

The outcome of intralesional vitamin D₃ (alphacalcidol) injection in treatment of cutaneous warts

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Abstract

Objective The objective of this study was to see the efficacy of intralesional vitamin D₃ injection in treatment of warts. The efficacy was assessed in the term of $\geq 50\%$ improvement in warts after treatment at 3rd month.

Methods This was a descriptive case series study and was completed in 6 months duration in dermatology department, Mayo hospital Lahore. A total of 97 cases of cutaneous warts fulfilling inclusion criteria were enrolled after getting approval from hospital ethical committee. All cases were included through OPD of Dermatology, Mayo Hospital Lahore after taking informed consent. Initially, lesions were anaesthetized with 0.1 ml of prilocaine (20 mg/ml). A 21-gauge syringe was used to inject 0.2 ml of vitamin D₃ (7.5 mg/ml) slowly into the base of each wart. According to the treatment protocol, injections of vitamin D₃ were given monthly with a maximum of 2 sessions. Per single session, the total amount injected into a patient was 7.5 mg. The whole procedure was done by consultant dermatologist having more than 5 years of experience. The treatment response $\geq 50\%$ was recorded as per operational definition at 3rd month. All data was recorded by researchers themselves on the prescribed proforma.

Results The mean age of all cases was 40.94 ± 11.53 with minimum and maximum age as 18 and 60 years. There were 56 (57.7%) male and 41 (42.3%) female cases. A total of 79 (81.4%) cases achieved efficacy of treatment while in 18 (18.6%) cases efficacy was not seen. Efficacy was seen in 77.5% cases who had duration of disease < 6 months and 92.3% of cases who had duration of disease since ≥ 6 months. The frequency of efficacy was statistically same in both genders and both duration of disease groups. These results showed that intralesional vitamin D₃ was effective in the treatment of different types of cutaneous warts with high significance level.

Conclusion It was concluded that intralesional vitamin D₃ injection was highly effective in treatment of cutaneous warts. Hence, intralesional vitamin D₃ being an effective, inexpensive and safe treatment must be opted for this common problem in our society.

Key words

Intralesional; Vitamin D₃; Human papillomavirus (HPV); Cutaneous warts.

Introduction

Warts are common benign epidermal growths that occur on the skin and the mucosa.^{1,2} They are caused by the hundred different types of

human papillomavirus (HPV).³ It has a role in both benign and malignant neoplasia.⁴

Human papilloma virus and warts are usually cleared and cured by the immune system.⁵ This virus targets the basal layer of epidermis and then it enters into latent phase. It induces hyperkeratosis and hyperplasia during epidermal growth.¹

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The life time risk of being infected among both men and women is 50%.⁶ The most common types, which are linked to carcinogenesis are HPV 16 and 18. Both types are preventable by treatment with vaccination.⁵ They affect children more than adults and commonly affect the face and extremities.⁷ The commonly encountered clinical types of warts are genital and non-genital warts, the latter subdivided into common, palmoplantar, plain, digitate/ filiform and mosaic warts.⁸

T-cell immune responses has important role as the host has been infected with human papillomavirus virus. Humoral immunity reduces the likelihood of reinfection and may prevent the spread to the distant sites.

Diagnosis is made clinically and usually no laboratory investigations are required. The histological feature is vacuolation in the granular layer, along with basophilic bodies representing viral particles and eosinophilic bodies composed of abnormal keratohyaline granules. This effect is mostly accompanied by epidermal papillomatosis and acanthosis.⁹ On Dermoscopic examination, warts reveal presence of typical pinpoint thrombosed blood vessels.¹⁰

Many immunotherapeutic and destructive modalities are available for the treatment of various types of warts.^{11,12} Immunotherapeutic treatments have included intralesional administration of *Candida albicans* antigen immunotherapy and tuberculin, mumps, measles, rubella vaccine.^{12,13}

Many destructive treatment modalities may result in scarring and post-inflammatory hyperpigmentation, while less aggressive treatment options can lead to recurrence.¹

Intralesional vitamin D₃ injections has gained popularity due to stimulation of the cell-

mediated immunity and effectively clearing of warts. When topically applied, it is involved in the formation of antimicrobial peptides and it also regulates epidermal cell proliferation.^{13,14}

Warts are commonly seen in our society. Newer cost effective treatment modalities like intralesional vitamin D₃ should be opted to treat such problems to achieve complete eradication of this disease in our set up. Hence, we conducted this study to determine the efficacy of intralesional vitamin D₃ in the treatment of cutaneous warts.

Methods

A total of 97 wart cases fulfilling inclusion criteria were taken after getting approval from hospital ethical committee. All cases were included after taking informed consent. Initially, warts were anaesthetized with 0.1 ml of prilocaine which is equivalent to 20 mg/ml. Then, 21-gauge syringe was used to administer 0.2 ml of vitamin D₃ which was equivalent to 7.5 mg/ml at the base of each wart slowly. According to the treatment protocol vitamin D₃ was administered on monthly basis with maximum of two sessions. Per session, the maximum dose of 7.5 mg was administered. All procedure was done by consultant dermatologist having more than 5 years of experience. The treatment response $\geq 50\%$ was recorded as efficacious as per operational definition at 3rd month. All data was recorded by researchers themselves on prescribed proforma.

Results

There were 38 cases with ages of 18-39 years old and 59 cases with of 40-60 years old. There were 56 male and 41 female cases. According to types of warts, 41 cases had Plain, 26 cases had Filiform and 30 cases had Verrucous type of warts (**Figure 1**). A total of 79 (81.4%) cases

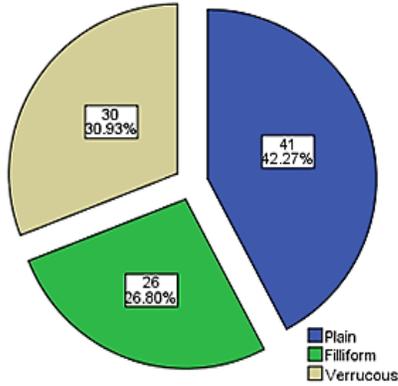


Figure 1 Distribution of warts types.

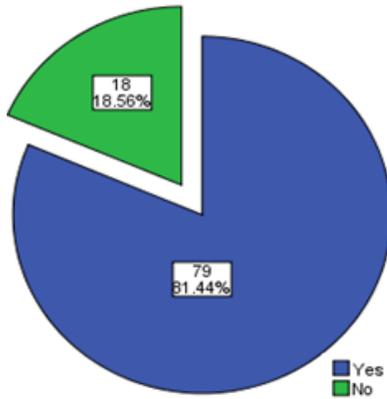


Figure 2 Distribution of efficacy of treatment.

achieved efficacy of treatment while in 18(18.6%) cases efficacy was not seen (**Figure 2**).

When data was stratified for age, in 18-39 years cases efficacy was seen in 81.6% while in 40-60 years old cases efficacy was seen in 81.4% cases. The frequency of efficacy was statistically same in both age groups, p-value >0.05 (**Table 1**).

In male cases efficacy was seen in 85.7% while in female cases efficacy was seen in 75.6% cases. The frequency of efficacy was statistically same in both genders, p-value >0.05 (**Table 2**).

In Plain form of warts efficacy was seen in 82.9%, in Filliform for of warts efficacy was seen in 76.9% cases and Verrucous form of warts efficacy was seen in 83.3% of the cases.

Table 1 Comparison of efficacy with respect to age groups (years).

Age (years)	Efficacy		Total
	Yes	No	
18-39	31(81.6%)	7(18.4%)	38(100.0%)
40-60	48(81.4%)	11(18.6%)	59(100.0%)
Total	79(81.4%)	18(18.6%)	97(100.0%)

Chi-square = 0.001, P-value = 0.978 (Insignificant).

Table 2 Comparison of efficacy with respect to gender.

Gender	Efficacy		Total
	Yes	No	
Male	48(85.7%)	8(14.5%)	56(100.0%)
Female	31(75.6%)	10(24.4%)	41(100.0%)
Total	79(81.4%)	18(18.6%)	97(100.0%)

Chi-square = 1.599, P-value = 0.206 (Insignificant).

The frequency of efficacy was statistically same in different types of warts groups, p-value > 0.05 (**Table 3**).

Efficacy was seen 77.5% cases who had duration of disease <6 months and 92.3% of cases who had duration of disease since ≥6 months. The frequency of efficacy was statistically same in all types of duration (**Table 4**).

Discussion

Warts are common and benign epidermal growths affecting all age groups. They are caused by different strains of human papillomavirus. They are mostly asymptomatic and have an unsightly appearance.¹

Recalcitrant warts continue to increase in number and size despite treatment with conventional therapeutic options.¹¹ They are

Table 3 Comparison of efficacy with respect to types of warts.

Types of warts	Efficacy		Total
	Yes	No	
Plain	34(82.9%)	7(17.1%)	41(100.0%)
Filliform	20(76.9%)	6(23.1%)	26(100.0%)
Verrucous	25(83.3%)	5(16.7%)	30(100.0%)
Total	79(81.4%)	18(18.6%)	97(100.0%)

Chi-square = 4.482, P-value = 0.786 (Insignificant)

Table 4 Comparison of efficacy with respect to duration of disease.

Duration of disease	Efficacy		Total
	Yes	No	
< 6 mon.	55(77.5%)	16(22.5%)	71(100.0%)
≥6 mon.	24(92.3%)	2(7.7%)	26(100.0%)
Total	79(81.4%)	18(18.6%)	97(100.0%)

Chi-square = 2.774, P-value = 0.096 (Insignificant).

frustrating and infuriating to the patient and physician. Primary treatments include topical treatment with imiquimod, salicylic acid and 5-fluorouracil, excision, cryotherapy, electrocautery and laser vaporization.¹⁵ Conventional treatment options are not considered best for patients with distant lesions as they act locally.

Recently, treatment with immunotherapy has been used to overcome this shortcoming.¹⁶ In this regard, many treatment options are available like immune stimulants, including pro-inflammatory cytokines (IL-2), interferons, candida and trichophyton, intralesional antigens like PPD (purified protein derivative), vaccines like the MMR, BCG (bacillus calmette guerin) and Mycobacterium W; immune enhancers like zinc sulfate and sensitizers like topical diphencyprone.¹⁷

Stimulation of cell mediated immunity by targeted therapy enables patient's immune system to combat warts and human papilloma virus. Immunotherapy is cost effective and has high recovery rates. Vitamin D regulates both cytokine production and epidermal proliferation. It also serves as an immunotherapeutic agent when used as an intralesional injection.¹³

In current study, the mean age of all cases was 40.94±11.53 with minimum and maximum age as 18-60 years. There were 56 (57.7%) male and 41 (42.3%) female cases. A total of 79 (81.4%) cases showed efficacy while in 18 (18.6%) cases showed no efficacy. Efficacy was seen in 77.5% cases who had duration of disease <6 months

and 92.3% of cases who had duration of disease since ≥6 months.

Similar results were found in 2015, in a study conducted by Aktas *et al.* that showed the efficacy of intralesional vitamin D₃ treatment for plantar warts. 16 out of 20 patients (80%) showed complete clearance of warts while one patient showed partial response and no response was observed in three patients. No adverse effects and recurrence were observed.¹³

Kavya *et al.* observed the efficacy of intralesional vitamin D₃ in treatment of warts. 78.57% of patients (33 out of 42 patients) showed complete resolution of warts, while remaining patients showed mild-moderate response and recurrence was observed in one patient. No adverse effects were reported.¹⁸ These results are aligned with our results having effectiveness in 80% patients with no recurrence and side effects.

Raghukumar *et al.* performed a study to evaluate the immunotherapeutic action of vitamin D₃ in treatment of warts along with its topical effects. 90% of patients showed complete eradication of warts. Their study showed comparable effectiveness of vitamin D₃ treatment as that of our study.¹⁴

Conclusion

The intralesional vitamin D₃ injection was highly effective in treatment of warts with no recurrence in these cases. It was also safe and an inexpensive treatment. In future further research with large sample size can be more beneficial to reveal its effectiveness and safety in the treatment of this common skin problem of the society.

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