



CODEN [USA]: IAJPB

ISSN: 2349-7750

INDO AMERICAN JOURNAL OF  
PHARMACEUTICAL SCIENCES

<http://doi.org/10.5281/zenodo.2638946>

Available online at: <http://www.iajps.com>

Research Article

EFFICACY OF INTRALESIONAL VITAMIN D3 THERAPY  
VERSUS CRYOTHERAPY IN THE TREATMENT OF  
PLANTAR WARTS

Dr. Muhammad Khurram Shahzad\*, Dr. Ayesha Ambreen\*\*, Dr. Javed Iqbal\*\*\*

\*Department of Dermatology, Nishtar Hospital, Multan

\*\*Department of Histopathology, Combined Military Hospital, Multan

\*\*\*Independent Medical University, Faisalabad

Article Received: February 2019 Accepted: March 2019 Published: April 2019

**Abstract:**

**Objective:** Comparison between intralesional vitamin D3 therapy and cryotherapy in the treatment of plantar warts.

**Methods:** A total of 128 patients aged between 18-35 years, having plantar warts, were randomly assigned into groups A and B (n=64, in each group. Patients in group A were given intralesional injection of vitamin D3 in each wart at 4 week interval for a maximum of 2 sessions. Patients in group B were given cryotherapy at weekly intervals for a maximum of 5 sessions. Patients were followed at 2<sup>nd</sup>, 3<sup>rd</sup> and 6<sup>th</sup> week, and both therapies were compared.

**Results:** Out of 128 patients, 69 (53.91%) were males and 59 (46.09%) were females with male to female ratio of 1.2:1. The mean efficacy of intralesional vitamin D3 therapy was seen in 85.63% patients, while efficacy of cryotherapy was seen in 62.61% patients (p=0.002).

**Conclusion:** This study concluded that intralesional vitamin D3 has more efficacy than cryotherapy in the treatment of plantar warts.

**Keywords:** plantar warts, vitamin D3, intralesional cryotherapy.

**Corresponding author:**

Dr. Muhammad Khurram Shahzad,  
Department of Dermatology, Nishtar Hospital,  
Multan, Pakistan  
Cell No. +923354847957  
E-mail: [dr.khurram178@gmail.com](mailto:dr.khurram178@gmail.com)

QR code



Please cite this article in press Muhammad Khurram Shahzad et al., *Efficacy of Intralesional Vitamin D3 Therapy Versus Cryotherapy in The Treatment Of Plantar Warts.*, Indo Am. J. P. Sci, 2019; 06(04).

**INTRODUCTION:**

Planter warts are benign proliferations of skin and mucosa caused by the human papillomavirus (HPV)<sup>1</sup> caused by HPV genotypes 3 and 10.<sup>2</sup> Clinically they present as firm papules with irregular surface (ranging in size  $\leq 1\text{mm}$  to  $\geq 100\text{mm}$ ) and can coalesce to form large masses.<sup>3</sup> They are more common among the children and young people<sup>4</sup> and are mostly painful when infected.<sup>5</sup> Plantar warts may eventually clear up naturally, but this may take couple of weeks to years. However, most patients desire faster relief.<sup>6</sup> Destructive modalities like podophyllotoxin, trichloroacetic acid, cantharidin, 5-fluorouracil, bleomycin, electrocautery, cryotherapy, curettage, surgical excision, laser ablation and photodynamic therapy have been used previously to treat planter warts, which are painful and recurrence is high.<sup>6</sup> Cryotherapy/cryosurgery remains one of the commonly used methods for treating warts and response rate to this modality range from 39% to 60%.<sup>7,8</sup> Recently researchers used Vitamin D3 topically and intralesional injections for the treatment of viral warts.<sup>9</sup> Vitamin D3 has shown its biological actions in epidermal cells resulting in cell proliferation, differentiation and the modulation of cytokine production.<sup>10</sup> Intralesional vitD3 therapy resulted complete clearance of recalcitrant viral warts in 80% and 90% patients, and it is declared safe and inexpensive treatment for recalcitrant warts.<sup>11</sup> However, an efficient treatment resulting in high efficiency has not been explored yet.<sup>12</sup> Intralesional vitamin D3 therapies, has not been practiced in Pakistan previously, therefore, this study was planned to compare the efficiency of intralesional vitamin D3 injection versus cryotherapy in the treatment of viral warts.

**METHODS:**

Present study was conducted on 128 patients suffering from planter warts in the Department of Dermatology, Nishtar Medical College Multan during 6<sup>th</sup> October 2016 to 5<sup>th</sup> April 2017. Approval from ethical committee of the hospital was taken before conduction of clinical trial. Patients included in the study were male and females aged between 18-35 years, having characteristic hyperkeratotic firm papules of  $\leq 3$  in number and  $\leq 3$  cm in size with a rough surface present on soles examined grossly, suffering for  $< 3$  months, have not taken any therapy for warts previously and willing to participate in clinical trials with a written consent. The excluded

criteria, was pregnant/lactating women, patients having periungual warts suffering from cauliflower-like thickened skin located in the longitudinal groves of the proximal nail folds, diabetics, hypertensive and lost follow ups.

Patients were randomly assigned in to two equal groups (n=64). Group A, patients were given 0.2 ml of vitamin D3 (7.5 mg/mL) as intralesional injection into the base of each wart after giving prilocaine (0.1 mL of 20 mg/mL). A maximum of 2 injections were given at 4-week interval. Patients in group B were given cryotherapy at weekly intervals for a maximum of 5 sessions. Cryotherapy was performed by applying liquid nitrogen with a cotton tip applicator for 10 to 30 seconds, till the ice ball formation spreaded to involve 1 mm margin of surrounding normal skin. Patients were followed at 2<sup>nd</sup>, 3<sup>rd</sup>, and 6<sup>th</sup> week. At the completion of trial, treatment modalities were evaluated by percent efficacy in respect of gender, age of patient; numbers and size of warts and duration of the disease. Independent-Samples T-Test was applied and 2-tail significance was calculated to determine the variation between means using SPSS computer software.

**RESULTS:**

Data regarding the percent efficacy of intralesional vitamin D3 therapy and cryotherapy are presented in table 1. A number of 69 men and 59 women qualified the inclusive criteria for this study. Females showed significantly ( $P < 0.005$ ) higher response to intralesional vitamin D3 therapy in treating planter warts compared to males. While, non-significant ( $P < 0.185$ ) difference was recorded between intralesional vitamin D3 injection and cryotherapy in males.

Efficacy of both modalities in treatment of planter warts was significantly ( $P < 0.005$ ) high in patients of low age (18-25 years) group compared to patients of high age (26-35 years) group. Efficacy of intralesional vitamin D3 therapy (85.19%) was significantly ( $P < 0.005$ ) higher than that of cryotherapy (48.0%) in high age group. Patients having 1-2 planter warts showed significantly ( $P < 0.05$ ) higher response to both of the modalities, however, the efficiency of intralesional vitamin D3 therapy was significantly ( $P < 0.021$ ) higher compared to cryotherapy. The efficacy of intralesional vitamin D3 therapy in the treatment of planter warts of various sizes and of various durations was significantly higher

than that of cryotherapy. Moreover, warts of smaller size ( $\leq 1.0$  cm) and of short duration (1-6 week) showed significantly higher response to both therapies. The overall mean efficacy of intralesional vitamin D3 therapy

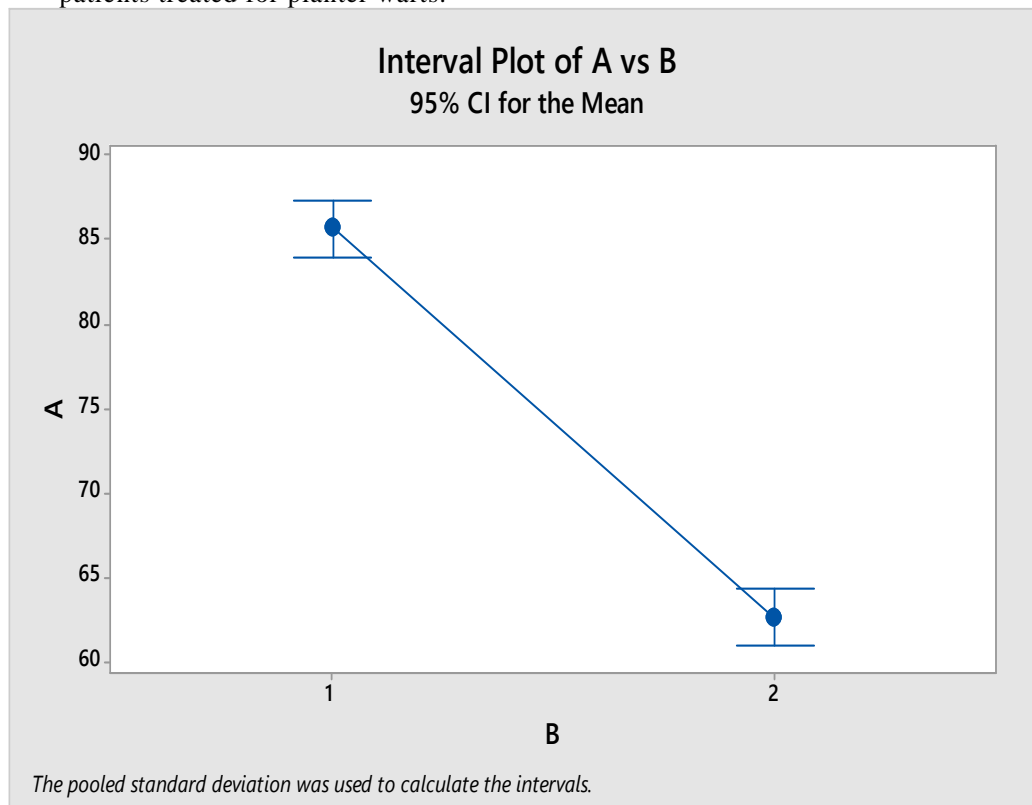
(group A) versus cryotherapy (group B) in patients treated for planter was calculated being 84.91 and 64.18% and is presented in figure 1.

Table 1: Efficacy of intralesional vitamin D3 injection versus cryotherapy in the treatment of planter warts.

		Group A			Group B			Mean	P-value
		Group A			Group B				
		T	R	E (%)	T	R	E (%)		
Gender	Men	38	31	77.50	31	21	67.74	72.62±0.45	0.185
	Women	26	24	92.31	33	20	60.61	76.46±0.41	0.005
Age (Years)	18-25	37	32	87.49	39	29	74.36	80.93±0.45	0.185
	26-35	27	23	85.19	25	12	48.00	66.60±0.41	0.005
No. of warts	1-2	33	31	93.94	35	25	71.43	82.70±11.30	0.015
	3	31	24	77.42	29	16	55.17	66.30±11.30	0.068
Size of warts (cm)	$\leq 1$	39	35	89.74	40	31	77.53	84.87±4.87	0.142
	1-1.5	25	20	80.00	24	10	41.67	59.60±4.90	0.006
Duration of disease (Weeks)	1-6	26	23	88.46	27	19	70.37	79.87±5.46	0.104
	7-12	38	32	84.21	37	22	59.46	71.80±5.46	0.017

T = Treated, R = Recovered, E = Efficiency

Figure 1: Mean efficacy of intralesional vitamin D3 (group A) versus cryotherapy (group B) in patients treated for planter warts.



**DISCUSSION:**

Warts are common viral infections on the skin caused by human papilloma virus (HPV) and some of them may be premalignant. Warts can appear at any age. The prognosis of warts cannot be predicted. In some patients they may spontaneously disappear, whereas others show persistence and progression with spread to other body sites, leading to physical and emotional distress to the patients.<sup>13</sup>Nofal et al. 2013 reported that intralesional immunotherapy with various antigens has shown reasonable efficacy in treating warts. Immunotherapy is based on the activation of the immune system to deal with the virus and suppress its activity. Such therapy may be applied either topically or through intralesional injection or through systemic administration<sup>14</sup>. Previously, anogenital and refractory warts has been successfully removed by using topical administration of vitamin D and the effect of vitamin D on warts was speculated to be derived from its potential to regulate epidermal cell proliferation and differentiation and modulate cytokine production. In addition, Toll-like receptor activation of human macrophages upregulates the expression of VDR and vitamin D 1-hydroxylase gene, leading to expression and secretion of antimicrobial peptides.<sup>15</sup>

During the present study 64.18% patients were successfully recovered from planter warts by the use of cryotherapy, while Focht et al. 2002 and Bruqqink et al. 2010 reported that efficacy of cryotherapy was not more than 60% in the treatment of planter warts. The efficacy of intralesional Vit D3 therapy was higher than found by Aktas et al. 2016, who reported clearance of planter warts in 80.0% patients. However, the efficacy of intralesional Vit D3 therapy during the present study was lower than reported by Raghukumar et al. 2017<sup>11</sup> and Kavya et al. 2017<sup>16</sup> (84.91% Vs 90%). They concluded that intralesional vitamin D3 is a safe, effective, and inexpensive treatment option for recalcitrant and multiple cutaneous warts.<sup>16</sup> Variations in the efficacy of intralesional vitamin D3 therapy and cryotherapy reported by various researchers might be due to different dose rate and number of treatments given in treating the variable size of viral warts. The vitamin D has multiple physiological and pharmacological effects mediated by action of the vitamin D receptors (VDRs). Recently, VDR activators (VDRAs) have been shown to inhibit cell replication and have immunomodulatory properties.<sup>17</sup> An important observation was reported which

suggested that Toll-like receptor (TLR) activation of human macrophages upregulated expression of vitamin D receptor and vitamin D-1-hydroxylase genes, leading to induction of the antimicrobial peptide.<sup>18</sup> Immunotherapy of cutaneous warts is simple, safe and effective, moreover, this procedure was within tolerable pain for planter warts.<sup>19</sup>

**CONCLUSION:**

Intralesional therapy with vitamin D3 has more efficacy than cryotherapy in the treatment of planter warts. It is simple, effective, safe and this procedure is within tolerable pain for the patients suffering from planter warts.

**REFERENCES:**

1. Moscarelli L, Annunziata F, Mjeshtri A, Paudice N, Tsalouchos A, Zanazzi M, et al. Successful treatment of refractory wart with a topical activated vitamin D in a renal transplant recipient. *Case Rep Transplant* 2011;368623.
2. Sterling JC, Gibbs S, Haque-Hussain SS, Mohd-Mustapa MF, Handfield-Jones HE. British association of dermatologists' guidelines for the management of cutaneous warts. *Br J Dermatol* 2014;171(4):696-712.
3. Sterling J. Viral infections. In: Burns T, Breathnach S, Cox N, Griffiths C. *Rook's Text book of Dermatology*. 8th ed. UK: Wiley-Blackwell; 2010. p. 37-59.
4. Mun JH, Kim SH, Jung DS, Ko HC, Kim BS, Kwon KS. Oral zinc sulphate treatment for viral warts. An open-label study. *J Dermatol*. 2011;38(6):541-5.
5. Abeck D. and Holst RF. Quadrivalent human papillomavirus vaccination: A promising treatment for recalcitrant cutaneous warts in children. *ActaDermVenereol* 2015; 95: 1017-9.
6. Nofal A, Nofal E, Yosef A, Nofal H. Treatment of recalcitrant warts with intralesional measles, mumps, and rubella: a promising approach. *Int J Dermatol* 2015;54(6):667-71.
7. Bruqqink SC, Gussekloo J, Berger MY, Zaaijer K, Assendelft WI, de-Waal MW, et al. Cryotherapy with liquid nitrogen versus topical salicylic acid application for cutaneous warts in primary care. Randomised controlled trial. *J Can Med Assoc* 2010;182(15):1624-30.
8. Focht DR, Spicer C, Fairchok MP. Efficacy of duct tape versus cryotherapy in the treatment of verruca vulgaris. *Arch Pediatr Adolesc Med* 2002;156(10):971-4.
9. Aktaş H, Ergin C, Demir B, Ekiz Ö.

- Intralesional vitamin D injection may be an effective treatment option for warts. *J Cutan Med Surg*. 2016; 20(2):118-22.
10. El-Khalawanya M, D. Shaabanb, S. Aboeldahab. Immunotherapy of viral warts: myth and reality. *Egypt J of Dermatol and Venereol* 2015; 35:1–13.
  11. Raghukumar S, BC Ravikumar, KN Vinay KN, MR Suresh, AAggarwal and DP Yashovardhan. Intralesional Vitamin D3 injection in treatment of recalcitrant warts: a novel proposition. *J Cutan Med Surg* 2017;21(4):320-4.
  12. Singh SK, Mohan A, Gupta AK, Pandey AK. A comparative study between intralesional PPD and vitamin D3 in treatment of viral warts. *Int J Res Dermatol* 2018;4:197-201.
  13. Lynch MD, J Cliffe and R Morris-Jones. Management of cutaneous viral warts. *BMJ* 2014; 348: g3339.
  14. Vender R, Bourcier M, Bhatia N, Lynde C. Therapeutic options for external genital warts. *J Cutan Med Surg* 2013; 17 Suppl 2:61-7.
  15. Rind T, Oiso N, Kawada A. Successful treatment of anogenital wart with a topical vitamin D(3) derivative in an infant. *Case Rep Dermatol* 2010;2:46-9.
  16. Kavya M, BasavapuraMadegowdaShashikumar, MuddanahalliRajegowda Harish, Bhadbhade P Shweta. Safety and efficacy of intralesional vitamin D3 in cutaneous warts: An open uncontrolled trial. *J CutanAesthetSurg* 2017;10(2):90-94.
  17. Abo Elela IM, MD Elshahid and AR Mosbeh. Intradermal vs intralesional purified protein derivatives in treatment of warts. *Gulf J DermatolVenereol* 2011; 18:21–6.
  18. Egawa K, Ono T. Topical vitamin D3 derivatives for recalcitrant warts in three immunocompromised patients. *Br J Dermatol* 2004;150:374-6.
  19. Alaa E.A. Moubasher, Osama M. Hassan, Eman M.K. Youssef and Marwa M.A. Sabek. Intralesional injection of purified protein derivatives versus zinc sulfate 2% in recalcitrant palmar and/or plantar warts. *J Egypt Women DermatolSoc*, 2016; 13:151–8.