Comparative Study on the effectiveness of Pulsed Dye Laser Therapy with and without Salicylic Acid in Plantar Warts

Thesis

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بسم الله الرحمن الرحيم
"قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ"
صدق الله العظيم
سورة البقرة آية (32)

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CONTENTS

LIST OF ABBREVIATIONS

AGEP : Acute Generalized ExanthematousPustulosis
ALA : Aminolaevulinic Acid
BC : Before Christ
CO2 : Carbon dioxide
DCP : Diphenocyprone
DNA : Double-stranded Nucleic Acid
DNCB : Dinitrochlorobenzene
DPCP : Diphenylcyclopropenone
ECT : Electrochemotherapy
Er:YAG : Erbium: Yttrium/Aluminum/Garnet
HIV : Human Immuodiffiency Virus
HPV : Human Papilloma Virus
INFs : Interferones
ISH : In Situ Hybridization
IL : Intralesional
KS : Kaposi Sarcoma
LN2 : Liquid Nitrogen
mRNA : Messenger Ribo Nucleic Acid
Nd:YAG : Neodymim :Yttrium/Aluminum/Garnet
NEH : NeutrophilicEccrineHidradenitis
PDL : Pulsed Dye Laser
PPD : Purified Protein Derivative
SADBE : Squaric Acid Dibutyl Ester
SA : Salicylic acid
TGF- β : Tumor Growth Factor-Beta
TRT : Thermal Relaxation Time
VEGF : Vascular Endothelium Growth Factor

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INTRODUCTION

Warts are benign epithelial proliferations induced by several types of the human papillomavirus (HPV) ***(Schellaas et al., 2008).*** HPVs are divided into separate genotypes depending on the bases of their DNA sequence. Different HPV types may infect either cornified stratified squamous epithelium of skin or uncornified mucous membranes. The appearance of the lesion is influenced not only by viral type but also by environmental and host factors ***(Sterling et al., 2001).*** Warts on the feet are most frequently caused by subtypes 1 or 4 ***(Kopera, 2003).***

Verrucae plantaris is one of the most common and challenging dermatologic lesions to treat ***(Jain and Storwick, 1997).*** Plantar warts represent about 30% of the cutaneous warts; they appear as thick, endophytic papules on the sole and lateral aspect of the feet, with gently sloping sides and a central depression. These on the sole are painful on pressure when walking due to deep inward growth ***(Egawa, 2003).***

Many treatments have been used for viral warts, but no single optimal treatment has been determined. Common therapeutic modalities for viral warts include cryotherapy, keratolytics, topical immunotherapy with contact sensitizer, oral cimetidine, antimitotic agents, carbon dioxide laser, electrosurgery, topical immune response modifier, photodynamic therapy and intralesional injection of antigens ***(Park and Choi, 2008).***

Laser treatment is based on the principle of the photothermal or photomechanical destruction of the target tissue. Monochromatic coherent light of a certain wavelength and fluence is absorbed by specific target structures. Light energy is converted to thermal energy, thus affecting the target structure. According to the pulse duration and

energy density, this effect may result in the coagulation (photothermal effect) or blasting (photomechanical effect) of these structures ***(Kopera, 2003).***

The spectrum of clinical applications of the pulsed dye laser has continued to advance rapidly over several years. This progress has been especially apparent in the treatment of benign cutaneous blood vessel diseases and is being expanded to include many benign nonvascular conditions as well ***(Kristen and Jerome, 2000).***

Pulsed dye laser (PDL) has been commonly used in the treatment of viral warts. Although the mechanism of action for PDL treatment for warts is not fully known, it is thought that this method is based on the specific destruction of superficial dilated capillaries in warts by selective photothermolysis of oxyhemoglobin within the microvasculature. The damage of virally-infected keratinocytes by PDL may contribute to the treatment of warts because the human papilloma virus is heat-sensitive ***(Park and Choi, 2008).***

Salicylic acid (SA) is a keratolytic agent usually used as an adjunct therapy as it increases the penetration of compounds such as 5 fluorouracil (5-FU), podophyllotoxin, imiquimod or cryotherapy by softening the tissue ***(Akarsu et al.,2006).***

Aim of the Work

Our aim of the work is to compare the effectiveness of pulsed dye laser therapy with and without salicylic acid application in treating patients with plantar warts.

PLANTAR WARTS

Plantar warts are extremely common and very painful. Although they don't cause serious health problems, the pain and cost associated with the treatment of warts can be substantial. Warts are caused by human papilloma virus which is a double-stranded DNA virus with 8,000 base pairs. More than 100 types of human papilloma virus have been identified. Plantar warts are caused by human papilloma virus subtypes 1, 2, 4 and 63, with types 2 and 4 composing most of the mosaic type plantar warts and type 1 human papilloma virus has been shown to have the highest viral particle density, an important factor in the transmission of plantar warts **(*Sallk and Douglas,2006*).**

Incidence and Prevalence

Plantar warts are estimated to occur in up to 10% in children and adolescents and up to 4.5% in adults aged 25-34 years, the range of greatest incidence is between 12 and 16 years of age. Plantar warts occur with greater frequency in girls than in boys. The peak incidence is at 13 years of age in females and 14.5 years of age in males **(*Plasencia, 2000*).**

Human Papilloma Virus (HPV)

HPV is a double-stranded DNA virus. The virus is 55 nm in diameter and its capsule lacks an envelope, making the virus very stable, infectious for years and resistant to many therapeutic agents. The HPV ds-DNA genome is composed of 8000 nucleotide base pairs which encode eight gene proteins. E gene ("early", six genes) and L gene ("late" two genes). The E gene interferes with the cell cycle regulation, which is related to tumor formation, genome replication and release of the virus, the L gene interferes with the proteins forming the capsule ***(Brown et al., 1999).***

Pathogenesis of Human Papilloma Virus Infection

The viral replication cycle appears to be linked to epithelial differentiation and keratinocytes maturation. HPV lesions are thought to arise from the proliferation of infected keratinocytes. Infection typically occurs when the basal cells in the host are exposed to

infectious virus through a disturbed epithelial barrier after minor skin abrasions or trauma. Following infection, viral genomes are contained in the nucleus as episomes, at approximately 50 to 100 copies per cell, and replicate with cellular DNA replication. The infected daughter cells migrate from the basal cell layer to suprabasal layer and begin differentiation, remain active in the cell cycle and enter into S-phase, while uninfected cells exit the cell cycle as they detach the basement membrane. So, viral genomes are amplified to thousands of copies per cell, late genes are expressed and production of mature virions is induced ***(Fehrmann et al., 2003)*** **(Figure 1)** ***(Lowy and Schiller, 2006).***

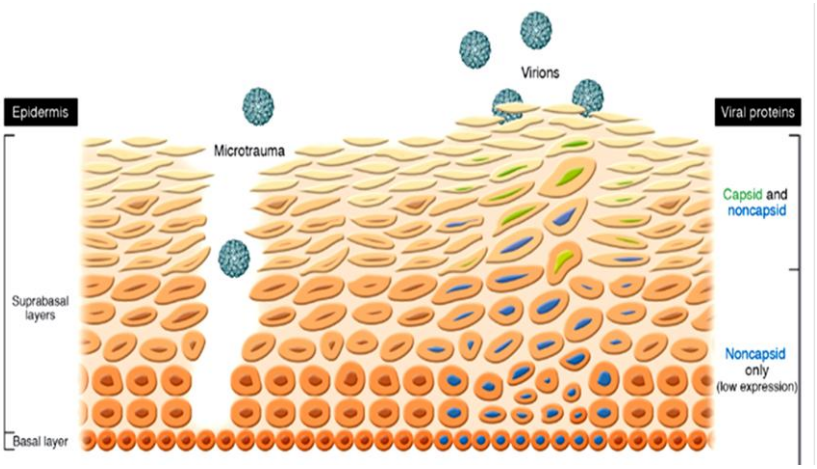

Fig (1): Human papilloma virus life cycle. To establish infection, the virus must infect basal epithelial cells that are long lived or have stem cell like properties. Micro trauma to the suprabasal epidermal cells probably enables the virus to infect the cell within the basal layer. The viral genome maintains itself as an episome in basal cells, where the viral genes are poorly expressed. Viral replication takes place in suprabasal layers and is tied to the epidermal differentiation process. The presence of the virus causes morphological abnormalities in the epithelium, including papillomatosis, parakeratosis and koilocytosis. Progeny virus is released in desquamated cells ***(Lowy and Schiller, 2006).***

The HPV can survive for many months at low temperature without a host; therefore, an individual with plantar warts can spread the virus by walking barefooted ***(Sanclemente and Gill, 2002).***

Clinical Presentation of HPV infection

Human papilloma viruses (HPVs) produce epithelial tumors of the skin and mucous membranes. More than 100 HPV types have been detected, and the genomes of more than 80 have been completely sequenced. There are three categories used to describe HPV clinically as non-genital cutaneous warts, non-genital mucosal warts and anogenital warts **(Table 1)** ***(Gearhart, 2006*****).**

Table (1): Diseases and associated HPV subtypes ***(Gearhart, 2006).***

Diseases	HPV Subtypes
Non genital Cutaneous Disease	
Common warts	1,2,4,26,27,29,41,57,65
Plantar warts	1. 2, 4, 63
Flat warts	3, 10,27,28,38,41,49
Butcher's warts	1,2.3,4,7,10,28
Mosaic warts	2, 27,57
Ungual squamous cell carcinoma	16
Epidermodysplasia verruciformis	5,8,9,10,14,17,20,21, 22, 23
Non genital Mucosal Disease	
Respiratory papillomatosis	6,11
Squamous cell carcinoma of lung	6,11,16,18
Laryngeal papilloma	6,11,30
Laryngeal carcinoma	16
Maxillary sinus papilloma	57

Squamous cell carcinoma of the sinuses	16, 18
Conjunctival carcinoma	16
Oral focal epithelial hyperplasia (Heck's disease)	13,32
Oral carcinoma, Oral leukoplakia	16,18
Anogenital Disease	
Condyloma accuminatum	6, 11,30.42,43,44,45,51,52
Bowenoid papulosis	16, 18,34,39,42,45
Buschke-Lowenstein tumors	6, 11
Intraepithelial neoplasia	30, 34,39, 40,53,57,59, 61, 62
Carcinoma of vulva	64,66,37,68,69
Carcinoma of vagina and cervix	6,11,16,18
Carcinoma of penis	16,18,31

Transmission of Plantar wart Infection

Human papilloma virus is transmitted between the hosts through direct contact. For infection and replication to occur, the virus requires a compromised skin surface. The virus attacks the granular and keratin layers of the epidermis, and viral DNA and protein production occur in the upper spinous layer, with final virus assembly occurring in