Immunotherapy with Intralesional Candida Albicans Antigen in Plane Warts

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Abstract

Background: Warts are a frequent skin condition. Human papillomavirus is the culprit (HPV). One of the warts treatments is intralesional immunotherapy utilizing the Candida antigen.
Objectives: To evaluate the efficacy of candida antigen in treatment of patients with plane warts.
Patients and methods: Sixty Egyptian patients were randomly assigned into two groups for this study, each with clinically obvious plane warts: Thirty patients were divided into two groups: group (A) received injections of Candida antigen, and group (B) received intralesional saline. Before each injection, one month later, and six months following the final injection, all patients were clinically and visually assessed.
Results: The mean age of the studied group was 21.8 ± 6.6 years with 53.7% males and 46.3% females, for the cases group, and the mean age was 24 ± 7.5 years with 46.3% males for the control group. We showed statistical significant difference (p-value < 0.001) between studied groups as regard response at 1 month, 2 month and 6 month. We found Statistically significant (p< 0.001) increased percentage of complete resolution in group I (11 patients, 36.7%) when compared with group II (0 patients, 0%). There was statistical significant (p2 < 0.001) increased percentage of partial resolution (12 patients, 40%) in group I when compared with group II. During the current study, no serious adverse events were observed, and no patients discontinued treatment as a result of side effects. Erythema (26.7%) and edoema (23.3% of all adverse events) were the most common.
Conclusion: Intralesional Candida antigen immunotherapy is safe, promising and efficient treatment approach for warts.
Keywords: Warts; Candida; Intralesional.

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Introduction

Warts or verrucae are known as human Papilloma Virus-induced cutaneous and mucosal infections. Due to a variety of causes, treating cutaneous warts as a long-standing clinical issue that seems to never go away is essential. The first is the prevalence of cutaneous warts, which is high both in Egypt and globally. The lack of a specific antiviral medicine and the many unproven efficacy of available treatments increase how serious the issue is **(Nassar et al., 2021).**

In children and young adults, plane warts are primarily caused by HPV serotypes 3, 10, 28, and 41. These papules often have the colour of the skin but can also be hyperpigmented. They can be smooth, slightly raised, or flat. Sizes range from 1 to 5 mm, and they are either polygonal or circular. The face, palms, and forearms are the primary locations where plane warts prefer to grow **(Abu El-Hamd and Aboeldahab, 2021)**.

Usually, damaging therapies like cryotherapy, electrocoagulation, topical salicylic acid, topical 5-fluorouracil, or laser are used to treat or remove warts. In essence, all of these therapies are painful, time-consuming, and frequently recurrent. **(Fathy et al., 2019).**

Intralesional immunotherapy has gained important attention as a warts treatment method. It has been reported that intralesional antigens, including the MMR (measles, mumps, and rubella) vaccination, skin test antigens (Mumps, Candida, and Trichophyton), and the BCG (Bacillus Calmette-Guerin) vaccine, are effective treatments for many types of warts. Injecting immunotherapeutic agents intralesionally makes use of the immune system's capacity to mount a delayed type hypersensitivity response to a variety of antigens, including the wart tissue, which causes the production of Th- 1 cytokines and the activation of cytotoxic and natural killer cells to eradicate HPV infection. In contrast to conventional wart remedies, this eliminates not just nearby warts but also distant warts **(Nofal et al., 2013).**

The aim of our study was to evaluate the efficacy of candida antigen in treatment of patients with plane warts.

Patients and methods

Sixty patients with clinically evident plane warts divided randomly into two groups: **Group (A)**: 30 patients received Candida antigen injection**. Group (B)**: 30 patients received intralesional saline at a dose of 0.3ml into the largest wart.

Inclusion criteria included: Patients between the ages of 16 and 60 years proved as having with clinically evident plane warts.

While participants on immune suppressive medications, people with significant co-morbidities or concurrent cancers, people with any eczematous skin condition, those with a history of Candida albicans antigen hypersensitivity, and people who are pregnant or nursing were all excluded from the study.

The study was approved by Qena Faculty of Medicine institutional ethical committee. All patients signed an informed consent before their inclusion in this study.

Ethical approval code :SVU-MED-DVA021-2-21-9-233.

All patients underwent the following:

All patients were subjected to the following:

I. History and Clinical Examination: -

1. Complete history taking, including information on the length of time the wart has been there, its progression, and any prior treatments.

2. Full Clinical Examination: A full clinical assessment included a sufficient clinical dermatologic examination of the location, kind, and quantity of warts as well as the existence of distant warts at the initial examination and at each subsequent appointment. Throughout the research time, patients were told not to utilise any additional wart-directed therapies.
3. Anthropometric measurments: Height and weight were measured, and body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

II. Treatment protocols:

Sixty patients were divided randomly into two groups:

1. **Group (A):** Thirty patients got injections of Candida antigen. Intradermally into the skin of the forearm, 0.1 millilitres of the C. albicans antigen were administered as a test dosage. When there was 5 mm of erythema and induration after 48–72 hours, a reaction was deemed positive. We just included reactors. Without pre-sensitization, 0.3 ml of 1/1000 Candida antigen solution (Candida albicans 1:20 w/v 10 ml vial, Allergy labs, INC, Oklahoma City, USA) was injected into the biggest wart in all patients that were included. Three injections altogether, administered over three weeks.
2. **Group (B):** Saline was injected intralesionally into the largest wart of 30 patients at a dose of 0.3 ml every two weeks until full clearance was achieved, or for a maximum of five treatment sessions.

III. Follow-up

Before each injection, one month later, and six months following the final injection, all patients were clinically and visually assessed. Patients were assessed and given the following grades for improvement: Warts can be resolved in one of four ways: (a) entirely, if they vanish totally; (b) partially, if they vanish 50% or less; (c), minimally, if they vanish less than 50%; or (d), if they don't vanish at all.

Statistical analysis

Version 26.0 of the Statistical Software for Social Sciences (SPSS) was used to analyse the data. Using the Student's t-test, quantitative data were compared as mean standard deviation (M SD). Quantitative information was presented as frequency and percentage number (%) and. To compare non-parametric data, the chi-square test was applied. Significant results were represented by P value < 0.05.

Results

Baseline characteristics

The distribution of sociodemographic factors was illustrated in (**Table 1).** Cases and controls were matched for all sociodemographic factors. The mean age of the studied group was 21.8 ± 6.6 years with 53.7% males and 46.3% females, for the cases group, and the mean age was 24 ± 7.5 years with 46.3% males for the control group.

Efficacy

The results of current study showed statistical significant difference (p-value < 0.001) between studied groups as regard response at 1 month, 2 month and 6 month. We found statistically significant (p< 0.001) increased percentage of complete resolution in group I (11 patients, 36.7%) when compared with group II (0 patients, 0%). There was statistical significant (p2 < 0.001) increased percentage of partial resolution (12 patients, 40%) in group I when compared with group II (**Table 2)**

We observed statistical significant (p-value < 0.001) increased percentage of

occurrence of side effects in group I (11 patients, 36.7%) when compared with group II (0 patients, 0%). Regarding the description of side effects occurred in group I, we noted that there was swelling in 7 patients (23.3%), erythema in 8 patients (26.7%), itching in 1 patient (3.3%), fever in 1 patient (3.3%) and myalgia in 1 patient (3.3%) (**Table .3)**

Table 1. Distribution of demographic data between the 2 groups

Variables		Candida antigen group N=(30)	Controls group N=(30)	P value
Age		21.8 ± 6.6	24.0 ± 7.5	0.3
BMI		25.0 ±1.8	24.5 ±1.5	0.6
Sex	female	14 (46.7%)	16 (53.3%)	0.6
	male	16 (53.3%)	14 (46.7%)	
Occupation	student	17(56.7%)	12 (40.0%)	0.2
	House wife	6 (20.0%)	5 (16.7%)	
	Driver	1(3.3%)	0	
	employer	6 (20.0%)	13 (43.3%)	
Socioeconomic status	Lowe	14 (46.7%)	14 (46.7%)	1.00
	moderate	16 (53.3%)	16 (53.3%)	
Residence	rural	13 (43.3%)	14 (46.7%)	0.8
	urban	17 (56.7%)	16 (53.3%)	
Smoking	smoker	9(30.0%)	8 (26.7%)	0.7
	no	21 (70.0%)	22 (73.3%)	

Table 2. Distribution of the response for injection after 1 month ,2 month and 6 months and the occurrence of recurrence between the 2 studied groups

Variables		Candida antigen group N=(30)	Controls group N=(30)	P value
Duration		12.06 ±6.7	14.7 ±6.5	0.1
Onset	Acute	5 (16.7%)	7 (23.3%)	
	Gradual	25 (83.3%)	23 (76.7%)	0.5
at 1 month	complete response	11(36.7%)	0	<0.001**
	partial response	12 (40.0%)	3 (10%)	
	no response	7 (23.3%)	27 (90.0%)	
at 2 month	complete response	11(36.7%)	0	<0.001**
	partial response	12 (40.0%)	3 (10%)	
	no response	7 (23.3%)	27 (90.0%)	
6 month post last injection	complete response	11(36.7%)	0	<0.001**
	partial response	12 (40.0%)	3 (10%)	
	no response	7 (23.3%)	27 (90.0%)	

Recurrence	**No**	**11(36.7%)**	**0**	**<0.001****
	Already no enhancement	**19 (63.3%)**	**30 (100%)**	

Table3. Distribution of the side effects after injection between the 2 studied groups

Variables		**Candida antigen group N=(30)**	**Controls group N=(30)**	**P value**
Swelling	**Yes**	**7(23.3%)**	**0**	**0.005****
	No	**23 (76.7%)**	**30 (100%)**	
Erythema	**Yes**	**8 (26.7%)**	**0**	**0.002****
	No	**22 (73.3%)**	**30 (100%)**	
Itching	**Yes**	**1 (3.3%)**	**0**	**0.5**
	No	**29 (96.7%)**	**30 (100%)**	
Fever	**Yes**	**1 (3.3%)**	**0**	**0.5**
	No	**29 (96.7%)**	**30 (100%)**	
Myalgia	**Yes**	**1 (3.3%)**	**0**	**0.5**
	No	**29 (96.7%)**	**30 (100%)**	

***statistically significant at <.05**

Discussion

According to findings of the present study, there was a statistically significant difference (p-value 0.001) between the groups that were examined in terms of reaction after one month, two months, and six months. We discovered that group I had a statistically significant (p 0.001) higher percentage of complete and partial resolution than group II.

The current study's results concurred with those of Nassar et al., who assessed 92 adult patients with intractable warts. For five sessions spread out over two weeks, all patients received 0.3ml of a 1/1000 Candida antigen solution intravenously into the largest wart. 80 of the 92 patients (92.3%) responded to therapy, with complete resolution attained in 55 patients (59.7%), moderate improvement in 25 patients (27.1%), and no improvement in 12 patients (13%) being seen **(Nassar et al., 2021).**

A study by **Majid and Imran (2013)** included 34 patients with resistant or recurring warts who tested positive for the C. albicans antigen. Three doses of a pure C. albicans antigen solution were administered intralesionally to patients over a period of three weeks. Injection-related warts and other untreated warts were observed in the patients, and 56% of them showed complete wart clearance in all locations. Additionally, 38% did not exhibit any reaction, while 6% displayed a partial or complete clearance of treated warts but no impact on untreated warts.

Also, **Alikhan et al. (2015)** conducted a study on 100 patients using intralesional candida antigen, and found that 20 patients showed no response to the injections, 39 patients showed a complete response, and 41 patients showed a partial response. 12 patients (33.3%) of the 36 patients who received intralesional candida antigen showed complete clearance, according to another study by **Nofal et al (2018)** on numerous resistant warts.

In a recent trial by **Kim et al., (2010),** 18 patients with at least two cutaneous, nongenital, nonfacial warts underwent

intralesional injections of 0.3 mL of Candida antigen into their largest wart at the baseline visit and then at each subsequent appointment every three weeks after that. Nine of the 11 patients who finished the research had their treated warts completely gone (82%), one had a partial wart disappearance (9%), and one had no reaction (9%). Six out of eight patients (75%) saw the first distant untreated warts completely disappear, whereas six out of six patients (100%) saw the second distant warts completely disappear.

Our findings demonstrated that no serious adverse events or treatment discontinuation as a result of adverse events were reported during the current research. Swelling and erythema occurred the most frequently (23.3 and 26.7%, respectively).

The current study's findings were consistent with a prospective study done by Abd El Azeem et al. on 28 individuals who had common warts on their hands and feet and were given intralesional Candida antigen. The 28 patients, who ranged in age from 18 to 56 and had a mean age of 33.36 ± 14.37 years, included 8 men and 20 women. 22 of the patients had received prior treatment. After the fourth session, there was a significant decrease with patients showing partial responses (64.3% of patients) and complete responses (35.7% of patients). No patient in the study had to stop receiving therapy due to moderate, acceptable side effects such as burning sensation, edoema, erythema, or flulike symptoms. No recurrence was noted during the six-month follow-up **(Abd El Azeem et al., 2021)**.

In a previous study by **Marei et al.,** 24 individuals were examined for recalcitrant warts. At intervals of two weeks, 0.1 ml of a 1/1000 C. albicans antigen solution was injected. Throughout the course of treatment, the warts on 14 patients (58.3%) completely disappeared, six patients (25%) partially responded, and four patients (16.7%) exhibited no response. Tolerable discomfort during injection was noted in all patients, along with erythema, edema/induration, and flu-like symptoms in a small number of individuals. These side effects, however, were minor, mild, and did not signal therapy cessation. (**Marei et al., 2020**).

In a different recent trial, 64 adult patients with numerous refractory genital warts—defined as warts that lasted for more than 2 years and didn't respond to at least two different treatment modalities—were included. Two groups of 32 patients each were randomly assigned to the patients. In the tuberculin group, 9 patients (32.1%) and the Candida antigen group, 12 patients (41.3%) both experienced complete wart removal. During the 6-month follow-up period, neither group experienced any recurrence of the mild and temporary side effects **(Nofal et al., 2020).**

Conclusion

Warts can be treated effectively, safely, and effectively with intralesional Candida antigen immunotherapy.

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