

Original Article

Role of *Candida* antigen in treatment of viral warts: a placebo-controlled study

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Abstract *Background* Warts are a common skin disorder. They are caused by human papillomavirus (HPV). The currently available therapies are based on local destruction of the lesion. Other treatment options include immunotherapy. *Candida* antigen acts as an immune modulator. It causes resolution of warts in the vicinity of the injection and also at distant sites, when given intralesional and intradermal simultaneously.

Objectives To determine the efficacy and safety of intradermal and intralesional *Candida* antigen in comparison with the placebo in the treatment of viral warts.

Patients and methods It was an interventional (quasi experimental) study, carried out in out-patient, Department of Dermatology, Unit II, Mayo Hospital, Lahore. Patients were divided into two groups of 30 each. Group A was given 0.1 ml of *Candida* antigen and group B was given 0.1 ml of normal saline intradermally and intralesionally. Maximum of 1 ml was given per visit. Total of three doses were given each one month apart. Patients were followed up for three months after the last dose.

Results The treatment was effective in about 67% of patients receiving *Candida* antigen therapy, whereas, in the control group only 20% patients showed improvement ($p < 0.05$). The results were statistically significant. The antigen was well tolerated and the side effects produced were mainly local and only transient.

Key words

Candida antigen, viral warts, intradermal, intralesional

Introduction

Viral warts are a common dermatological problem. Patients with warts present not only to the dermatologist but also to family physicians and general surgeons.^{1,2,3} In our setup patients also approach homeopathic practitioners, quacks and barbers for treatment. Though not life threatening in immunocompetent patients, they are a source of discomfort, embarrassment and occasionally pain.

The treatment options presently available are electrocautery, cryotherapy, lasers, topical chemotherapeutic agents and surgical excision.^{4,5,6} All of these are associated with side effects and have varying percentage of recurrence and failure rate which is frustrating both for the patients and doctors alike. There is still room for new effective and safe treatment modalities for viral warts.

Immune mechanisms have been suggested to explain spontaneous resolution of warts.⁷ It is basically the cell-mediated immunity that plays a role in regressing viral warts.⁸ If immunity could be stimulated, lasting resolution can occur.⁹ The stimulated immune system will destroy warts scattered on various parts of the

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body relieving the necessity of local treatment for each wart.¹⁰

Candida antigen has been used as an immunotherapeutic agent for the treatment of viral warts.¹¹ It offers several advantages over currently available therapies. It is safe and inexpensive. It does not require specialized expertise and equipment. It can also be used safely in pediatric age group.¹²

The present study was undertaken to assess its role in the treatment of viral warts in our patients.

Patients and methods

It was an interventional (quasi-experimental) study carried out in the outpatient section of Dermatology Department, Unit II, Mayo Hospital, Lahore. The total duration of this study was six months. Patients were given 3 doses of *Candida* antigen or placebo each 4 weeks apart and were then followed up for another 3 months.

A total of 60 patients (aged above 2 years, with verruca plana, verruca vulgaris and plantar warts, willing to give informed consent were enrolled in the study. Pregnant or lactating females, and patients with genital or facial warts, immunodeficiency states, hypersensitivity to *Candida* antigen, hypersensitivity to lignocaine, or who had had any treatment for warts during last one month were excluded. They were divided into two equal groups of 30 patients each (group A, the study group and group B, the control group).

A predevised pro forma was completed for all patients. An informed consent was taken from the patient or parents in case of children. Detailed history regarding concurrent systemic or cutaneous diseases and their treatment was

noted. A history of hypersensitivity to vaccines and drugs was carefully recorded. All the patients were photographed (with permission) prior to the commencement of therapy and on each follow-up visit.

In the study group (group A), hypersensitivity to *Candida* antigen and lignocaine was separately checked prior to the therapy. The patients were given a 1:1000 solution of *Candida* antigen diluted in equal proportion with 2% lignocaine.

With a 1ml syringe, 0.1ml of *Candida* antigen/lignocaine solution was given intradermally on a flexor aspect of left forearm of the patient. Then approximately 0.1ml of this solution was given intralesionally at the base of each wart. A maximum of 1.0ml of solution was given per visit. Both intradermal and intralesional injections were repeated every four weeks for a total of three doses.

Sterile normal saline was injected intradermal and intralesional to the patients of group B (control group) in the same manner as for group A.

Prior to the administration of the next dose, response to the previous was noted in terms of clearance of number of warts. Any local and systemic side effects to the last dose were also recorded. After the completion of 3 doses patients were followed up monthly for the next three months.

Reduction in the number of warts measured the efficacy. If $\geq 60\%$ improvement was seen the therapy was considered effective.

Results

Sixty patients with verruca plana and vulgaris were enrolled in the present study. They were

Table 1 Demographic data and disease characteristics in two groups.

Characteristics	Group A (n=30)	Group B (n=30)
Age range (years)	3½- 65.	6-54
Mean age (years)	16	20
Male	16 (53.3%)	20 (66.7%)
Females	14 (46.7%)	10 (33.3%)
<i>Sites involved</i>		
Feet (including soles)	17 (56.6%)	18 (60%)
Hands	13 (43.3%)	12 (40%)
<i>Symptoms</i>		
No symptom	17 (56.6%)	10 (33.3%)
Pain	11 (36.6%)	19 (63.3%)
Itching	1 (3%)	1 (3%)
Bleeding	1 (3%)	-
<i>Treatment already used</i>		
Cryotherapy	4 (13.3%)	3(10%)
Cautery	3(10%)	6 (20%)
Cryo + cautery	2(6%)	3(10%)
Topical keratolytic	3(10%)	-
Excision	2 (6%)	-
Homeopathic treatment	2(6%)	1(3%)
Corn cap	1(3%)	-

Table 2 Side effects noted in two groups.

Side effects	Group A (n=30)	Group B (n=30)
Erythema(at inj. site)	11 (36.6%)	6 (20%)
Swelling(at inj. site)	11 (36.6%)	6 (20%)
Itching(at inj. site)	8 (26%)	6 (20%)
Blister formation	1 (3%)	0
Fever	1 (3%)	0
Myalgias	1 (3%)	0

divided into two equal groups of thirty patients each. Age and sex distribution are given **Table 1** and **2**. Ten out of sixty (16.6 %) patients, five each in study and control group, were of pediatric age. Their ages ranged from three and half to twelve years.

Family history of viral warts or history of contact with a person with warts was present in ten out of sixty patients. Eight of them were in group A and two in group B.



Figure 1 Warts on fingers before treatment.



Figure 2 Disappearance of warts after treatment,

The lesions were mainly present on and around hands and feet in all patients as genital and facial warts were excluded from the study. The duration of warts ranged from two weeks to two and half years while one patient had them for six years and another claimed of having warts for last fifteen years.

Half of the patients were asymptomatic. Eleven patients in the study group and 19 in the control group had pain in the lesions. In group A, 17 and in group B, 13 patients had already tried some other treatment modality for warts (**Table 1**).

Twenty-four out of thirty patients completed the study in group A. Out of these 24 the treatment was effective in 67% (**Figures 1** and **2**). In group B, 20 patients completed the study out of which only 20% group B, 13 patients had

already tried some other treatment modality for warts (**Table 1**). showed good response ($p < 0.05$).

The side effects experienced by the patients were mainly local and these too were only transient not persisting beyond a few hours (**Table 2**). They did not cause any hindrance in their daily routines. Similarly, the patients who reported myalgias and fever settled by taking NSAIDs only.

Discussion

The use of immune modulation as a treatment of viral warts is a relatively newer concept. Various antigens are used to stimulate the immune response e.g. mumps, *Candida albicans* and *Trichophyton* etc.¹³

C. albicans antigen stimulates cell-mediated immunity of otherwise immunocompetent wart patients.¹¹ There is resolution of lesions in the vicinity of intradermal injection due to local immune response and also at distant sites due to generalization of the immune response.¹⁴

The technique of intralesional and intradermal *Candida* antigen injection is easy to learn and can be taught to paramedical staff. No sophisticated equipment is required as for cauterization and cryotherapy. The materials used are inexpensive like disposable polythene glove, 1 ml syringes, and injectable lignocaine. The *C. albicans* antigen is used in a very diluted form so that the cost is almost negligible.

All material used are disposable, like gloves and syringes, so the risk of spread of HPV, HIV, HBV, HCV etc. is minimized.

Due to easy technique and inexpensive disposable materials it is possible to treat a large

number of patients per day. Similarly a large number of warts can be treated at the same time thus improving patients' compliance and reducing the load of patients in OPD.

The technique is associated with minimal pain as a very small gauge (G-30) hypodermic needle is used to inject the antigen/lignocaine solution. Diluting the antigen with lignocaine further reduces pain. Due to minimal pain and discomfort, patients have a better compliance.

In this study 67% of patients showed improvement. These results are better than Horn *et al.*¹³ in which only about half (54 %) of the patients responded. Our results are comparable with that of Phillips *et al.* in which the therapy was effective in 70 % of the patients.¹⁰ In a large proportion of the patients in the present study and Phillips *et al.* the warts were cleared either after the first or second dose of *Candida* antigen barring further treatment. Even those warts that did not resolve completely were reduced in size making further dosage even more effective.

In Phillips *et al.* the response with plantar warts was not as good as with warts on the other sites of body. We could not find any difference in the results between lesions on various sites of the body.

In the present study 20% of the patients in the control group also showed improvement. This appears to be due to natural resolution of warts, which is not uncommon.¹⁵

The antigen was used not only in adults but also in pediatric patients. The later constituted around 16.6% of the patients enrolled for the study. It was well tolerated and was found to be safe and effective in children too, giving this therapy an advantage over cauterization and excision/paring in pediatric patients.

The side effects were experienced by only 33% patients in our study. These were mostly mild and transient. In the study of Phillips *et al.*¹⁰ side effects though transient were seen in nearly half (54 %) of the patients. As the technique was same the difference might be due to better tolerance in our patients including children.

We found that *Candida* antigen was effective because the stimulated immune response destroyed all warts on the body relieving the necessity of local treatment of every wart. Even patients who did not have complete cure had some improvement in the number and size of warts.

It is suggested that more number of patients should be studied for intralesional *Candida* antigen. Also a follow up of longer duration is required to assess the incidence of recurrence of warts following this therapy.

Conclusion

Intradermal and intralesional injection of *Candida* antigen is effective in the treatment of viral warts. The procedure is easy to learn and the antigen if made available is inexpensive. It is also safe and has an advantage of treating the warts located at distant sites on the body.

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