



## The value of 5% topical imiquimod cream for the treatment of flat warts in a sample of Iraqi patients

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### Article History:

Received on: 05.01.2019

Revised on: 24.01.2019

Accepted on: 02.02.2019

### Keywords:

Topical imiquimod cream,  
Flat warts,  
Human papilloma virus

### ABSTRACT

Flat warts are mainly caused by HPV type 3 and 10. The condition is usually seen in young people in visible skin areas such as the back of hands, face, and forehead. Medical treatment may be prolonged in some situations for months and rarely for years making patients unsatisfactory. Surgical approaches such as electrocoagulation, cryosurgery, and laser are used when medical treatment fails to control the disease, but surgical removal carries the risk of scar formation and is usually costly. The current study was planned and carried out to evaluate the response of plane warts to 5% imiquimod cream in a sample of Iraqi patients with plane warts. The present cohort study included 20 patients with plane warts. Those patients were selected from the pool of patients visiting the dermatology consultation unit at Al-Diwaniyah teaching hospital, Al-Diwaniyah Province, Iraq during the period from September 2018 through June 2019. Age, gender, and duration of disease were the main variables included in the study; the outcome was a response to treatment classified as complete, partial, and incomplete. All patients were treated by topically applied 5% imiquimod cream once daily and were followed up for a period of time, ranging from 2 weeks to 12 weeks. The results of the current study revealed that treatment duration and response to treatment is shown in Table 2. Mean duration of treatment was  $7.95 \pm 3.33$  weeks, and it ranged from 2 to 12 weeks. Complete response was seen in 60 %, partial response was identified in 30 %, and no response was the outcome in 10 % of patients. Treatment response was not correlated to the age or gender of patients, but longer duration of disease predicted poor response to treatment. In view of available data in the current study and in previous reports, 5% topical imiquimod cream appears to be an efficient and safe mode of treatment for flat warts.



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ISSN: 0975-7538

DOI: <https://doi.org/10.26452/ijrps.v10i2.1374>

Production and Hosted by

IJRPS | <https://ijrps.com>

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### INTRODUCTION

Human papilloma virus can infect the skin and mucous membranes of human being leading to the development of benign lesions called warts (Bialecka *et al.*, 2018). Indeed, there are more than 100 types of human papilloma virus (Braaten and Laufer, 2008). The clinical manifestations are also variables including Genital warts, Common warts, Deep palmoplantar warts (Myrmecia), Flat warts, Epidermodysplasia verruciformis, Focal epithelial hyperplasia and Plantar cysts (Bacaj and Burch, 2018). The transmission of the disease can

happen following direct or indirect contact, particularly when epithelial barriers are disrupted (Lipke, 2006). The virus is often restricted to epithelial surfaces, and systemic invasion is unusual. The virus prefers to replicate in upper epithelial layers; however, it can be isolated from basal epidermal layers (Kawana *et al.*, 2001). The disease is very common, and approximately a significant proportion of the population worldwide, and no age is immune (Baseman and Koutsky, 2005). The disease is highly frequent among school-age children. The disease is more frequent in patients with immune suppression and in those who are involved in meat handling. There is no sex predilection, and either sex is affected nearly equally (Baseman and Koutsky, 2005).

Flat warts are mainly caused by HPV type 3 and 10 (Bialecka *et al.*, 2018). The condition is usually seen in young people in visible skin areas such as the back of hands, face, and forehead (Bialecka *et al.*, 2018). From a histological point of view, the lesions caused by flat warts are similar to those seen in the common wart. Typical cells with pyknotic basophilic nuclei that are centrally located and are surrounded by perinuclear halos are characteristic (Jin *et al.*, 2011). The most frequent therapeutic ways include topically applied retinoids such as isotretinoin, tretinoin, and tazarotene, in the form of liquids or ointments (Bialecka *et al.*, 2018).

Nevertheless, these agents are accompanied by a number of side effects such as exfoliation, erythema, and skin irritation. When treatment lasts for a long period, these side effects become very disturbing as they happen in visible skin areas. Anti-mitotic agents are also used for the treatment of warts, such as podophyllotoxin liquid and 5-fluorouracil ointment; however, their use is frequently associated with hypersensitivity reactions (Gibbs *et al.*, 2002). Topical agents may be avoided in children. Medical treatment may be prolonged in some situations for months and rarely for years, making patients unsatisfactory (Gibbs *et al.*, 2002). Surgical approaches such as electrocoagulation, cryosurgery, and laser are used when medical treatment fails to control the disease, but surgical removal carries the risk of scar formation and is usually costly. Spontaneous remission is possible; however, a long period of time may pass before this to happen (Kavya *et al.*, 2017; Tagami *et al.*, 1980). Some forms of immunomodulating agents have been used such as imiquimod cream with variable and conflicting results (Schwab and Elston, 2000; Durani and Jappe, 2002; Minh *et al.*, 2019). Therefore, the current study was planned and carried out to evaluate the response of plane warts to 5% imiquimod cream in a sample of

Iraqi patients with the plane wart.

## PATIENTS AND METHODS

The present cohort study included 20 patients with plane warts. Those patients were selected from the pool of patients visiting the dermatology consultation unit at Al-Diwaniyah teaching hospital, Al-Diwaniyah Province, Iraq during the period from September 2018 through June 2019. Age, gender, and duration of disease were the main variables included in the study; the outcome was a response to treatment classified as complete, partial, and incomplete. All patients were treated by topically applied 5% imiquimod cream once daily and were followed up for a period of time, ranging from 2 weeks to 12 weeks.

The study was approved by the institutional ethical approval committee, and verbal consent was obtained from each participant or his parents, in case of children, after full illustration of the purpose and the procedure of the current study.

### Statistical analysis

Obtained data were then transferred into an SPSS (version 23) spreadsheet. Numeric data were expressed as mean, range, and standard deviation, whereas, categorical data were expressed as number and percentage. The correlation was assessed using the Spearman correlation test. The level of significance was set at  $P \leq 0.05$ .

## RESULTS AND DISCUSSION

The demographic characteristics of the study sample are shown in Table 1. The age ranged from 3 to 35 years with a mean of  $14.70 \pm 8.47$  years; 9 (45.0%) were children, and the rest were adults. Male patients accounted for 13 (65.0%) whereas female patients accounted for 7 (35.0%). The duration of disease varied from 3 to 60 months averaging  $16.25 \pm 14.63$  months, Table 1. Treatment duration and response to treatment is shown in Table 2. Mean duration of treatment was  $7.95 \pm 3.33$  weeks, and it ranged from 2 to 12 weeks. Complete response was seen in 60%, partial response was identified in 30%, and no response was the outcome in 10% of patients, Table 2. Treatment response was not correlated to age or gender of patients, but longer duration of disease predicted poor response to treatment, Table 3.

A plane wart is a common dermatologic disease in daily clinical practice, and it involves areas of skin that are usually exposed; therefore, patients usually seek medical advice because of significant embarrassment associated with such skin disfigurement

**Table 1: Demographic characteristics of patients with the plane wart**

Characteristic	Value
Age (years)	
Mean $\pm$ SD	14.70 $\pm$ 8.47
Range	3 - 35
< 15 years	11 (55.0 %)
$\geq$ 15 years	9 (45.0 %)
Gender	
Male	13 (65.0 %)
Female	7 (35.0 %)
Disease duration	
Mean $\pm$ SD (months)	16.25 $\pm$ 14.63
Range (months)	3 - 60
<1 years	10 (50.0 %)
1-3 years	9 (45.0 %)
> 3 years	1 (5.0 %)

**Table 2: Treatment duration and response**

Characteristic	Value
Treatment duration (weeks)	
Mean $\pm$ SD	7.95 $\pm$ 3.33
Range	2 -12
2 Weeks	1 (5 %)
3 Weeks	2 (10 %)
4 Weeks	1 (5 %)
5 Weeks	1 (5 %)
6 Weeks	1 (5 %)
8 Weeks	8 (40 %)
12 Weeks	6 (30 %)
Response to treatment	
No response	2 (10 %)
Partial response	6 (30 %)
Complete response	12 (60 %)

**Table 3: Correlations of treatment response to demographic characteristics**

Characteristic	r	p
Age	0.222	0.346
Gender	0.021	0.930
Duration of disease	- 0.495	0.027 *

in addition to the well-known contagious nature of the disease by the community. Currently used medical treatment options are frequently associated with disabling side effects and treatment failure; in addition, the surgical approach is associated with a scar formation on some occasions and is often expensive. Therefore, the search for a more satisfactory mode of medical treatment is mandatory. In the current study, and based on previous reports that 5% topical imiquimod cream may offer a satisfactory response in a substantial proportion of patients with flat warts, this mode of treatment was tested on a number of Iraqi patients with the plane wart. It was found that complete response was the outcome in 60% of patients, a proportion that is more than satisfactory for most dermatologists. Moreover, partial response was seen in 30 % of cases. Only 2 out of 20 patients showed no response to treatment. Several authors reported satisfactory results following the use of topical imiquimod cream for the treatment of plane wart (Schwab and Elston, 2000; Durani and Jappe, 2002; Minh *et al.*, 2019). The current study demonstrates a non-significant correlation between age or gender of patients and treatment response; however, the longer the duration of disease, the worse the response is, a finding that is similar to that of other authors (Minh *et al.*, 2019). Some known side effects accompanying the use of topical imiquimod cream are pruritus, erosions, erythema and burning (Hengge *et al.*, 2000) however, we found minimal and negligible side effects in association with the use of 5% topical imiquimod cream, a finding that is supported by previous authors (Schwab and Elston, 2000; Durani and Jappe, 2002; Minh *et al.*, 2019). Imiquimod was approved by the FDA in 1997. It acts as an immune modulator through upregulation of interferon-alpha, beta, and gamma, and tumor necrosis factor, causing a reduction in HPV mRNA synthesis with consequent wart regression (Tyring *et al.*, 1998).

## CONCLUSION

In view of available data in the current study and in previous reports, 5% topical imiquimod cream appears to be an efficient and safe mode of treatment for flat wart.

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