

Original Research Article

A study on safety and efficacy of intralesional vitamin D3 in cutaneous warts

Amruthavalli Potlapati*, Narendra Gangaiah, Neethu Mary George

Department of Dermatology, Sri Siddhartha Medical College, Agalakote, Tamkur, Karnataka , 572107

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*Correspondence:

Dr. Amruthavalli Potlapati

E-mail: amrutha.potlapati@gmail.com

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ABSTRACT

Background: Immunotherapy is an upcoming treatment modality for cutaneous warts. Majority of the treatment modalities used for warts are destructive and can be painful, causes scarring and are not suitable for multiple warts. Immunotherapy overcome these shortcomings and it has shown good response both in injected and distant warts. Literature shows only very limited data on the use of immunotherapy, especially vitamin D3, in case of cutaneous warts. Objective was to evaluate the safety and efficacy of intralesional vitamin D3 in cutaneous warts and to assess the treatment response and adverse effects of the same.

Methods: Sixty patients of age more than 18 years of both sexes with cutaneous warts were given intralesional vitamin D3 of maximum five doses two weeks apart after obtaining an informed written consent. Patients were monitored for reduction in size and number of warts and also for any side effects.

Results: Out of the total 60 patients, 46 (76.6%) patients had complete resolution of warts following injection, 12 (20%) cases showed partial response and 2 (3.4%) cases had no response.

Conclusions: Intralesional vitamin D3 was found to be an effective treatment modality for multiple and recalcitrant warts.

Keywords: Warts, Immunotherapy, Vitamin D3, Intralesional injection, Verrucae

INTRODUCTION

Warts or verrucae are benign epidermal proliferation of the skin and mucosa caused by human papilloma virus (HPV). Common warts are the commonest followed by plantar, plane, filiform and anogenital warts. Incubation period of warts is two to three months after initial contact. Warts are transmitted mainly by direct skin-to-skin contact; also, through fomites and vertical transmission. The fact that they can recur even after complete physical removal makes them extremely frustrating both for the patient and the physician. Recalcitrant warts may reflect a localized or systemic cell-mediated immune (CMI) deficiency to HPV. Various reasons like lack of production of memory T-cells to target HPV infection, failure of clonal expansion of

lymphocytes to adequate stimulation, inability of T-lymphocytes to traffic to sites of infection and weak effector response mechanism have been hypothesized.

Warts are usually self-limiting, but spontaneous resolution takes months to years within which there are chances of spread to other sites and other persons. Local destruction of warts is a commonly employed treatment modality performed by using either topical keratolytic, electrocoagulation, cryotherapy or laser therapy.¹⁻² All these modalities of treatment can be painful, causes scarring and are not suitable for multiple warts. Hence to overcome these shortcomings, immunotherapy is being tried widely for the treatment of warts over the last few years. Various antigens have been tried including measles,

mumps, rubella (MMR); tuberculin purified protein derivative (PPD); mycobacteria vaccine, candida antigen and vitamin D3.³⁻⁶ Our study evaluated the safety and efficacy of intralesional vitamin D3 in cutaneous warts and assessed the treatment response and adverse effects of the same.

METHODS

Sixty patients of age more than 18 years of both sexes who presented with cutaneous warts in dermatology outpatient department at Sri Siddhartha Medical College, Tumkur from January 2019 to September 2019 were enrolled in this study. Patients who have taken any form of treatment in the past 6 months, pregnant females, lactating mothers and those on immunosuppressive drugs were excluded.

A detailed history pertaining to the demographic data, occupation, duration of wart and previous treatment taken will be collected using a questionnaire, after obtaining written informed consent. Photographs will be taken at each visit to support the recorded data.

Larger warts will be considered for injection. A maximum of two warts will be treated at each session. Injections will be repeated at two-weekly intervals for a maximum of five injections. If complete clearance will be achieved before four injections, treatment will be stopped, and patient will

be followed up for recurrence. Patients will be evaluated for treatment efficacy and adverse reactions every two weeks for first two months and monthly thereafter to record for any recurrence, for six months.

Method of administration of vitamin D3 injection

Vitamin D3 injection (arachitol) is available in vials containing 6,00,000 IU of cholecalciferol in 1 ml (15 mg). The selected warts will be injected first with 0.2 ml of lignocaine (20 mg/ml); after few minutes, 0.2 ml of vitamin D3 (15 mg/ml) will be injected into the base of each wart with a 27 g insulin syringe.⁷ Post treatment, patients will be advised not to use any topical and oral medications.

RESULTS

Out of the total 60 patients, 38 (63.3%) were males and 22 (36.7%) were females with a male:female ratio of 1.7:1. Majority (47, 78%) belonged to age group of 18-29 years with a mean age of 24.8 years. The duration of warts ranged from one month to four years (mean= 9.5 months). Age-sex distribution of the total patients presented is given in Table 1. Table 2 shows distribution based on type of warts.

No patient took treatment in the past 6 months and except for 6 patients, 54 patients had not taken any treatment in the whole course of the disease.

Table 1: Age-sex distribution of patients presented with cutaneous warts.

Age distribution (years)	Gender		Total
	Male	Female	
18-29	29	18	47
30-39	5	3	8
40-49	2	0	2
50-59	2	1	3
Total	38	22	60

Table 2: Distribution of subjects based on types of warts.

Wart type	Frequency	%
Plantar	35	52.2
Common	28	41.8
Periungual	2	3.0
Filiform	2	3.0
Total	67*	100.0

*some patients had more than one type of wart.

Out of the total 60 patients, 46 (76.6%) patients had complete resolution of warts following injection, 12 (20%) cases showed partial response and 2 (3.4%) cases had no response, after 6 months following last injection. The average number of injections needed for complete resolution of warts were 3.02.

Maximum number of injections given were 5 but most (36.6%) of the patients responded to 3 injections. The number of injections needed based on type of wart is given in Table 3.

The patients were followed up for 6 months after the last injection during which no patients showed recurrence.

DISCUSSION

Immunotherapy is an effective modality that is emerging in cases of resistant and recalcitrant warts which acts on the basic principle of enhancing the cell mediated immunity, regulating epidermal cell proliferation and differentiation, modulating cytokine production and induction of Adenosine monophosphate (AMPs) by upregulation of vitamin D receptors in the skin for the clearance of warts.⁸

In our study, intralesional vitamin D3 showed 76.6% of cases with complete resolution which was similar to that found by other studies.⁷ (Figure 1) Based on the type of wart, complete resolution was obtained maximum in case of plantar warts (82.8%) followed by common warts (67.8%), periungual and filiform (50% each). (Figure 2) periungual warts being a condition that is difficult to treat and has high chance of recurrence, this modality can be considered as a promising one. As we have noticed resolution of distant warts along with injected warts, there is a possibility of resolution of periungual warts extending into nail bed without going for nail avulsion.

Table 3: Clearance (complete) based on type of wart and number of injections.

Number of injections	Type of wart				Total
	Plantar	Common	Periungual	Filiform	
1	2	0	0	0	2
2	8	6	0	0	14
3	14	6	1	1	22
4	3	5	0	0	8
5	2	2	0	0	4
Total	29	19	1	1	50*

Table 4: Comparison of previous studies on vitamin D3.

S. no.	Authors	Number of injections	Interval between sessions	Percentage of complete response	Other findings
1	Raghukumar et al ⁹	Maximum of 4 injections/ till resolution	3 weeks	90%	-
2	Banoth ¹¹	Maximum of 3 sessions/ till resolution	3 weeks	76.92%	Compared to control group with normal saline (8% showed partial response)
3	Kavya et al ²	4 sessions or till complete clearance	2 weeks	78.57%	-
4	Singh et al ¹⁰	Maximum of 4 sessions/ till resolution	2 weeks	72.5%	Compared to intralesional PPD (80% clearance)
5	Kareem et al ¹²	2 sessions	1 month apart	40%	Significant response compared to control group (normal saline) (p<0.001)

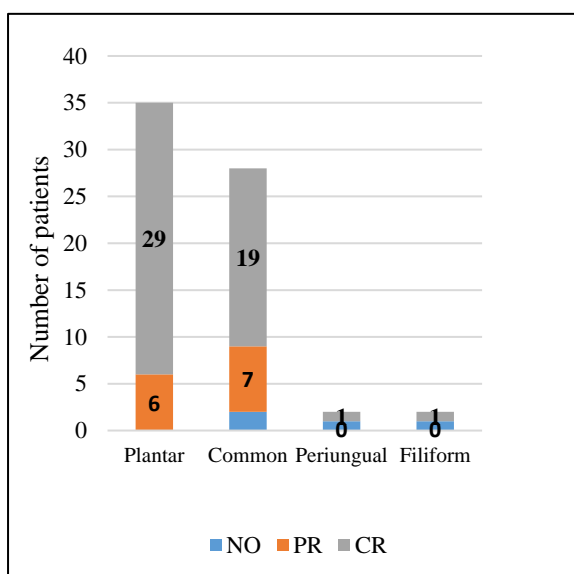
**Figure 1: Clearance based on types of warts.****Figure 2: Complete resolution of multiple and recalcitrant common warts on the dorsum of bilateral feet after 2 injections.**



Figure 3: Hyperpigmented nodule on the dorsum of foot at the site of injection.

The average number of injections to which patient responded was 3.02 unlike the study by Raghukumar et al which showed 3.66.⁹ A maximum of 4 sessions were adopted in studies by Singh et al and Manjunath et al.^{2,10}

The response was better with warts of shorter duration than those with longer duration of warts and was found to be statistically significant by Spearman's rank correlation test (correlation value -0.282 and p value 0.029). This was unlike the study by Raghukumar et al.⁹

The side effects noted were only minimal and included pain, localized swelling which resolved in a day or two and bruising. One patient had a nodule formation post injection which responded after stopping the injection with clearance of the overlying warts (Figure 3).

Comparison with other studies that has used vitamin D3 injections are given in Table 4.

CONCLUSION

In conclusion, we have found vitamin D3 to be a promising, safe and effective mode of treatment especially in cases of multiple warts and those at unusual sites. More number of studies are needed to assess the dose injected, number of sessions and interval between injections.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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