Effectiveness of Photodynamic Therapy for Management of Primary Palmar Hyperhidrosis

Thesis

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List of Abbreviations

Abb.	Full term
AKs	*Actinic Keratosis*
ALA	*Aminolevulinic acid*
BCC	*Basel cell carcinoma*
BD	*Bowen's disease*
BTX	*Botulinum toxin*
CL	*Cutaneous lesihmaniasis*
DAG	*Diaclyglyceorl*
ETS	*Endoscopic thoracic sympathectomy*
GM-CSF	*Granulocyte-macrophate colony stimulating factor*
HDSS	*Hyperhidrosis Disease Severity scale*
HS	*Hyperhidrosis*
IL	*Interleukin*
IP3	*Inositol triphosphate*
IPL	*Intense pulse light*
MAL	*Methyl aminolevulinic acid*
MB	*Methylene blue*
Nd;YAG	*Neodymium-doped yttrium aluminum garnet*
OTC	*Over-the-counter clinical-strength antiperspirants*
P.acnes	*Propionibacterium*
PDT	*Photodynamic therapy*
PS	*Photosensitizer*
RL	*Red light*
ROS	*Reactive oxygen species*
SCC	*Squamous cell carcinoma*
TNF	*Tumor necrosis factor*

1. INTRODUCTION

Hyperhidrosis is defined as sweating beyond what is necessary to maintain thermal equilibrium. It is a disorder characterized by visible, excessive, bilateral, and relatively symmetrical sweating without definitive cause ***(Hornberger et al., 2004; Haider and Solish, 2005).*** The excessive sweating is independent of the process of thermoregulation ***(Murray et al., 2007)***.

Hyperhidrosis may be primary (idiopathic, essential) or secondary to a number of diseases and prescribed drugs. Hyperhidrosis occurs as a primary disorder in palms, axillae, soles or craniofacial region and can result in occupational, psychological, physical impairment and potential social stigmatization ***(Hornberger et al., 2004).*** It is often distressing and interfering with patient's daily activities ***(Weber et al., 2005).*** Based on the severity of hyperhidrosis and the degree of interference with daily activities, a 4-point scale, hyperhidrosis disease severity scale, was designed to classify and assess patients with hyperhidrosis. Patients classified on high grades of this scale, grade 3 and 4, showed barely tolerability of the condition with frequent interference with the daily activities, and intolerability with constant interference, respectively. Also, the grade 1of the scale indicate that sweating is noticeable and does not interfere with daily activities and grade 2 of the scale indicate that sweating is tolerable and sometimes interfere with daily activities ***(Hornberger et al., 2004).***

A number of medical and surgical remedies are available for the treatment of hyperhidrosis. Surgical options include minor skin excision together with subcutaneous curettage, liposuction curettage, and endoscopic transthoracic sympathectomy ***(Moran and Brady, 1991; Zacherl et al., 1998; Fox et al., 1999).*** A minor invasive modalities using ND:YAG laser which is delivered subdermal through a tiny incision was tried and showed a significant clinical improvement with minimal side effects ***(Goldman and Wollina, 2008).*** Iontophoresis is one of the simplest and safest, treatments which were traditionally used for treatment of palmar and plantar hyperhidrosis and it depends on the introduction of an ionized substance through intact skin by the application of a direct current ***(Stolman, 2008).***

Medical treatment modalities using a diversity of topical and systemic drugs have been implied with different success rate. Topical agents include aluminum chloride, anticholinergics, boric acid, 2–5% tannic acid solutions, resorcinol, potassium permanganate, formaldehyde, glutaraldehyde, and methenamine. All of these agents are limited by staining, contact sensitization, irritation, or limited effectiveness ***(Atkins and Bulter, 2002; Connolly and Barker, 2003).*** Systemic anticholinergics have been tried, but unfortunately the dosages required to achieve reduced sweating also result in adverse effects including xerostomia, mydriasis, cycloplegia, and bowel and bladder dysfunction ***(Stolman, 2008).*** The anticholinergics oxybutynin

and benztropine showed effectiveness in some cases of hyperhidrosis ***(Murray et al., 2007; Stolman, 2008).***

Photodynamic therapy (PDT) involves the use of photosensitizer agents as amino levulinic acid, methyl amino levulinic acid, methylene blue and eosin followed by exposure to light source to trigger the production of reactive oxygen species (ROS) which have destructive powers ***(Mitra and Stables, 2006).*** PDT has been used for treatment of hidradenitis suppurativa and acne vulgaris through destruction of sebaceous gland with good success rates ***(Gold, 2007; Rose and Stables, 2008; Saraceno et al., 2009; Schwiger et al., 2011; Guglielmetti et al., 2012).*** Although its use in various diseases and it has shown effectiveness for treatment of diseases with sebaceous gland disorders and its capability to destruct sebaceous glands effectively, a paucity of studies has examined its efficacy for sweat glands disorders***. Salah and Attia (2011); Mordon et al. (2014)*** reported a remarkable efficacy of PDT for treatment of axillary hyperhidrosis through application of eosin as a photosensitizer.

2. Aim of the Work

To evaluate the efficacy and safety of photodynamic therapy in the treatment of palmar hyperhidrosis. A comparison will be done between two types of photosensitizers (liposomal eosin hydrogel and methylene blue).

Chapter 1

3.1. HYPERHIDROSIS

Hyperhidrosis is defined as sweating beyond what is necessary to maintain thermal equilibrium. Primary hyperhidrosis is a disorder characterized by visible, excessive, bilateral, and relatively symmetrical sweating without definitive cause, the excessive sweating is independent of the process of thermoregulation ***(Hornberger et al., 2004; Haider and Solish 2005; Murray et al., 2007).***

Hyperhidrosis or excessive sweating of the hands, axillae, and soles of the feet can be a debilitating condition. Patients suffering from palmar hyperhidrosis find difficulties with writing or holding a pen and subsequently their academic work may suffer. The patient may become withdrawn and find difficulty mixing socially with peers. Occasionally, hyperhidrosis affects the whole body but the debilitating areas for which they seek treatment are usually the palms and axillae ***(Crabbe and Parikh, 2009).***

3.1.1. Epidemiology of hyperhidrosis

Hyperhidrosis affects 1–3% of the population. The condition is more common in hot humid climates, and in certain racial groups especially Middle Eastern Jews, Japanese, and Taiwanese. Most cases are idiopathic. Secondary hyperhidrosis is exceedingly rare in childhood but lymphoma, hyperthyroidism,

phaeochromocytoma, and anxiety disorders should be considered in the differential diagnosis **(Strutton et al., 2004).**

3.1.2. Anatomy of Sweat Glands

Sweat glands are widely distributed over the skin. The total number lies between 2 and 4 million. There are 2 types of sweat glands that are distinguished according to development, morphology and function: eccrine sweat glands forming the majority and apocrine sweat glands which are present just in limited areas **(Kredyen et al., 2002)**.

3.1.2.1. Eccrine Sweat Glands

Eccrine sweat glands are distributed over nearly the entire body surface. They are most numerous on the sole of the foot and the forehead followed by the palms and the cheek and are rare on the back, the thigh and the scrotum. They are absent from the tympanic membrane, margins of the lip, nail bed, nipple, inner preputial surface, labia minora, glans penis and glans clitoridis ***(Burns et al., 2004)***.

The duct consists of a single layer of inner or luminal cells and two or three outer rows of cells. Cornification takes place within the duct, and the horn cells become part of stratum corneum of the epidermis. The straight dermal portion of the duct is composed of a double layer of cuboidal epithelial cells and is lined by an eosinophilic cuticle on its luminal side. The secretory acinar portion of the unit, or coil gland, is formed

within the panniculus near the junction of dermis and subcutis. An inner layer of epithelial cells, the secretory portion of the gland is surrounded by a layer of flattened myoepithelial cells. The secretory cells are of two types: glycogen-rich, large pale cells, and smaller, darker-staining cells. The pale glycogen-rich cells are considered to initiate the formation of sweat **(Prost-Squarcioni, 2006).**

Eccrine sweat is a sterile dilute electrolyte solution that consist of sodium chloride, potassium and bicarbonate primarily, and antimicrobial peptides proteolytic enzymes, glucose, pyruvate, lactate, urea, ammonia, calcium, amino acids, epidermal growth factor, cytokines and immunoglobulins. Also organic compounds, heavy metals and drugs are also excreted in sweat **(Schittek et al., 2004; Schaller and Plewig, 2008)**.

Eccrine sweat glands have an important thermoregulatory function, but they also respond to emotional and gustatory stimuli. The secretory rate is far greater than that of other exocrine glands. Under severe heat stress, they are capable of producing up to 10 liters of sweat per day **(Burns et al., 2004)**.

3.1.2.2. Apocrine Sweat Glands

Adult apocrine units develop as outgrowths, not from the surface epidermis, but of the infundibular or upper portion of the hair follicle. They are therefore intimately related, at least anatomically, if non functionally, to pilar units. Although