investigating the efficacy of PDL in treating nail psoriasis. Substantial improvement was noted in psoriatic nail matrix and nail bed lesions after treatment with PDL. The Pulsed Dye Laser was reported safe and well tolerated, the reported side effects included: pain, purpura, and hyperpigmentation; more pain was seen with longer pulse durations, but those side effects were transient and did not affect patients' acceptance to treatment ***(Fernández-Guarino et al., 2009; Oram et al., 2010; Treewittayapoom et al., 2012; Huang et al., 2013; Goldust and Raghifar, 2013*** *and* ***Al-Mutairi et al., 2014).***

Despite the promising findings of the previously done studies, more trials on a larger scale are still needed to further prove the efficacy of PDL in the treatment of nail psoriasis.

The Aim of the work

The aim of this work is to further prove the efficacy of PDL in the treatment of nail psoriasis in a controlled study.

Psoriasis

Psoriasis is a common, chronic, inflammatory, immune-mediated disease of the skin and joints. Psoriasis can be a debilitating chronic illness with marked physical, psychological, and social effects although it is rarely life threatening ***(Witman, 2001).*** It is usually characterized by sharply demarcated erythematous plaques with silvery scales which appear typically over the extensor surfaces; however, the entire skin may be involved. Its course is usually relapsing and remitting with variation in severity and clinical manifestations even within the same individual ***(Godie, 2004****; **Campalani and Barker, 2005*** *and* ***Langley et al., 2005).***

1.1. Epidemiology:

1.1.1. Incidence:

Psoriasis is one of the most common chronic inflammatory skin disorders. There are no specific data on the prevalence rates as the majority of studies reported estimates only. Psoriasis affects almost 2% of the general population. Prevalence rates in Europe are estimated to be 1.5%, while in the United States of America it is estimated to be 4.6%. Lower prevalence rates have been witnessed in East Africans, American blacks, Indians; and among the Chinese population, the lowest prevalence rates were

observed (0.4%). This incurable, chronic, immune-mediated disease is characterized by periods of remission and relapse ***(Christophers, 2001*** *and* ***Griffiths and Barker, 2007).***

1.1.2. Climate:

Climate seems to have an effect on psoriasis prevalence. Many patients reported improvement of symptoms in the summer and worsening in the winter ***(Witman, 2001).*** The Dead Sea climatotherapy led to reversal of the immunopathologic abnormalities of psoriasis ***(David et al., 2005).***

1.1.3. Age:

The first manifestation of psoriasis has two peaks of onset; either around the age of 20 or between 50 and 60. However, psoriasis may manifest at any age. Psoriasis can be differentiated into two subgroups: type I which begins before the age 40 and accounts for almost 75% of psoriasis patients, and type II which begins after the age 40 ***(Henseler and Christophers, 1985).*** Type I psoriasis is associated with a more severe course of disease, limited success of treatment, increased prevalence of certain human leucocyte antigen (HLA) types and stronger hereditary ties ***(Sabat et al., 2007).***