Zagazig University Medical Journal

Volume 27
Issue 1 *January, 2021*

Article 38

April 2021

The efficacy and safety of Intralesional Candida Injection in Treatment of Common Warts.

Mai Mohamed Sharaf Abd El Azeem
Dermatology, Venereology and Andrology Department, faculty of Medicine, Zagazig University, Egypt,
mai.sharaf1987@gmail.com

Amany Nassar
Dermatology, Venereology and Andrology Department, faculty of Medicine, Zagazig University, Egypt,
dramany_nassar@yahoo.com

Ola Elasser
Dermatology, Venereology and Andrology Department, faculty of Medicine, Zagazig University, Egypt,
aasser2013@gmail.com

Zagazig University Medical Journal
www.zumj.journals.ekb.eg

Manuscript ID ZUMJ-1909-1484 (R2)
DOI 10.21608/zumj.2019.16568.1484

ORIGINAL ARTICLE.

The Efficacy and Safety of Intralesional Candida Injection in Treatment of Common Warts

Amani Nassar [1], AlShimaa Mohamed Ibrahim [2], Mai M. Sharaf Abd Elazeem [3]
1: Professor and Head of Dermatology, Venereology & Andrology Department, Faculty of Medicine, ,Zagazig University
2: Lecturer of Dermatology, Venereology & Andrology, Faculty of Medicine, Zagazig University
3: M.B.B.Ch.

Corresponding author:
Mai M. Sharaf Abd Elazeem
Dermatology, Venereology & Andrology Department, Zagazig University Hospitals, Zagazig, Egypt.
Email:
mai.sharaf1987@gmail.com

Submit Date 2019-09-06
Revise Date 2019-09-30
Accept Date 2019-10-04

ABSTRACT

Background: Warts are a common sight in Dermatology clinics and they constitute the commonest cutaneous manifestation of human papilloma virus (HPV) infection. A variety of procedures has been used and treatment may be invasive and/or conservative. Therefore, the aim of this study was to evaluate the efficacy and safety of intralesional Candida antigen injection in the treatment of common warts. **Methods:** At outpatient Dermatology clinic, 28 patients with common warts of the hands and feet were treated with intralesional Candida antigen. Side effects as well as improvements in texture after each session and after the final treatment were documented. The patients treated by 0.1 intralesional candidal injection once weekly maximum for 5 sessions for 5 weeks or less if complete recovery occur. **Results:** Patient's response to treatment was assessed clinically and we found disappearance of the wart and return of the normal skin markings in 35.7% of patients following intralesional candida injection. All reported side effects were mild, transient and tolerable, and did not necessitate stoppage of treatment in any of the studied patients. No recurrence reported during 6 months follow up. **Conclusion:** Intralesional Candida injection is an effective and safe modality for the treatment of common warts.

Keywords: Warts, Candida injections, Immunotherapy

INTRODUCTION

Common warts or verrucae vulgaris benign proliferations of the skin or mucosa caused by human papilloma virus (HPV) infection, they are commonly caused by HPV-2 as it continue to form new genomic variants and situated on the back of hands and fingers but also may occur anywhere on the skin [1]. Infection with HPV occurs by direct skin contact with trauma sites. The incubation period is about two to six months. Diagnosis is made by examination and typical features observation. Investigations are not usually used [2].

Warts are commonly treated by traditional treatments as destructive procedures such as cryotherapy, electrocoagulation, chemical cautery, and laser. All of these treatments can be painful; time consuming or expensive and none of them is considered the gold standard [3].

Candida is the first antigen that was tried for immunotherapy of warts and was reported

January. 2021 Volume 27 Issue 1 10.21608/zumj.2019.16568.1484

success in majority of patients. Candida immunotherapy has even been reported in all body warts even genital warts and also in children with recalcitrant warts [4].

The present study was aimed to evaluate the efficacy and safety of intralesional Candida antigen injection in the treatment of common warts.

METHODS

The present study was carried at Dermatology, Venereology and Andrology department, Zagazig University Hospitals. All patients were recruited from Dermatology, Venereology and Andrology outpatient clinics of Zagazig University Hospitals in the period from February 2017 to February 2018.

The present study included 28 adult patients of both sexes with common warts of different sites, sizes and durations and no concurrent use of systemic or topical treatments of warts. After excluding hypersensitivity patients to Candida antigen, acute febrile illness, and immunosuppressive diseases e.g. systemic lupus erythematosus, concomitant immunosuppressive drugs intake, past history of allergic skin disorders such as generalized eczema or urticarial and history of meningitis or convulsions, pregnancy and lactation.

Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Patients were subjected to history taking regarding age and sex, history of dermatological disease: including, onset, course, duration, site, and history of previous treatment for the disease, and history of associated other dermatological diseases, and history of systemic diseases and drug intake. Local examination of warts to determine the type, number, size, sites of warts and the presence or absence of distant lesions. The diagnosis of warts was made by clinical examination, and patients were advised not to use any other wart treatment during the study period.

All patients were directly injected with 0.1 ml of Candida antigen (Candida albicans 1:20 w/v 10 ml vial) was brought from Allergy Laboratories, INC. Oklahoma City, USA) into the largest wart using an insulin syringe, which is held parallel to the skin surface with the bevel facing upward. Injections were done at 1-week intervals until complete clearance was achieved or for a maximum of five treatment sessions. Response to treatment in both groups was evaluated by the decrease in size of warts and photographic comparison at base line and at each visit. Immediate and late adverse effects of both antigens were also evaluated after each treatment session.

The results were evaluated as follows; Complete response: disappearance of the wart and return of the normal skin markings. Partial response: 50-99% reduction in wart size and no response: 0-49% decrease in wart size [5]. Follow up evaluation was done every month for six months after completion of the treatment for detection of any wart recurrence.

Statistical analysis

All data were collected, tabulated and statistically analyzed using SPSS 24.0 for windows (SPSS Inc., Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) and Fisher exact was used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as mean ± SD (Standard deviation) for parametric and median and range for non-parametric data. Independent T test and Mann Whitney test were used to calculate difference between quantitative variables in two groups for parametric and non-parametric variables respectively. All statistical comparisons were two tailed with significance Level of P-value $\leq$ 0.05 indicates significant, p <0.001 indicates highly significant difference while, P> 0.05 indicates Non-significant difference.

RESULTS

The 28 patients included 8 males and 20 females with ages ranged from 18 to 56 years old, with a mean of 33.36 ± 14.37 years old, 22 patients of them were on previous therapy;

January. 2021 Volume 27 Issue 1 10.21608/zumj.2019.16568.1484

6 patients were on Cryo-cautery, 8 chemical cautery, 4 electro- cautery, 2 immunotherapy and 2 surgery before starting this study. Clinical data of all patients are shown in table 1. The significant reduction appeared from 4th session with (35.7%) for complete response and (64.3%) of patients showed partial response as shown in table 2 and figures 2&3. Side effects as burning sensation, edema and erythema were mild, tolerable, and transient as shown in figure 1.

Table 1. Clinical data of the warts of the patients (results section).

Variable		***Studied patients (n=28)***
Warts site *n (%)*	*Dorsum of Rt hand*	6 (21.4)
	Dorsum of Lt hand	8 (28.6)
	Dorsum of both hand	2 (7.1)
	Periungual	4 (14.3)
	Dorsum of Rt foot	6 (21.4)
	Dorsum of Lt foot	2 (7.1)
Duration (months) *Median (Range)*		17 (3 – 32)
Recalcitrant, *n (%)*		12 (42.9)
Warts size *n (%)*	*< 1 cm*	24 (85.7)
	> 1 cm	4 (14.3)

Table 2. Therapeutic response among the patients (results section).

Response		***Studied patients (n=28)***
1st Session *n (%)*	*No response*	6 (21.4)
	Partial response	22 (78.6)
2nd Session *n (%)*	*Partial response*	28 (100)
	Complete response	---
3rd Session *n (%)*	*Partial response*	28 (100)
	Complete response	---
4th Session *n (%)*	*Partial response*	24 (85.7)
	Complete response	4 (14.3)
5th Session *n (%)*	*Partial response*	18 (75)
	Complete response	6 (25)
Final results	*No response*	---
	partial response	18 (64.3)
	Complete response	10(35.7)

January. 2021 Volume 27 Issue 1 10.21608/zumj.2019.16568.1484

Table 3. Relation between the therapeutic response and demographic & clinical data (results section).

		Partial response (N=18)	***Complete response (N=10)***	***P***
Age (years) Mean ± SD		36.11 ± 15.19	28.4 ± 12.7	.641
Female, n (%)		12 (66.7)	8 (80)	.600
Duration (months) Mean ± SD		19.33 ± 7.81	11.2 ± 12.01	**.04**
Previous therapy, n (%)		16 (88.9)	4 (40)	.060
Size, n (%)	*< 1 cm*	1 (25)	7 (53.8)	.650
	> 1 cm	3 (75)	--	
Recalcitrant		12 (66.7)	---	**.02**

Table 4. The most common immunotherapeutic methods for the treatment of warts (discussion section)

Topical therapy	Intralesional therapy	Systemic therapy
Diphencyprone	Bleomycin	Cimetidine
Dinitrochlorobenzene	Interferon	Levamisole
Diphenylcyclopropenone (DPCP)	*Candida albicans* antigen	Zinc sulfate
Fluorouracil	Measles, mumps, and rubella (MMR) vaccine	Acupuncture
Imiquimod	Lipid garlic extract (LGE)	Purified protein derivative (PPD)
Bacillus Calmette–Guérin (BCG)	Bacillus Calmette–Guérin (BCG) vaccine	Autowart injection
Activated vitamin D	*Mycobacterium indicus pranii* vaccine	
Squaric acid dibutylester (SADBE)		
Sinecatechins		

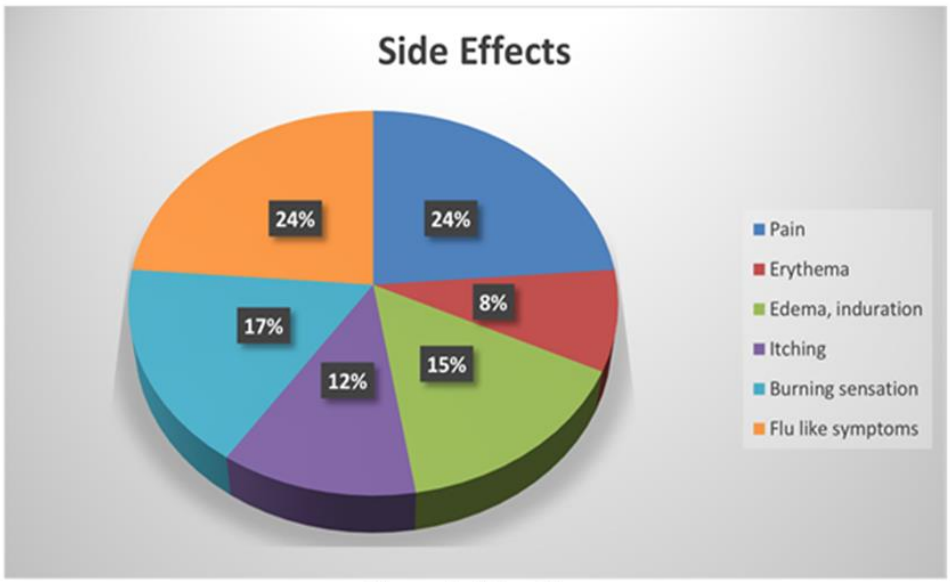

Figure 1. *Side effects*

January. 2021 Volume 27 Issue 1 10.21608/zumj.2019.16568.1484

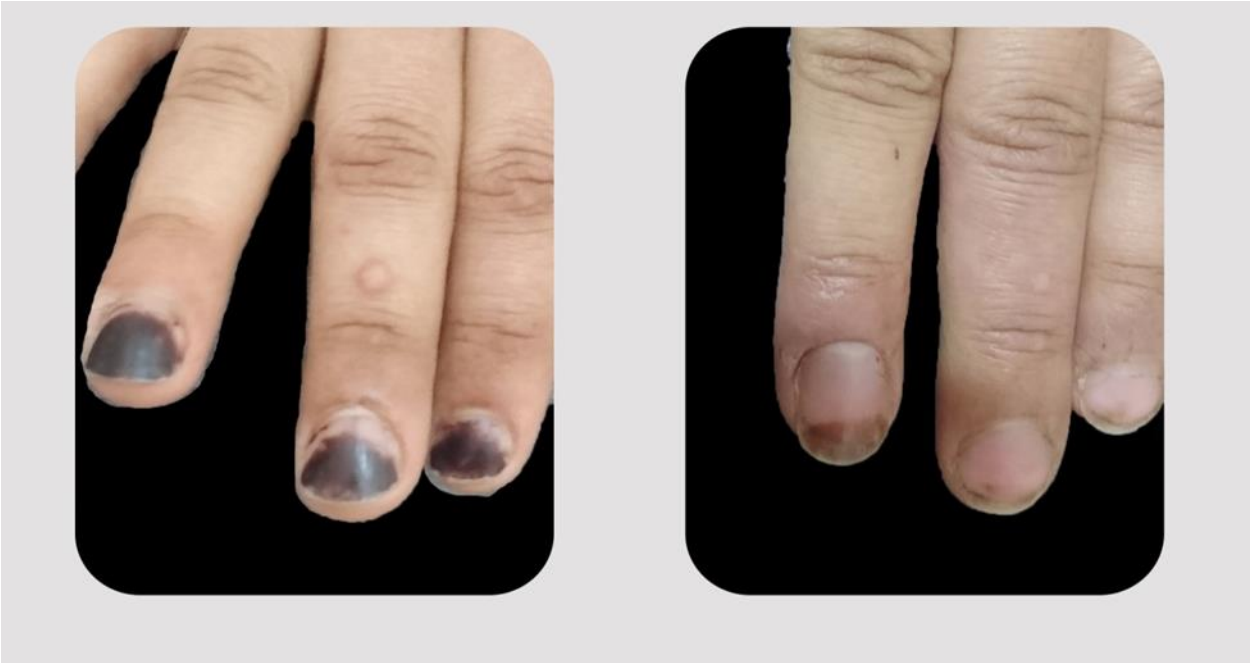

Figure 2. Partial response of common wart after 5 sessions of intralesional candida antigen injection

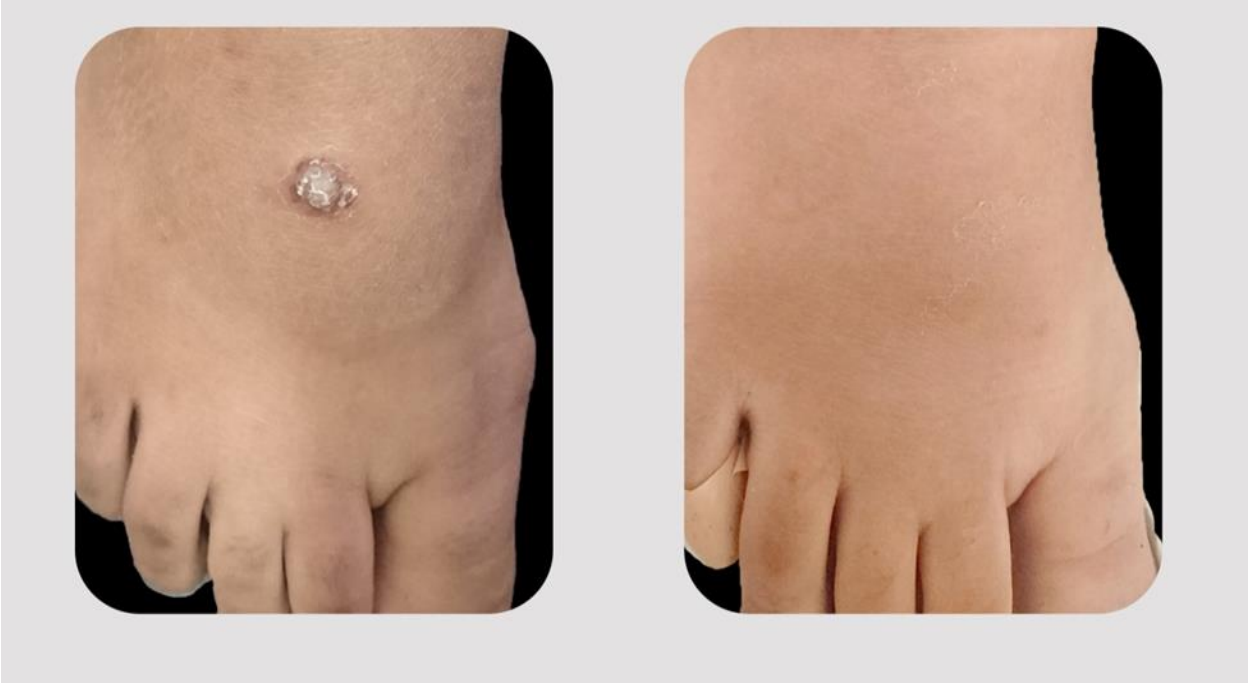

Figure 3. Complete response of common wart after 5 sessions of intralesional candida antigen injection.

DISCUSSION

Warts treatment represents a challenge for both patients and physicians. Most of the current procedures such as cryotherapy, electrodessication and laser therapy depend on the ablation of warts, and they are commonly associated with significant pain, tissue destruction and high recurrence rate [3,5,6].

Several immunotherapeutic agents have been used for the treatment of warts to overcome the challenges associated with the use of destructive therapies. Among these agents, is intralesional antigen immunotherapy that has shown a promising

January. 2021 Volume 27 Issue 1 10.21608/zumj.2019.16568.1484

efficacy and safety in the treatment of different types of warts [7-9].

Based on the previous observations, we designed our study to evaluate the efficacy and safety of one of the effective immunotherapeutic agent, intralesional Candida antigen in the treatment of common warts.

The various immunotherapeutic agents used for the treatment of different types of warts. The immunotherapeutic agents were classified according to the mode of administration into three main categories - topical, intralesional, and systemic as shown in table 4 [14].

In the current work, we did not make a pre-sensitization skin test for candida antigen because of the high incidence of Candia infection in our community makes the sensitivity to the injected Candida antigen highly expected.

Collectively, the study revealed complete response was achieved in 35.7% of the studied patients, while partial response was reported in the other 64.3% of patients with no recurrence in the 6- month follow-up period. This rate of success was lower than that reported by Clifton et al. [10] (47%), Alikhan et al. [11] (39%) and Nofal et al. [5] (61.1%), but it was higher than reported by Nofal et al. [12] (33.3%).

Factors which may explain the different response to candida antigen; the differences in the studied population selected for treatment, the studied patients number, the injected antigen sensitivity degree, and the warts number, type, duration and resistance may be responsible for the difference between the results of our study and other studies.

In this study, no statistically significant relationship was found between the therapeutic response to candida antigen injection, and the different clinical variables, including age, sex, site, type, size or previous therapy of warts, but a significant inverse relationship was found between the therapeutic response and disease duration (the shorter the duration of warts, the higher the response) (as illustrated in table 3). In consistency with our results, Nofal et al. [5] reported comparable findings. This finding may be attributed to the higher viral load expected to increase with the longer duration of the warts. In addition recalcitrant warts showed poor response than non-recalcitrant types.

This study revealed clearance of untreated warts, including the nearby and distant lesions. This observation comes in agreement with those reported by other studies utilizing intralesional antigen injection for the treatment of warts [4]. Also, Alikhan et al. [11] (39%) and Clifton et al. [10] (47%) were similar to our results. This strongly indicates the development of a widespread cell-mediated immunity against HPV as a response to candida antigen injection; an observation that represents a great advantage of Candida antigens over traditional procedures.

In our study, all reported side effects as burning sensation, edema, erythema and flu-like symptoms were mild, tolerable, and transient and did not necessitate stoppage of treatment in any of the studied patients. These findings were in agreement with studies done by Clifton et al. [10] and Nofal et al. [5]

In the present study, no recurrence was observed in any of the studied patients after the 6-month follow-up period. Similar observations have also been reported by similar related studies with Candida antigen done by Maronn et al. [13] and Nofal et al. [5, 12] This finding represents an important and promising advantage of candida antigen immunotherapy over traditional modalities.

In addition to Fathy et al. [15] reported the beneficial role of intralesional Candida antigen injection in multiple recalcitrant plantar warts as a simple, safe, effective treatment modality with minimal side effects, very low recurrence rate.

CONCLUSION

Intralesional Candida injection is an effective and safe therapy for common warts treatment.

Conflict of Interest: Nothing to declare.

Financial Disclosures: Nothing to declare.

REFERENCES

[1] Saini S, Dogra N, and Dogra D. "A prospective randomized open label comparative study of efficacy and safety of

January. 2021 Volume 27 Issue 1 10.21608/zumj.2019.16568.1484

intralesional measles, mumps and rubella vaccine versus 100% trichloroacetic acid application in the treatment of common warts." Int Res J Med Med Sci. 2016; 4(5): 1529-1533.

[2] Radley D, Saah A, and Stanley M. Persistent infection with human papillomavirus 16 or 18 is strongly linked with high-grade cervical disease. Human vaccines & immunotherapeutics. 2016; 12(3): 768-772.

[3] Gharib IEl, Aly DG, Emam HM, and Khater OH. Evaluation of Acitretin in the Treatment of Multiple Recalcitrant Common Warts: A Pilot Study. Pigmentary Disorders. 2015; 2:183.

[4] King M, Johnson SM and Horn TD. Intralesional immunotherapy for genital warts. Arch Dermatol. 2005; 141: 1606–1607.

[5] Nofal A, Marei A, Amer A, and Amen H. Significance of interferon gamma in the prediction of successful therapy of common warts by intralesional injection of Candida antigen. Int J Dermatol. 2017; 56(10):1003-1009.

[6] Aldahan AS, Mlacker S, Shah VV, Kamath P, Alsaidan M, Samarkandy S, et al. Efficacy of intralesional immunotherapy for the treatment of warts: A review of the literature. Dermatologic therapy. 2016; 29(3): 197-207.

[7] Eassa BI, Abou-Bakr AA and El-Khalawany MA. Intradermal injection of PPD as a novel approach of immunotherapy in anogenital warts in pregnant women. Dermatol Ther 2011 ;24(1):137-143.

[8] Abd-Elazeim FM, Mohammed GF, Fathy A, Mohamed RW. Evaluation of IL-12 serum level in patients with recalcitrant multiple common warts, treated by intralesional tuberculin antigen. J Dermatolog Treat. 2014; 25(3): 264-367.

[9] Kim SY, Jung SK, Lee SG, Yi SM, Kim JH, Kim IH. New alternative combination therapy for recalcitrant common warts: the efficacy of imiquimod 5% cream and duct tape combination therapy. Ann Dermatol. 2013; 25(2):261–263.

[10] Clifton MM, Johnson SM, Roberson PK, Kincannon J, Horn TD. Immunotherapy for Recalcitrant Warts in Children Using Intralesional Mumps or Candida Antigens. Pediatr Dermatol. 2003; 20(3):268-271.

[11] Alikhan, A, Griffin, J, Newman, C. Use of Candida antigen injections for the treatment of verruca vulgaris: a two-year mayo clinic experience. J Dermatolog Treat. 2015; 11: 1–4.

[12] Nofal A, Khattab F2, Nofal E2, Elgohary A. Combined acitretin and Candida antigen versus either agent alone in the treatment of recalcitrant warts. Journal of the American Academy of Dermatology. 2018; 79(2): 377-378.

[13] Maronn M, Salm C, Lyon V, Galbraith S. One-year experience with Candida antigen immunotherapy for warts and molluscum. Pediatr Dermatol. 2008; 25:189-192.

[14] El-Khalawany M, Shaaban D, Aboeldahab S. Immunotherapy of viral warts: myth and reality. Egypt J Dermatol Venerol. 2015;35:1-13.

[15] Fathy G, Sharara MA, Khafagy AH. Intralesional vitamin D3 versus Candida antigen immunotherapy in the treatment of multiple recalcitrant plantar warts: A comparative case-control study. Dermatol Ther. 2019: e12997.

Cite This Article

Abd El Azeem, M., Nassar, A., Ibrahim, A. The efficacy and safety of Intralesional Candida Injection in Treatment of Common Warts.. *Zagazig University Medical Journal*, 2021; (148-154): -. doi: 10.21608/zumj.2019.16568.1484