Comparative study of therapeutic efficacy of intralesional vitamin D3 versus intralesional purified protein derivative in the treatment of warts

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Abstract

Introduction: Warts are benign epidermal proliferations of skin and mucosa caused by human papilloma virus. Destructive therapeutic modalities are limited by cost, pain, scarring. Immunotherapy is a new modality which acts on enhancing cell mediated immunity.

Objective: This study aims to evaluate and compare efficacy of intralesional vitamin D3 and purified protein derivative (PPD) in treatment of warts.

Materials and Methods: It is a prospective hospital based comparative study among 40 patients with warts. Patients were randomly and equally divided. Group A patients were given intralesional vitamin D3 (0.2ml of 15mg/ml into each wart) and Group B patients were given intralesional PPD (0.2ml of 5TU/ml into each wart). The injections were repeated every 2 weeks until complete clearance. Decrease in size and number of lesions were evaluated and photographic record was maintained. Patients were followed up after 3 months. Unpaired t test was used for statistical analysis.

Results: The study found that 14 out of 20 patients (70%) of Group A showed complete response after 4 sessions and 6 patients (30%) showed moderate response. 17 out of 20 patients (85%) of Group B showed complete response, 2 patients (10%) showed moderate response, 1 patient (5%) showed no response. Recurrence was observed in 1 patient after 3 months who received vitamin D3. No serious adverse effects were observed.

Conclusion: Both vitamin D3 and PPD showed positive results with PPD having faster and better efficacy in treatment of multiple common warts.

Keywords: Immunotherapy, Warts, Intralesional, Vitamin D3, Tuberculin purified protein derivative.

Introduction

Warts are one of the commonest skin infections of the epidermis caused by virus i.e. human papillomavirus (HPV). Destruction of local tissue is the method used commonly in the treatment of warts which is not practical in cases of multiple lesions, facial lesions because it might lead to scarring or pigmentation.

Various destructive modalities like electrocoagulation, cryotherapy, laser surgery, 5-fluorouracil etc. are used in treating warts. These treatments are expensive, time consuming, painful and are associated with recurrences.[1,4]

Immunity plays an important role in clearance of warts. Warts are known to undergo spontaneous regression due to development of cell mediated immunity to the virus. Therefore immunotherapy is a potential modality to treat warts which depends on the principle of enhancing the cell mediated immunity. Immunotherapy can cause complete resolution without scarring and decreased recurrences.[5,7]

Several studies have been done in the past with various immunotherapeutic agents like trichophytin, candidin, measles, mumps, rubella (MMR) vaccine, purified protein derivative, intralesional vitamin D3, cimetidine, imiquimod, interferons.[8,1]

Aims and Objectives

The present study is taken up with an objective to prove and compare the efficacy of intralesional tuberculin purified protein derivative and intralesional vitamin D3 in the treatment of warts.

Materials and Methods

The study was conducted between February 2018 and August 2018. Patients with warts, attending the department of Dermatology in A.J. Institute of Medical Sciences, Mangalore, were taken up for the study. A proper clinical history with detailed examination and a written informed consent was obtained from all the patients. A total of 40 patients who were aged ≥ 18 years having single or multiple viral warts, with no other concurrent treatment for warts were taken up for the study. Patients with active systemic illness/ infection, pregnant and lactating women, patients on immunosuppressive drugs, patients with genital warts and those with keloidal tendency were excluded from the study. Institutional ethics committee clearance had been obtained for the study 40 patients with warts were taken up for the study and were randomly divided into 2 groups i.e. group A and group B, the patients were explained regarding the objectives as well as the method of study.

Group A: Patients were given intralesional injection of 0.2ml of 15mg/ml (6 lakh IU) vitamin D3 per wart.

Group B: Patients were given intralesional injection of 0.2ml of 5TU/ml purified protein derivative (PPD) per wart.

Injections were repeated every 2 weeks until complete clearance. Response was evaluated by decrease in size and number of lesions and photographic record was maintained.

The response was evaluated as:

1. Complete response – complete absence of clinically apparent wart
2. Partial response – decrease in size > 25%
3. No response – < 25% decrease in size.

Patients were followed up for 3 months after the last injection to detect any recurrence. Unpaired t test, chi-square test were used for statistical analysis.

Results

In this study the maximum number of patients were in the age group of 20- 40 years which was 28 (70%) followed by >40 years which was 12 (30%). The age of patients in group A, who received intralesional vitamin D3 ranged between 18-60 years with mean age ± standard deviation (SD) 25.1± 4.41 and that of group B, who received PPD ranged between 20-60 years with mean age ± standard deviation (SD) 26.95± 5.49 as shown in Table 1.

Table 1: Distribution of patients according to age

Age of Patients	Group A (VIT D3)	Group B (PPD)
Range (years)	18-60	20-60
Mean Age ± SD	25.1 ± 4.41	26.95 ± 5.49

Male outnumbered female in both the groups with male: female ratio of 1.8:1 and 1.2:1 in group A and B respectively as shown in table 2.

Table 2: Gender distribution in both groups

Group	Male	Female	Male : Female
A (VIT D3)	13	7	1.8:1
B (PPD)	11	9	1.2:1

Amongst group A and B patients majority of the patients had verruca vulgaris followed by plantar warts and periungual warts. Distribution of patients according to the type of wart is depicted in Fig. 1.

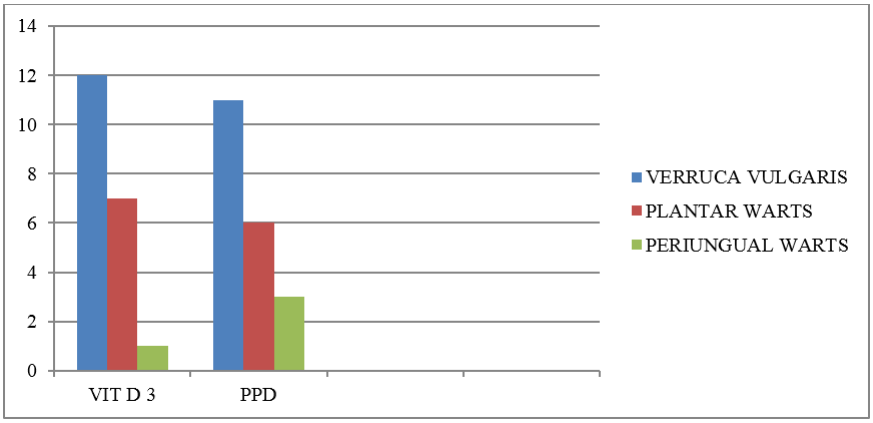

Fig. 1: Distribution based on type of warts

The study showed that in group A who received intralesional vitamin D3 out of 20 patients, 14 (70%) showed complete clearance while 6 patients (30%) showed partial response (shown in Fig. 2)

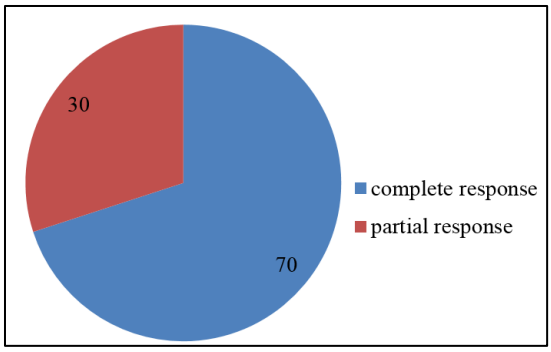

Fig. 2: Response with vitamin D3

In group B, patients who received intralesional PPD, out of 20 patients 17 (85%) showed complete response, 2 patients (10%) and 1patient (5%) showed no response (shown in Fig. 3)

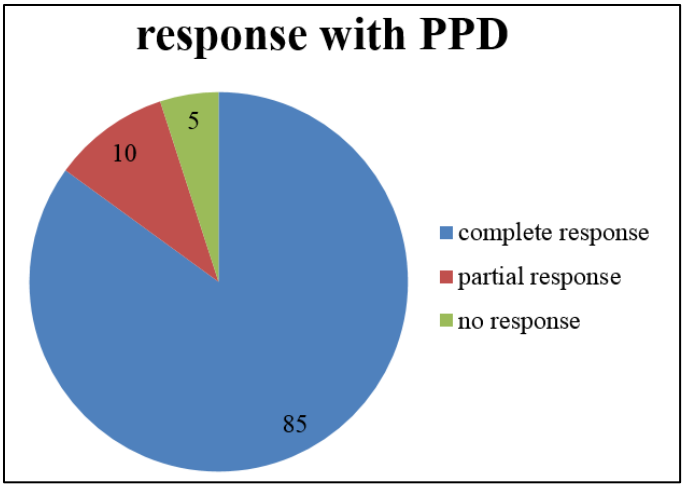

Fig. 3: Response with PPD Comparison of responses with vitamin D3 and PPD are shown in Fig. 4

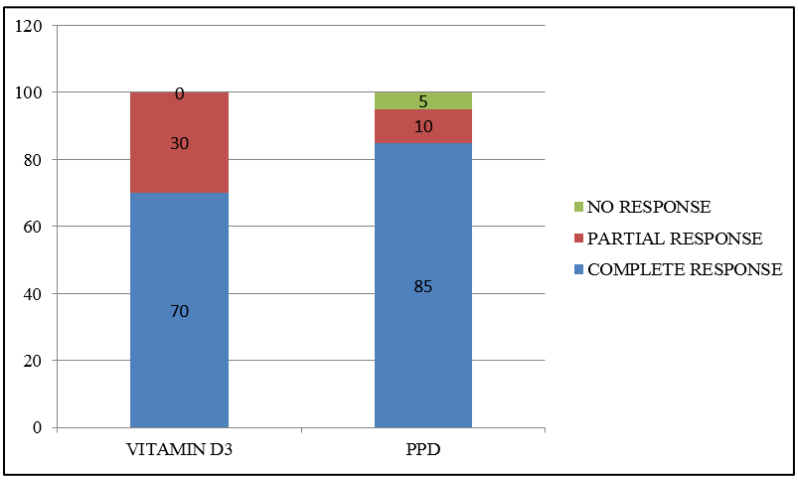

Fig. 4: Comparison of responses with vitamin D3 and PPD

Different outcomes are observed with both the drugs when injected into various types of warts. In group B patients complete clearance is seen in 90.9% of patients with verruca vulgaris and that of group A complete clearance was seen in 83.3% in case of plantar warts complete clearance was seen in 83.3% and 42.8% in group B and group A respectively. Efficacy of vitamin D3 and PPD is compared in different types of warts as shown in table 3.

Table 3: Efficacy of both drugs in various types of warts

Type of wart	Count	Response						P Value
		Vit D3			PPD			
		Complete	Partial	No	Complete	Partial	No	
Verruca vulgaris	Number	10	2	-	10	-	1	0.58
	%	83.3%	16.66%	-	90.9%	-	9%	
Plantar	Number	3	4	-	5	1	-	0.13
	%	42.8%	57.1%	-	83.3%	16.6%	-	
Periungual	Number	1	-	-	2	1	-	0.70
	%	100%	-	-	66.6%	33.3%	-	

P value obtained by applying unpaired t test to the above data is greater than 0.05 thus the difference is not considered as statistically significant. No recurrences were observed at the end of follow up period. Patients

experienced adverse effects like mild pain at the injection site and swelling which subsided on its own. No serious adverse effects observed.

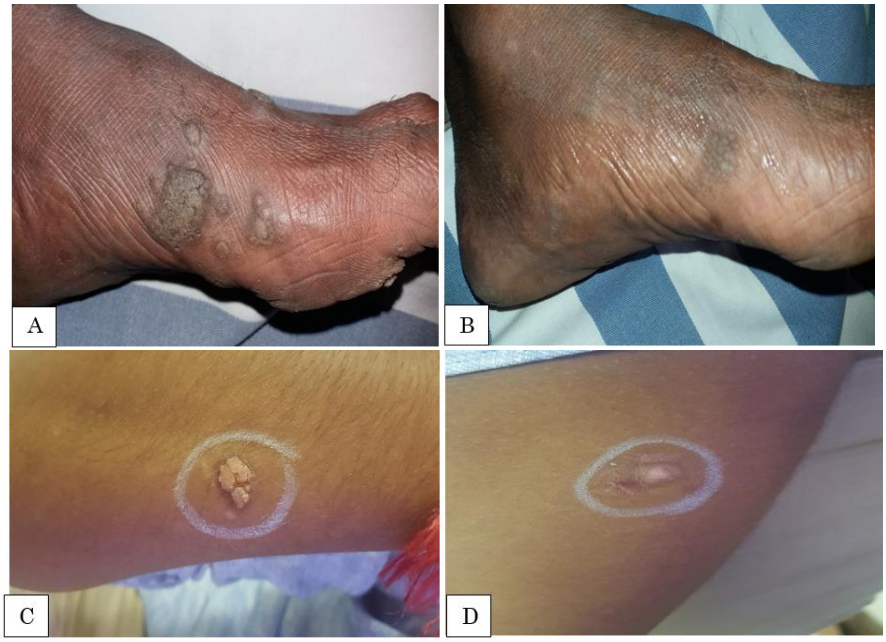

Fig. 5: (A) pre procedure; (B): post procedure photographs of plantar warts after intralesional vitamin D3; (C): Pre and; (D): Post procedure photographs of verruca vulgaris after intralesional vitamin D3 (from left to right)

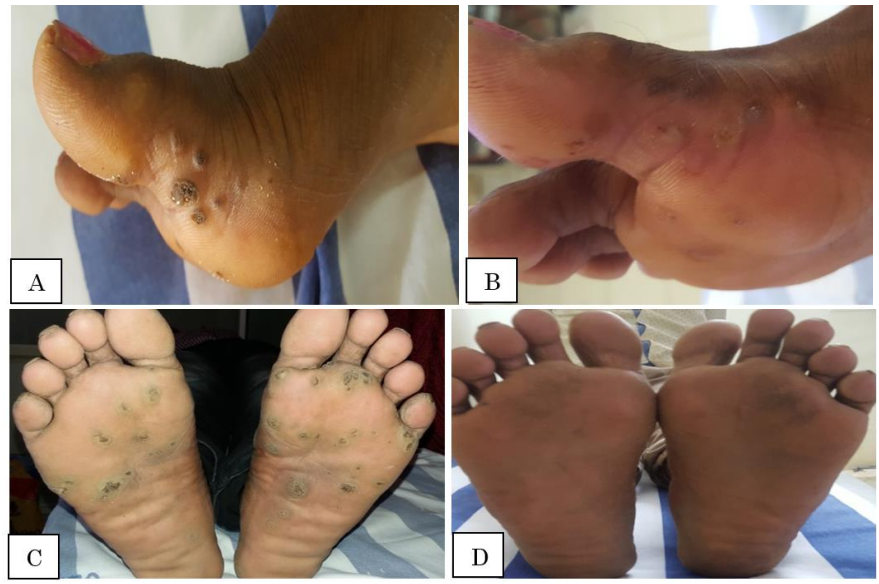

Fig. 6: (A, C) pre and post (B,D) procedure photographs of plantar warts in two patients after intralesional PPD

Discussion

Immunotherapy is emerging as a new modality in the treatment of warts. Immunotherapy is defined as a type of biological therapy that uses substances to stimulate or suppress the immune system to help the body to fight cancer, infection and other diseases. It mounts a delayed type hypersensitivity response to various antigens and wart tissue which helps in clearing local as well as distant warts. Various intralesional immunotherapeutic agents are used in treatment of warts, for example, purified protein derivative, vitamin D3, MMR vaccine, BCG vaccine, candida, trichophytin antigen etc.[13-17] The present study clearly demonstrates that warts can be treated successfully with intralesional vitaminD3 and PPD injection.

The role of vitamin D3 in treatment of warts is still not well understood. The probable mechanism if vitamin D3 in treatment of warts was proposed to be due to its ability to regulate epidermal cell proliferation and differentiation and modulate cytokine production. It can also lead to induction of anti-microbial peptide expression in the skin.[18,19] According to a research conducted earlier injecting PPD into the wart, which is caused due to the infection by human papilloma virus (HPV), induces cell mediated immunity nonspecifically by production and activation of Th1 cytokines which will activate cytotoxic and natural killer cells which help in eradicating HPV.[16-19]

In our study, out of 20 patients who received vitamin D3, majority (60%) had verruca vulgaris, followed by (35%) plantar warts and then (5%) periungual warts. Amongst 20 patients who received PPD, majority (55%) had verruca vulgaris, then plantar warts (30%) and then followed by periungual warts (15%).

In our study, amongst group A patients, 70% of patients showed complete response and 30% of patients showed partial response. These results are comparable to studies done by Kavya M et al (78.5%)[22] and Aktas et al (70%).[23] Also previously a study done by Raghu Kumar et al with intralesional vitamin D3 on 64 patients having warts showed that 90% of patients had complete clearance and 6.66% of the patients showed partial response.[24]

Amongst group B patients, 85% of patients showed complete response, 10% showed partial response and 5% of the patients showed no response. These results are similar to the results obtained by studies done by Wananukul et al (93%) and Nimbalkar et al (80%).[25,26]

In our study, we observed that efficacies varied among the two drugs in different types of warts. When given to verruca vulgaris patients complete clearance was observed in 90.9% of patients who received PPD and 83.3% of patients achieved complete clearance who received vitamin D3. In case of plantar warts complete clearance rates were 83.3% and 42.8% and partial response rates were 16.6% and 57.1% with PPD and vitamin D3 respectively. This shows that PPD is more effective in treatment of plantar warts than vitamin D3. When vitamin D3 was injected into periungual warts 100% complete clearance is seen and with PPD the complete and partial responses are 66.6% and 33.3% respectively.

The number of sessions required achieving complete response varied between both the drugs with PPD ranging from 3-4 sessions and vitamin D3 required more than 6 sessions. No recurrences were observed in patients who received PPD one patient who received vitamin D3 reported relapse at the same site.

Immunotherapy with vitamin D3 and PPD are well tolerated. The side effects observed were minimal and not serious. The common side effects noted were pain at the time of injection, mild swelling and erythema. Both are cost effective with PPD slightly cheaper than vitamin D3.

Overall, both the modalities proved to be effective in treatment of warts with intralesional PPD being superior over vitamin D3.

Conclusion

Both vitamin D3 and PPD were found to be effective and well tolerated. Amongst the two drugs, Intralesional PPD is found to be more effective in terms of efficacy, less number of sessions and no relapse. It is safe and simple to perform and has no serious side effects.

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Conflicts of Interest: None.

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