BROADBAND UVA VERSUS PUVA IN THE TREATMENT OF EARLY STAGE MYCOSIS FUNGOIDES: A COMPARATIVE STUDY

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالُوا سبحانك لَا علْم لَنا إِلا ما علمتنا إِنك أَنت الْعليم الْحكيم

صدق الله العظيم

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ABSTRACT

Background: Mycosis fungoides (MF) is the most common type of cutaneous-T-cell lymphoma, with no established consensus for its treatment. The standard treatment for early stage MF is PUVA. UVA1 phototherapy was found to induce marked improvement in skin lesions of patients with stages IA and IB MF. Broad band UVA is composed of 80.1% UVA1, with similar mechanisms of action.

Aim of work: The aim of the present work was to compare the efficacy of PUVA versus broad band UVA as a substitute to UVA1 in the treatment of early stage MF (IA, IB, IIA).

Patients and methods; Thirty patients with early stage MF (IA and IB) were included in this prospective, randomized clinical trial. They were randomly divided into two equal groups; group A [15 patients receiving PUVA] and group B [15 patients receiving BBUVA at 20J/cm^2/ session]. The patients received 3 sessions/week for 13 weeks i.e. forty sessions. The patients were compared regarding clinical, histopathological, immunohistochemical (By measuring the bcl-2 level) and overall responses.

Results: Among each of the two groups, there was statistically significant improvement in the clinical, histopathological, immunohistochemical and overall responses. However there was no statistically significant difference between both groups in any of the aspects with comparable overall success rates; (93.3%) in the PUVA group and (80%) in the BBUVA group. Excellent overall response rates was higher in the BB-UVA group (41.7%) versus (14.3%) in the PUVA group, but still with no statistically significant difference (P=0.117).

As regards the side effects encountered in both groups; there was no statistically significant difference in the rates of tanning, pruritus, appearance of new lesions, photosensitivity or dryness. However discomfort was significantly higher among the BB-UVA group (P=0.032) and nausea was significantly higher among the PUVA group (P=0.003).

Conclusion: BB-UVA is a new, yet promising therapeutic modality in the treatment of early stage MF, as it is comparable to PUVA, as regards both the efficacy and safety. It could substitute the use of UVA1 in the treatment of early stage MF specially in pigmented skin (phototype ≥ III) that can withstand longer periods of phototherapy without phototoxicity.

Keywords: Mycosis fungoides, PUVA, Broad band-UVA, UVA1, phototherapy, Bcl-2.

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LIST OF ABBREVIATIONS

AIF	: Apoptosis inducing factor
AP-1	: Activator protein-1
APAF	: Apoptotic protease-activating factor
BB-UVA	: Broad band-ultraviolet A
BCNU	: Bischlorethyl nitrosuea
BH	: Bcl-2 homology
BSA	: Body surface area
CCL	: Chemokine ligands
CCR	: Chemokine receptors
CLA	: Cutaneous lymphocyte-associated antigen
CMV	: Cytomegalovirus
COX-2	: Cyclooxygenase-2
CT	: Computed tomography
CTCL	: Cutaneous T-cell lymphoma
DISC	: Death-inducing signaling complex
EBV	: Epstein-Barr virus
FADD	: Fas associated protein with death domain
FDA	: Food & drug administration
G-CSF	: Granulocyte colony stimulating factor
GM-CSF	: Granulocyte-macrophage colony stimulating factor
HD	: High dose
HIV	: Human immunodeficiency virus
HN-2	: Nitrogen mustard
HSV	: Herpes simplex virus
HTLV	: Human T-cell lymphotropic virus
ICAM-1	: Intercellular adhesion molecule-1

IL	: Interleukin
INF	: Interferon
LD	: Low dose
LN	: Lymph node
MD	: Moderate dose
MEL	: Monochromatic excimer light
MF	: Mycosis fungoides
MMP	: Matrix metalloproteinase
MOP	: Methoxypsoralen
mRNA	: Messenger RNA
MSH	: Melanocyte-stimulating hormone
NF-KB	: Nuclear factor-kappa Beta
PCR	: Polymerase chain reaction
PG	: Prostaglandin
PLE	: Polymorphous light eruption
PUVA	: Psoralen plus ultraviolet A
QOL	: Quality of life
RARs	: Retinoic acid receptors
RXRs	: Retinoid X receptors
sBCC	: Superficial basal cell carcinoma
SCC	: Squamous cell carcinoma
SMAD	: Transcription factor proteins
TBI	: Tumor burden index
TCR	: T-cell receptor
TCRGR	: T-cell receptor gene rearrangement
TGF	: Transforming growth factor
Th1	: T helper 1
Th2	: T helper 2

TLRs : Toll-like receptors

TNF : Tumor necrosis factor

TNF-α : Tumor necrosis factor-alpha

TNM : Tumor-node-metastasis

TNMB : Tumor-node-metastasis-blood

TSEB : Total skin electron beam

UV : Ultraviolet

UVA : Ultraviolet-A

UVB : Ultraviolet-B

α-MSH : Alpha-melanocyte stimulating hormone

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INTRODUCTION

Mycosis Fungoides (MF), a low grade lymphoproliferative disorder, is the most common type of cutaneous T-cell lymphoma. Typically, neoplastic T-cells localize to the skin and produce patches, plaques, tumors or erythroderma. Diagnosis of MF can be difficult due to highly variable presentations and sometimes non specific nature of histological findings ***(Nashan et al., 2007)***.

Several reviews and guidelines on the management of MF have been published; however, treatment strategies for patients with MF vary from institution to institution and no consensus has yet been agreed upon ***(Trautinger et al., 2006)***.

Treatment of MF is indicated to reduce symptoms, improve clinical appearance, prevent secondary complications, and prevent progression of disease, all of which may have an impact on survival. Treatment of MF includes topical and systemic therapies, which can be administered alone or in combination ***(Lundin and Osterborg, 2004)***.

MF is one of the major dermatologic conditions for which phototherapy continues to be a valuable treatment modality ***(Baron and Stevens, 2003)***.

The standard treatment for early stage MF is photochemotherapy with methoxsalen plus UVA (320 to 400 nm) exposures (PUVA therapy) ***(Zane et al., 2001)***. Irradiation devices that allow treatment of patients' skin with selected emission spectra are increasingly being used, as high dose UVA1 therapy (which selectively employs long wave UVA