

Original Research Article

Evaluation of therapeutic effectiveness of vitamin D3 injections in common warts in a tertiary care centre

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ABSTRACT

Background: Warts or verrucae are the benign cutaneous manifestations caused by human papilloma virus. The treatment of wart possess a therapeutic challenge, as a result multiple modalities are existing for the treatment of cutaneous warts, which is cumbersome and may result in cosmetic disfigurement, chances of recurrences. The aim of the present study was to determine the resolution of common warts in response to vitamin D3 injections and to compare the resolution of common warts in the group receiving vitamin D3 with placebo group receiving normal saline.

Methods: A total of 26 patients were enrolled and divided into Group A- received lesional injection of 0.2 ml vitamin D3 every 3 weeks for 3 months for the improvement in the size of warts. Group B- received 0.2 ml of normal saline injections as a control. The maximum of three sessions were carried in both groups. Clinical assessment was done by photographic evaluation at baseline, before each treatment session, and after completion of treatment.

Results: In group A, 76.92% (10) of the patients showed complete clearance of wart with vitamin D3 injection, while in group B 8% (1) of patients with normal saline showed partial response. This therapy was well tolerated except for the minimal side effects like pain, redness and swelling at the site of injection.

Conclusions: Intralesional Vit D3 injections may be a treatment option for warts, which has a good cosmetical acceptance and simple, well tolerated easily administrated in outpatient clinic rather than conventional treatment.

Keywords: Immunotherapy, Vitamin D3, Warts, Normal saline, Intralesional

INTRODUCTION

Cutaneous warts are the common benign condition caused by human papilloma virus (HPV) usually self-limiting papillomas.^{1,2} These are the one of the benign presenting complaints among the patients attending to OPD of dermatology. There are different modalities of treatment, mostly are of destructive nature such as cryotherapy, photodynamic therapy, pulse dye lasers, kerolytics like salicylic acid, immune stimulation (dinitrochloro benzene, interferons) or antimetabolic effects (bleomycin, fluorouracil).³ The currently available

treatment often fails and chances of recurrences. To overcome this complication immunotherapy is evolving and more popular treatment for cutaneous warts by inducing the host cell mediated immunity. Various topical and intralesional agents are used as immunotherapy of warts such as imiquimod, *Mycobacterium W* (MW), BCG, MMR vaccines, candida antigens, trichophyton skin antigens.⁴⁻⁹ Similarly, vitamin D is an effective and recent modality used in the treatment of wart. The aim of the present study was to determine the resolution of common warts in response to vitamin D3 injections and to compare the resolution of common warts in the group

receiving vitamin D3 with placebo group receiving normal saline.

METHODS

A randomised control trial was a study conducted in the department of dermatology in the Mamata General Hospital in period of six months from November 2016 to May 2017. A total of 26 patients of common warts were enrolled for the study, for each patient age, sex, duration, site of wart were noted. The patients in age group of 14 to 60 years, size of wart up to 10 cm were included. Pregnant, lactating mothers, immuno suppressed patients, history of intake of immune modulators, immunosuppressive drugs were excluded. We explained the procedure to all the patients, written and informed consent were obtained from them before the commencement of the study. Approval was obtained from the institutional ethical committee.

Patients of the study were equally divided into group A and group B. No prior sensitization dose was given to any of these patients. Group A received 0.2 ml/7.5 mg of injection vitamin d3 (arachitol-3l) using an insulin syringe at the base of a single wart per patient and the same procedure was repeated at an interval of every three weeks for three successive visits. Group B received 0.2 ml of 0.84% normal saline at the base of the single wart per patient; the same procedure was repeated for three successive visits at an interval of three weeks.

Clinical response was determined by photographic evaluation at baseline, before each treatment session and after completion of treatment (at the end of 12th week). Improvement of response was graded as complete clearance (total resolution of warts), partial clearance (decreased in apparent size of wart as assessed by clinician and photographic evaluation), no response (no decrease in apparent size of wart). Patients were followed up for 3 months after the last injection. Statistical analysis was done by chi square test using IBM SPSS software version 2.1.

RESULTS

In present study the maximum number of patients were in the age group of 20-30 yrs which were 18 (69.2%) followed by <20 yrs which were 8 cases (30.7%) mean age of the patient was 26.6 yrs±5.5 yrs. A total of 26 patients for treatment of warts among them 10 were females and 16 were males. Male to female ratio was 1.8:1. Most common occupation group in our study are students 14 (53.84%) followed by manual labourers 8 (30.76%), house wives 4 (15.38%) (Table 1).

In our study maximum number of patients having single wart were 22 (84.61%), more than one wart is seen in 4 patients (15.38%) (Figure 1). The commonest site of involvement is upper extremities among 17 members (65.38%) followed by lower extremities among 6

members (23.07%) while on trunk is among 3 members (11.53%) (Table 2). The maximum size of the wart in our study ranged from 0.5 cm to 2.5 cm (88.46%) and the mean duration of wart is 3.2±1.61 mean years.

Table 1: Socio-demographic profile of the subjects (n=26).

		No. of cases	%
Age (in years)	<20	8	30.7
	21-30	18	69.2
Occupation	Student	14	53.8
	Manual labourers	8	30.7
	House wives	4	15.38
Gender	Male	10	38.4
	Female	16	61.5

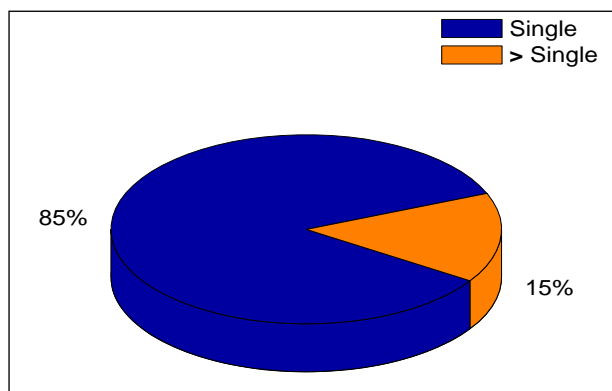


Figure 1: Distribution of cases showing number of warts.

Table 2: Distribution of cases according to site of warts.

Site of warts	No of cases	Percentage (%)
Upper extremities	17	65.38
Lower extremities	6	23.07
Trunk	3	11.53

In present study cosmetic concern is commonest complaint which constitutes 17 patients (65.38%) while others came with complaints of increasing in size with pain 9 (34.61%). The present study showed that in group A out of 13 patients, 10 (76%) showed complete clearance while 1 (7.5%) showed partial clearance in other 2 (16.5%) patient showed no response. In group B out of 13 patients, 1(7.5%) patient showed partial clearance and remaining patients showed nil response (Table 1). Maximum response was seen after 7 weeks treated with vitamin D.

Immunotherapy was well tolerated by the patients except for pain during injections followed by erythema and edema of the lesion; no allergic or systemic adverse reactions were noted. Minimal side effects were managed

by NSAIDS. In this study Group A is more responding to the treatment than Group B ($\chi^2=15.4$, d:f=1, $p<0.001$). Patients were followed up for three months, there is no recurrences were observed in Group A (Figure 2, and Table 3).



Figure 2: (A) Photographs showing initial lesion before start of intralesional injection of vitamin D3; (B) after three weeks (C) after twelve weeks.

Table 3: Distribution based on type of response.

	Response group	No response group
Group A (Vitamin D3)	11	2
Group B (NS)	1	12

DISCUSSION

Warts are the common viral infection on the skin and mucosa and are prevalent worldwide. Warts are caused by HPV (DNA virus), which has more than 100 strains. Some warts may spontaneously disappear while others persist and spread on other body sites provoking physical and emotional stress to the patient.¹⁰

Warts treatment depends on two main therapeutic options, the first line is conventional destructive and aggressive methods which includes treatment with chemical cauterly, cryotherapy, electrocauterly, surgical excision, laser ablation and second line of treatment includes immunotherapy which is based on activation of immune system to deal with HPV virus and suppress its activity. Such therapy applied topically, intralesionally or systemic administration.¹¹ Intralesional Immunotherapy utilises the immune system to mount a delayed type of hypersensitivity response to various antigens and also to wart tissue. Immunotherapy associated with production of Th1 cytokines that activate cytotoxic and natural killers to eradicate HPV infection. This clears not only local warts also distant warts unlike traditional wart therapy.¹²

In one study author have directly injected antigen to the largest wart without performing a preliminary intradermal testing. Warts are injected intralesionally using an insulin syringe which is held parallelly to the skin surface bevel facing upwards. This therapy is repeated every 3 weeks until complete clearance of warts for a maximum of three treatments with or without response.¹³ In our study patient subjected with vitamin D3 treatment every three weeks for a maximum of 3 sessions which is co-related with the above study.

We adopted this study with vitamin D3 due to economical price, easy availability and good compliance to the patient. An active form of vitamin D3 has been used for treatment of psoriasis vulgaris. It is well known that vitamin D3 analog have biological action in epidermal cell regulation, cell proliferation and modulation of cytokine production. Recent evidence demonstrates an effect on cell death, tumour invasion, angioma and cancer regulation.¹⁴ Intralesional vitamin D3 was first introduced by Aktas and co-workers for the treatment of plantar warts.¹⁵

The effect of vitamin D3 on verrucae by TLR activation of human macrophages, upregulates the expression of vitamin D receptors and vitamin D1 hydroxylase gene leading to antimicrobial peptide action.¹⁶ Topical vitamin D3 derivative used in a case of infant with ano-genital wart and also used to treat the warts in three immunocompromised patients of SLE, HIV and renal transplant recipients.¹⁷ Intralesional saline is generally used as placebo control for treatment of cutaneous warts.¹⁸ In some study patients were subjected to intralesional saline in a cutaneous wart showing a zero response.¹⁹ In the present study there is a partial clearance of the warts in one patient treated with normal saline.

While in our study 10 patients showed complete clearance of wart and one patient showed partial clearance and 2 patients showed no response with intralesional injections of vitamin D3, which is co-related with the earlier study.²⁰ We obtained partial clearance in one patient with intra lesional normal saline, which could be related to some amount of autoinoculation during intra lesional injection with normal saline.

CONCLUSION

Injection vitamin D3 is more effective in treatment of warts. This immunotherapy has better patient compliance, good therapeutic response without cosmetic disfigurement and capable of preventing recurrences. Thus, our observation open avenues of further randomised trials for the establishment of role of vitamin D3 in cutaneous warts.

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