



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



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شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



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Evaluation of Allograft Injection (Heterologous Verruca Vulgaris Lesion Extract) in the Treatment of Verruca Vulgaris

Thesis

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in Dermatology, Venereology and Andrology*

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List of Abbreviations

Abb.	Full term
°C	<i>Degree Celsius</i>
5-FU.....	<i>5-Fluorouracil</i>
A.....	<i>Ampere</i>
Ab.....	<i>Antibody</i>
ABMR	<i>Antibody-mediated rejection</i>
ACOG	<i>American College of Obstetricians and Gynecologist</i>
APC.....	<i>Antigen-Presenting Cells</i>
BCG	<i>Bacillus Calmette-Guérin</i>
Ca	<i>Calcium</i>
CD.....	<i>Cluster of Differentiation</i>
Co.....	<i>Cobalt</i>
DAMPs.....	<i>Damage associated molecular patterns</i>
DNA.....	<i>Deoxyribonucleic acid</i>
DPCP.....	<i>Diphenylcyclopropenone</i>
Eg.....	<i>Exempli gratia</i>
ELISA.....	<i>Enzyme-linked immunosorbent assay</i>
f.....	<i>Focal length</i>
G	<i>Gauge</i>
Ge.....	<i>General electric</i>
h.....	<i>Hour</i>
HBV.....	<i>Hepatitis B virus</i>
HCV.....	<i>Hepatitis C virus</i>
HIV	<i>Human immunodeficiency virus</i>
HPV	<i>Human papilloma virus.</i>
HS.....	<i>Highly significant</i>
HTLV.....	<i>Human T-lymphotropic virus</i>
IAEA.....	<i>International Atomic Energy Agency</i>
IBM SPSS	<i>Statistical Package for Social Science</i>
IFN- α	<i>Interferon-alpha</i>
IFN-g	<i>Interferon-Gamma</i>
IL	<i>Interleukin</i>

List of Abbreviations *cont...*

Abb.	Full term
<i>KGY</i>	<i>KiloGray</i>
<i>MHC</i>	<i>Major Histocompatibility Complex</i>
<i>MMR</i>	<i>Mumps-measles-rubella</i>
<i>MP</i>	<i>Megapixel</i>
<i>No.</i>	<i>Number</i>
<i>NS</i>	<i>Non significant</i>
<i>PPD</i>	<i>Purified protein derivative</i>
<i>PRR</i>	<i>Pattern recognition receptors</i>
<i>S</i>	<i>Significant</i>
<i>SA</i>	<i>Salicylic acid</i>
<i>SD</i>	<i>Standard deviation</i>
<i>sig</i>	<i>Significance</i>
<i>TCMR</i>	<i>T-cell mediated rejection</i>
<i>TGR</i>	<i>Transforming Growth Factor</i>
<i>Th</i>	<i>t-helper cells</i>
<i>TLR</i>	<i>Toll-Like Receptors</i>
<i>TNF</i>	<i>Tumor Necrosis Factor</i>
<i>TU</i>	<i>Tuberculin unit</i>
<i>VDRL</i>	<i>Venereal disease research laboratory</i>
<i>VV</i>	<i>Verruca vulgaris</i>

INTRODUCTION

Human papilloma virus (HPV) infections of keratinocytes are a very common type of cutaneous infections. Prevalence varies; it affects 7% to 10% of general population, commonly in teenagers and early adults. (*Paul et al., 2017*).

Verruca (or warts) are infective benign superficial cutaneous or mucosal lesions that can be transmitted by direct or indirect contact. Some HPV subtypes are associated with malignancies such as types 6, 11, 16, 18, 31, and 35. Malignant transformation usually is seen with patients with genital warts and immunocompromised patients (*Al Aboud and Nigam, 2020*).

Warts are usually self-limiting showing complete spontaneous remission in 42% of patients within 2 months, Many ablative modalities have been utilized as a treatment for verruca lesions including surgical removal by curettage and cautery, chemical cautery, cantharidin, cryotherapy, electrocautery, radiocautery ablation, infrared coagulation, topical treatments, photodynamic therapy, and lasers. Though effectiveness of these modalities in many cases, many side effects could occur such as scarring, high rate of recurrence, pain, and pigmentation (*Das, 2020*).

As a twist in the approach to treat such lesions, immunotherapy has been introduced with the aim of local or general stimulation of the body's own immune system so as to

affect eradication of the infective viral agent and subsequent resolution of the cutaneous lesion. Different modalities of immunotherapy exist whether topical, intralesional or systemic. In local techniques, the most likely mechanism of action is local stimulation of the immune system towards the injected or locally applied antigen followed by either nonspecific collateral destruction of the lesion and/or viral agent by the ensuing local inflammatory reaction or more specific action through simultaneous immune recognition of the virus and subsequent antiviral immune reaction (mostly cell- mediated). The latter is more likely keeping in mind the observed clinical resolution of lesions not only at the same site of application but also at distant sites (*Sefcik and Burkhart, 2017*).

After transplantation of liver or other organs, antibody-mediated rejection (ABMR), hyperacute vasculitic rejection can occur in individuals with preformed antibodies against the donor's major histocompatibility complex (MHC) class I–encoded antigens. Under most other circumstances, acute allograft rejection is initiated by the large number of recipient T cells that recognize donor alloantigens (mostly those encoded by the highly polymorphic MHC). Transplantation of MHC histoincompatible tissues therefore elicits a strong, cytopathic, T cell–dependent immune response to donor tissues. This immune response occurring during rejection can be collaterally used to treat HPV virus infection (*Sánchez–Fueyo and Strom, 2011*).

AIM OF THE WORK

The aim of the present study is to evaluate the efficacy of local allograft injection (heterologous verruca vulgaris (VV) lesion extract) as a line of immunotherapy treatment for patients with multiple VV.

Chapter 1

WARTS

Causative agent:

Papilloma viruses are a diverse group of small Deoxyribonucleic acid (DNA) viruses that induce warts in a variety of vertebrates including human. Some also have malignant potential. The papilloma virus causing infection in humans is called HPV. It has more than 200 different genotypes, with equal frequency in both sexes (*Allayali et al., 2017*). Most papilloma viruses have a specific cellular tropism. The lesions can be cutaneous or can involve mucosal squamous epithelium. The virus infects the basal layer of the epithelium, possibly stem cells, but virus replication takes place only in fully differentiated keratinocytes (*Brentjens et al., 2002; Sterling, 2004*).

Predisposing factors:

Several studies have revealed risk factors for children and adolescents having warts that include low social class, practicing gymnastics and sports, a large family size, and keeping household animals (*Yang et al., 2007; Allayali et al., 2017*).

Human immunodeficiency virus (HIV) infection and immunosuppression status or medications predispose a person for multiple verruca (*Porro et al., 2003*).

Mode of transmission:

There is no reliable information on the infectivity of common and plantar warts, but it is low. Warts spread by direct or indirect contact. Impairment of epithelial barrier function from trauma, maceration or both, can predispose to infection with HPV (*Brentjens et al., 2002*).

In adults, anogenital warts are transmitted through sexual contact in most patients (*Malloy et al., 2000*). Anogenital warts are uncommon in children and hence there is insufficient data to conclusively prove their sexual transmission. Infection from the mother's genital tract at delivery is regarded as a frequent source of childhood anogenital wart. Postnatal transmission from adults with genital warts may occur non-sexually. Thus, both sexual and non-sexual routes are significant in the transmission of anogenital warts in children (*Belinson et al., 2001; Bomfim et al., 2005*).

People with plantar warts can auto-inoculate HPV and spread infection to other parts of the body. For example, picking at warts with fingernails may result in transference of infection to the hands. Abrasive implements used to remove thickened wart skin, and clinical implements such as dermoscopes, have been shown to retain detectable HPV DNA (*Aubin et al., 2010; Penso-Assathiany et al., 2013*).

Prevalence:

Warts are common worldwide. They affect approximately 10% of the population and can occur at any age group. They are more common among immunosuppressed patients and meat handlers. In school-aged children, the prevalence is as high as 10% to 20%. Although warts are rare in infancy and early childhood, prevalence increases among school-aged children and peaks at 12 to 16 years. The male-to-female ratio is approximately equal (*Al Aboud and Nigam, 2020*).

Types:

HPV type 1, 2, 4, 27, 57 & 63 cause common warts. They occur largely between the age of 5 and 20 and only 15% occur after the age of 35 (*Brentjens et al., 2002*).

The occurrence of warts on the plantar skin is not uncommon. People who have the habit of rubbing their feet against rough surfaces while bathing or otherwise, are more prone to develop such lesions. They are mainly seen over the pressure points such as the heels or metatarsal heads. The common types causing plantar warts are HPV types 1, 2, 4, or 57 (*Brentjens et al., 2002*).

Plane warts are mainly due to HPV-3 and HPV-10. Anogenital warts are common, with an estimated 1.3 million new cases per year in the USA. They may be caused by HPV