

COMPARISON OF INTRALESIONAL VITAMIN D3 VERSUS CRYOTHERAPY FOR MANAGEMENT OF PLANTAR WARTS

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ABSTRACT

Objective: To compare the frequency of success of intralesional vitamin D3 versus cryotherapy for management of patients with plantar warts.

Study Design: Quasi experimental study.

Place and Duration of Study: Department of Dermatology, Pak Emirates Military Hospital, Rawalpindi, from Aug 2016 to Feb 2017.

Methodology: Total 60 patients, fulfilling the selection criteria, were included in the study. The patients were randomly divided in two groups by using lottery method. In group 1, Vitamin D3 was injected into the base of the warts after local anaesthetic agent, prilocaine. In group 2, cryotherapy was done by using a high-intensity regimen of one session every two weeks till 6 weeks. All patients were followed-up in Out-Patient Department (OPD) for 13 weeks. After 13 weeks, condition of warts was assessed. In case of complete resolution of warts, the success was labeled.

Results: In this study success rate of intralesional D3 was 63.3% and for cryotherapy success rate was 43.3% (p -value=0.121). Stratification of age and gender did not show any statistically significant difference between success rates of both treatment modalities. However patients with history of shorter duration ranging in between 11-15 days showed significant higher success rate for intralesional vitamin-D3 as compared to cryotherapy.

Conclusion: Frequency of success of intralesional vitamin-D3 was more than that of cryotherapy for treating planter warts.

Keywords: Cryotherapy, Intralesional Success, Plantar warts, Vitamin-D3.

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INTRODUCTION

Human papillomavirus (HPV) infection causes plantar warts, a common skin infection of foot and a therapeutic challenge despite many treatment options available¹.

More than 150 types of the human papillomavirus (HPV) causing plantar warts have been found, which probably infect the skin via areas of minimal trauma. Risk factors include use of communal showers, occupational handling of meat and immunosuppression. Warts are harmless and resolve as a result of natural immunity in immunocompetent individuals however HPV can remain infective for months or years^{2,3}.

Multiple modalities exist to combat plantar warts as they are more refractory to treatment than common warts². Many treatment options have been used with varying efficacies including destructive therapy, virucidal therapy, antimetabolic therapy, and immunotherapy (as well as a combination of these) are commonly being used with varying efficacies¹.

Many of the available therapeutic modalities for plantar warts are associated with unsatisfactory results and high recurrence rates so plantar warts treatment represents a continuing challenge for dermatologists. Efficacy of intralesional immunotherapy by different antigens in the treatment of all types of warts is proved in several clinical trials⁴.

Cryotherapy is widely used as first line therapy for the treatment of cutaneous warts. A

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study conducted by Bruggink *et al* has shown that with cryotherapy, success (complete resolution of warts) was achieved in 39.5% of patients⁵. In another study it was observed that patients of plantar warts who received intralesional vitamin-D3, showed complete resolution of warts (success) in 80% cases⁶.

Rationale of this study was to compare the frequency of success of intralesional vitamin-D3 versus cryotherapy for management of patients with plantar warts. We wanted to conduct this study to get local data so that in future we may be able to implement the use of more appropriate options for management of plantar warts. This will improve our practice and contribute to update local guidelines to manage such cases in future.

METHODOLOGY

This quasi experimental study was conducted at department of Dermatology, Pak Emirates Military Hospital Rawalpindi from 4th August 2016 till 5th February 2017. A sample size of 60 cases was calculated with 80% power of test, 5% level of significance and taking expected percentage of success i.e. 80% with intralesional vitamin-D3 and 49% with cryotherapy for management of warts.

sampling technique non probability consecutive sampling sample selection inclusion criteria patients of age between 20-70 years, either gender presenting with plantar warts (as per operational definition) exclusion criteria patients not willing for follow up recurrence of warts. Patients who had more than five warts (on clinical examination) Immunocompromised patients (on clinical examination) Patients with genital warts, seborrheic warts or warts >1cm in diameter (on clinical examination) Patients having undergone treatment for warts during last 2 months were excluded from this study.

After approval from hospital ethical committee, 60 patients, fulfilling the selection criteria were included in the study from OPD of Department of Dermatology, Pak Emirates Military Hospital, Rawalpindi. Written informed consent

was taken from all the patients. Demographic details including name, age, gender, duration of warts were also recorded. Then patients were randomly divided in two groups by using lottery method. In fig-1, Vitamin-D3 (0.2 mL, 7.5 mg/mL) was injected into the base of the warts after local anaesthetic agent prilocaine (0.1 mL, 20 mg/mL) injection. A maximum of 5 warts were treated in 1 session, with at maximum 2 injections performed at 4-week intervals. In fig-2, cryotherapy was done by using a high-intensity regimen of one session every two weeks till 6 weeks. During each session, the patients received three serial applications in which a wad of cotton wool saturated with liquid nitrogen was applied over the lesion. Each application was executed until a frozen halo of 2mm around the base of the wart appeared (usually after 2-10 seconds). Then all patients were followed-up in OPD for 13 weeks. After 13 weeks, condition of warts was assessed and if there was complete resolution of warts, then success was labeled (as per operational definition).

SPSS-21 was used for data entry and analysis. The quantitative variables and were presented as Mean \pm SD were. The qualitative variables were presented as frequency and percentage. Chi-square test was applied to compare success in both groups. The *p*-value ≤ 0.05 was taken as significant.

RESULTS

A total of 60 patients were included in study. Mean age of patients in IV-D3 and in cryotherapy group was 32.80 ± 8.65 and 32.87 ± 1.13 years respectively. In IV-D3 group 24 male and 6 female were included and in cryotherapy group 22 male and 8 female patients were included.

Average number of warts in IV-D3 and in cryotherapy group was 2.50 ± 1.00 and 2.47 ± 1.07 respectively (table-I). Mean duration of warts in IV-D3 and in cryotherapy group was 8.93 ± 5.58 and 7.60 ± 4.45 weeks. Effect of treatment of IV-D3 and cryotherapy (figure).

In IV-D3 group success of treatment was seen in 63.3% patients while in cryotherapy

group success was seen in 43.4% patients only (table-II). Success rate of IV-D3 was significantly higher in patients in the age group 41-50 years while in other age groups i.e. 19-30 years and 31-40 years no statistically significant difference was seen for success rate in both treatment groups (table-III).

Gender had no effect on the success of treatment. Patients with 1-5, 6-10 and 16-20 weeks of duration of warts did not show any statistically

Table-I: Descriptive statistics for number of wart .

	IV-D3	Cryotherapy
Mean ± SD	2.50 ± 1	2.47 ± 1.07
Minimum	1	1
Maximum	4	4

significant difference for success rate in each group (table-IV).

DISCUSSION

The conventional modalities being used in treatment of warts include destructive therapies such as salicylic acid, trichloroacetic acid,

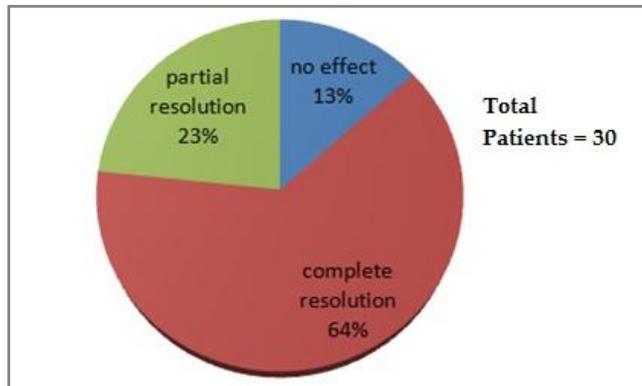


Figure: Treatment effect.

cryotherapy, silver nitrate, phenol, canthiridin, surgical interventions and lasers; antiproliferative agents such as bleomycin, vitamin-D3 analogs, podophyllin, podophyllotoxin, and 5-fluoro uracil; antiviral agents such as cidofovir and retinoids⁷. Immunotherapy is becoming more and more popular, especially in the treatment of refractory cutaneous and genital warts because of cumbersome procedures of conventional modalities and a high risk of recurrence⁸⁻¹⁰.

We have two main therapeutic options for the treatment of warts either conventional destructive and aggressive method like chemical cautery, cryotherapy, electrocauterization, surgical excision, and laser ablation. Second choice available is immunotherapy, which is based on the activation of the immune system leading to suppression of viral activity in skin lesions. This therapy is administered topically, through intra-

Table-II: Success of Treatment.

Success	IV-D3	Cryotherapy	p-value
Yes	19 (63.3%)	13 (43.4%)	0.121
No	11 (36.7%)	17 (56.7%)	
Total	30	30	

Table-III: Success of Treatment Stratified for age.

Age	Success	IV-D3	Cryo-therapy	p-value
19-30	Yes	6 (50%)	8 (57.1%)	0.716
	No	6 (50%)	6 (42.9%)	
31-40	Yes	6 (54.5%)	2 (25%)	0.198
	No	5 (45.5%)	6 (75%)	
41-50	Yes	7 (100%)	3 (37.5%)	0.010
	No	-	5 (62.5%)	
	No	2 (33.3%)	5 (62.5%)	

Table-IV: Success of Treatment Stratified for duration of wart (weeks).

Duration	Success	IV-D3	Cryo-therapy	p-value
1-5	Yes	5 (50%)	5 (38.5%)	0.580
	No	5 (50%)	8 (61.5%)	
6-10	Yes	8 (72.7%)	4 (50%)	0.311
	No	3 (27.3%)	4 (50%)	
11-15	Yes	3 (100%)	2 (28.6%)	0.038
	No	-	5 (71.4%)	
16-20	Yes	3 (50%)	2 (100%)	0.206
	No	3 (50%)	-	

lesional injection or given systemically^{11,12}.

Other immunotherapeutic agents like Corynebacterium parvum, contact immunotherapy, glycyrrhizinic acid, Echinacea, green tea extracts, and intralesional vitamin-D3 are being tried with variable results. Intralesional administration of agents i.e.

Measles, mumps, rubella vaccine; and Candida albicans antigen immunotherapy have shown promising results in treatment of warts¹¹.

In literature some cases of viral warts have been treated successfully with topical vitamin-D3. It acts via regulation of epidermal cell proliferation, differentiation and cytokine production modulation. Expression of antimicrobial peptide is mediated by upregulation of vitamin-3D receptors in the skin^{9, 10, 13}. To the best of our knowledge, intralesional vitamin-D3 is not been used for the treatment of warts.

Although success rate of IV-D3 in our study was higher as that of cryotherapy but it did not achieve statistical significance. Stratification of age and gender did not show any statistically significant difference between success rates of both treatment modalities. However patients with shorter duration ranging in between 11-15 days showed significant higher success rate for IV-D3 as that of cryotherapy.

A study conducted by Bruggink *et al* showed 39.5% success with cryotherapy in patients with plantarwarts success⁵. Aktaş *et al* in his study reported 80% cases of plantar warts showing complete resolution (success) with intralesional vitamin-D3⁶. His findings were in line with the results of our study showing higher success rate of IV-D3 for treating planter warts. Success rate of cryotherapy, reported by different studies ranges in between 13.6%-65.5%^{6,14,15}.

Side effects reported with cryotherapy are local pain, swelling, blister formation, ulceration, secondary infection, dyspigmentation, contracted scar, hypertrophic scar, skin atrophy and paraesthesia¹⁶.

Although vitamin-D3 mechanism of action is not clear against warts; it controls cell proliferation, differentiation and immunoregulation. Vitamin-D3 receptor (VDR) present over keratinocytes, melanocytes, fibroblasts, and immune system cells of the skin are targeted by vitamin-D3^{16,17}. Warts which are unresponsive to conventional therapy may be treated with intalesional vitamin-D3 as it is well tolerated, simple to administer in outpatient clinics. However large randomized placebo controlled clinical trials are

required to prove its efficacy in treatment of refractory warts¹⁸.

Few limitations were observed in our study like small sample size and inability for long term follow up of patients for recurrence of disease. Plantar warts in immunocompromised patients are difficult to treat and they were not included in the study. It is recommended that in future, studies may be carried out regarding role of vitamin-D3 not only in plantar warts but also in all types of warts.

CONCLUSION

Success rate of intralesional vitamin-D3 is higher as compared to that of cryotherapy in treating plantar warts.

CONFLICT OF INTEREST

There is no conflict of interest in this study to be declared by any author.

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