Effect of Photodynamic Therapy on Photoaging and Skin Field Cancerization

Thesis

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List of Abbreviations

Abb.	Full term
AKs	*Actinic Keratosis*
ALA	*Aminolevulinic Acid*
AP-1	*Activator Protein 1*
ATP	*Adenosine Triphosphate*
BCC	*Basal Cell Carcinoma*
BER	*Base Excision Repair*
Bp	*Base Pairs*
BRAF	*B-Raf Protein*
CDKN2A	*Cyclin-Dependent Kinase Inhibitor 2A*
CL	*Cutaneous Leishmaniasis*
CPDs	*Cyclobutane Pyrimidine Dimmers*
CTGF	*Connective Tissue Growth Factor*
ECM	*Extracellular Matrix*
ERK	*Extracellular Signal-Regulated Kinases*
IHC	*Immunohistochemistry*
JNK	*c-Jun Amino Terminal Inase*
LED	*Light Emitting Diodes*
MAL	*Methyl Aminolevulinate*
MAPK	*Mitogen-Activated Protein Kinases*
MF	*Mycosis Fungoides*
MMPs	*Matrix Metalloproteinases*
NF-kB	*Nuclear Factor Kappa-Light-Chain-Enhancer of Activated B Cells*
NMSC	*Non-Melanoma Skin Cancer*
P. acnes	*Propionibacterium Acnes*
PDT	*Photodynamic Therapy*
PS	*Photosensitizer*

List of Abbreviations (Cont...)

Abb.	Full term
PTCH	*Tumor Suppressor Gene Patched*
PTEN	*Phosphatase and Tensin Homolog*
ROS	*Reactive Oxygen Species*
SCC	*Squamous Cell Carcinoma*
SKs	*Seborrheic Keratosis*
TGF	*Transforming Growth Factor*
TGF-b	*Transforming Growth Factor b*
TIMPs	*Tissue inhibitor of Matrix Metalloproteinases*
Tn-C	*Tenascin C*
TP-53	*Tumor Protein 53*
TSP-1	*Thrombospondin-1*
UV	*Ultraviolet*
VEGF	*Vascular Endothelial Growth Factor*

ABSTRACT

Our study agrees with the previous studies done by other investigators using photosensitizers other than MB. Our results provide comparable results and further support the effectiveness of PDT in treatment of wrinkles thus photodynamic therapy can offer a good alternative as it provides better final cosmetic result with a non-invasive character.

Also there are advantages of using methylene blue instead of ALA as ALA is more expensive and needs longer contact time with the skin for 3-5 hours unlike methylene blue which is commercially available and needs 5-15 minutes contact with the skin. Also ALA may cause pain and erythema that last for at least 24 hours with residual skin pigmentation.

This study indicates that MB mediated PDT is safe, effective and an economic alternative to ALA in treatment of wrinkles.

Keywords: *Propionibacterium Acnes - Nuclear Factor Kappa-Light-Chain-Enhancer of Activated B Cells - Mitogen-Activated Protein Kinases*

INTRODUCTION

Aging is a frequent problem facing dermatologists in daily practice. It is a multisystem degenerative process that involves the skin and skin support system, with increased risk of developing benign and malignant neoplasms on photoaged skin ***(Sjerobabski-Masnec and Podujie, 2014)***.

Chronically sun-exposed skin develops several changes such as roughness, swallowness, dyschromia, wrinkles and fine lines, erythema, telangiectasias and sebaceous gland hypertrophy. These changes are referred to as the photoaging process ***(Kohl et al., 2011)***.

Sun-related changes in the skin involve the appearance of elastosis in association with degeneration and decrease of collagen, clinically apparent as yellow discoloration and coarse wrinkles. Histologically accumulated abnormal elastic fibers in the papillary dermis can be detected. As a result of UV-induced hyperplasia of melanocytes or increased melanogenesis, pigmentary alterations like ephelides, lentigines and a diffuse irreversible hyperpigmentation are apparent. Alterations in cutaneous microvasculature such as regression of small blood vessels and neoangiogenesis, resulting in telangiectasias, are seen on chronically light-exposed skin ***(Szemies et al., 2012)***.

Treatment of photoaged skin includes photoprotection, medications and procedures to reverse existing damage. Photoprotection employs measures to prevent against UV damage achieved by sunscreens, sun-protective clothing, and sun avoidance ***(Helfrich et al., 2008)***.

Reversal of the appearance of aging skin, includes injectable botulinum toxins and dermal fillers, micodermabrasion, non-ablative and ablative laser treatments, topical photosensizers with lasers and light sources, chemical peels, and a diverse array of topical agents, including prescription retinoids and bleaching agents. A combined approach is considered ideal for many patients, because it targets various different regions of the face as well as static and dynamic changes associated with aging ***(Tierney and Hanke, 2010)***.

Topical photodynamic therapy (PDT) has shown to be effective for the treatment of several aspects of skin ageing which includes improvement of fine wrinkles, mottled hyperpigmentation, tactile roughness and sallowness. These results are supported by immunohistochemical analysis that revealed both upregulation of collagen production and increased epidermal proliferation. Neocollagenesis as an indirect dermal effect of PDT is stimulated through cytokine induction ***(Khol et al., 2010)***.

PDT is based on a phototoxic reaction caused by a photosensitizer that is activated by light to form reactive oxygen species. In dermatology, PDT is performed using topical precursor molecules of the biosynthetic pathway of heme such as 5-aminolevulinic acid (ALA) or its methyl ester methyl aminolevulinate (MAL). These molecules are then converted in the skin into photoactivatable porphyrins, in particular protoporphyrin IX (PpIX) ***(Babilas et al., 2010)***.

Several studies have provided the evidence that PDT has the potential to reduce the carcinogenic potential in areas of field cancerization and promote improvement in certain aspects of photoaging ***(Morton, 2012)***. In skin rejuvenation, ablative lasers provide the best results, but post-procedure side effects like redness, hyperpigmentation and hypopigmentation display big drawbacks. PDT skin rejuvenation takes up a middle position between ablative and non-ablative skin rejuvenation, having superiority over ablative by fewer serious side effects and superiority over non-ablative by being achieving better results ***(Dover et al., 2005)***.

Numerous light sources including red light, blue light, Pulsed Dye Laser (PDL) and Intense Pulsed Light (IPL) have been used for photodynamic rejuvenation ***(Freeman et al., 2003; Babilas et al., 2006)***. Several studies have indicated that IPL devices are suitable for treatment of photodamage ***(Ruiz-Rodriguez et al., 2002; Kim et al., 2005)***. A series of full-face IPL-treatments without a photosensitizer resulted in an