

COMPARATIVE EFFICACY OF CRYOTHERAPY AND INTRALESIONAL VITAMIN D3 IN PATIENTS WITH PLANTAR WARTS

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ABSTRACT

Background: Plantar warts, caused by human papillomavirus (HPV), are common and often resistant to treatment. While cryotherapy is a standard approach, intralesional vitamin D3 has emerged as a newer, immunomodulatory option. Comparative evidence regarding their efficacy remains limited. **Objective:** To compare the efficacy of cryotherapy and intralesional vitamin D3 in the treatment of plantar warts. **Study Design:** randomized controlled trial. **Setting:** Combined Military Hospital (CMH), Nowshera. **Duration of Study:** 02-December-2024 to 02-June-2025. **Methods:** A total of 194 patients aged 15–45 years presenting with 1–3 plantar warts were enrolled and randomly assigned to two groups. Group A (n = 97) received cryotherapy using liquid nitrogen biweekly for six weeks. Group B (n = 97) received intralesional vitamin D3 (0.2 mL of 7.5 mg/mL) at the same interval. Treatment efficacy was defined as complete clinical clearance of all warts by six weeks. Statistical analysis was performed using a chi-square test; p-value <0.05 was considered significant. **Results:** The mean age was 31.55 ± 9.35 years in Group A and 32.23 ± 8.37 years in Group B. Cryotherapy showed a significantly higher clearance rate of 66.0% compared to 45.4% with intralesional vitamin D3 (p = 0.004). **Conclusion:** Cryotherapy is considerably more effective than intralesional vitamin D3 in achieving complete resolution of plantar warts over six weeks, and should be preferred as a first-line treatment in clinical practice.

Keywords: Plantar Warts, Cryotherapy, Intralesional Vitamin D3, Efficacy

INTRODUCTION

Plantar warts are skin lesions located on the plantar surface of the foot that arise from infection of keratinocytes by human papillomavirus (HPV). HPV is widespread, while the majority of individuals are silent carriers of HPV (1-4). Most cases occur in children as well as adolescents (5, 6). Immunocompromised patients demonstrate an elevated risk of developing plantar warts, which can result in pain and, in rare instances, cancer. Once a plantar wart develops, it releases HPV through the desquamation of epithelial cells. Viruses can infect additional sites as well as hosts. Current therapies for plantar warts, which focus on retroactive therapy of the wart, facilitate viral transmission (6, 7).

Current therapies exhibit variable efficacy, as lesions are known for their resistance to treatment and elevated recurrence rates. Moreover, several of these different treatment methods do not successfully address the underlying issue (8, 9). Established preventive programs primarily focus on managing the exposure of HPV, a task that is commonly impractical due to its broad prevalence (10). Due to the significant treatment resistance associated with plantar warts and the absence of effective prevention methods, medically centred HPV prophylaxis could be beneficial for populations with elevated instances of plantar warts in managing lesion dissemination as well as transmission (10, 11).

Cryotherapy is frequently used as a primary treatment for cutaneous warts. A study found that cryotherapy resulted in the complete resolution of warts in 39.5% of patients. A separate investigation found that patients with plantar warts who received intralesional vitamin D3 experienced complete disappearance of warts in 80% of instances (12, 13). Another study observed the efficacy of cryotherapy at 43% and intralesional vitamin D3 at 63.3% in cases of plantar warts (14).

Although cryotherapy is an established treatment modality for treating plantar warts, options such as intralesional vitamin D3 have conflicting results. Vitamin D3 has the advantage of being readily available and not requiring any special storage equipment or environmental conditions due to the paucity of literature on this subject locally. The goal of this study is to compare the efficacy of cryotherapy and intralesional vitamin D3 in treating plantar warts. The results of this study will be beneficial for our healthcare professionals to shed light on the effectiveness of cryotherapy and intralesional vitamin D3, providing valuable insights to inform clinical decision-making and optimise patient care in the management of plantar warts.

METHODOLOGY

A randomised controlled trial was conducted in the Dermatology Department of the Combined Military Hospital, Nowshera, from December 2, 2024, to June 2, 2025, following approval from the institute. We enrolled 194 patients, with 97 patients allocated to each treatment group using consecutive non-probability sampling. The sample size was evaluated based on previously reported efficacy rates of 43.3% for cryotherapy and 63.3% for intralesional vitamin D3, with 80% power and a 95% confidence level.

Participants included males and females aged 15 to 45 years with 1–3 plantar warts and a maximum wart duration of six months. Pregnant patients, patients on immunosuppressive therapy, those who had received wart treatment in the preceding four weeks, patients with systemic illnesses, those unwilling to adhere to follow-up protocols, and patients with mosaic plantar warts were excluded from the research. Consent was taken from the patients.

Patients were randomly assigned to two groups using block randomisation. Group A received cryotherapy administered via liquid nitrogen applied with a cotton wad until a 2 mm frozen halo appeared

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around the lesion base. Treatment sessions were conducted every two weeks for six weeks, with follow-up assessments to monitor progress. Group B received intralesional vitamin D3 (0.2 mL of 7.5 mg/mL) injected into the wart base after local anaesthesia with lidocaine (0.1 mL of 20 mg/mL), also administered biweekly for six weeks. Before each treatment, thickened skin was debrided to enhance therapeutic penetration.

Efficacy was defined as complete wart clearance, evidenced by the restoration of normal skin texture and the absence of palpable lesions, after six weeks. A consultant dermatologist evaluated outcomes on a fortnightly basis, and data were recorded on structured proformas. Demographic and clinical variables, including age, BMI, gender, comorbidities (diabetes and hypertension), socioeconomic status, place of residence, employment status, and education level, were documented.

SPSS 25 was used for data analysis. Frequencies and percentages were used to analyse gender, comorbidities (diabetes and hypertension), socioeconomic status, place of residence, employment status, and education level. The primary comparison of efficacy between groups was conducted using the Chi-square test, with a P value considered notable at ≤ 0.05 . Stratification analyses of efficacy in both groups, evaluating demographics and comorbidities, were performed using the Chi-Square test with a P value notable at ≤ 0.05 .

RESULTS

The study compared the efficacy of cryotherapy (Group A) with that of intralesional vitamin D3 (Group B). The mean age of the patients in Group A was 31.55 ± 9.35 years, while Group B had a slightly higher mean age of 32.23 ± 8.37 years. Body mass index (BMI) in Group A averaged 24.45 ± 1.39 kg/m² and Group B averaged 24.53 ± 1.53 kg/m².

The gender distribution revealed 42 (43.3%) males and 55 (56.7%) females in Group A, while Group B had 52 (53.6%) males and 45 (46.4%) females. Comorbidities, such as hypertension, were reported in 20 (20.6%) patients in Group A and 25 (25.8%) in Group B, while diabetes was present in 15 (15.5%) and 17 (17.5%) patients, respectively (Table 1).

Regarding efficacy, we observed that Group A demonstrated potentially higher efficacy, with 64 (66.0%) patients, compared to 44 (45.4%) in Group B ($p = 0.004$). Conversely, treatment failure was observed in 33 (34.0%) patients in Group A and 53 (54.6%) in Group B (Table 2). The table presents the stratification of efficacy in both groups with demographic variables and comorbidities

Table 1: Demographics and comorbidities

Demographics and comorbidities		Groups			
		Group A (Cryotherapy)		Group B (Intralesional vitamin D3)	
		n	%	n	%
Gender	Male	42	43.3%	52	53.6%
	Female	55	56.7%	45	46.4%
Education status	Educated	53	54.6%	46	47.4%
	Uneducated	44	45.4%	51	52.6%
Employment status	Employed	51	52.6%	42	43.3%
	Unemployed	46	47.4%	55	56.7%
Living place	Urban	41	42.3%	50	51.5%
	Rural	56	57.7%	47	48.5%
Hypertension	Yes	20	20.6%	25	25.8%
	No	77	79.4%	72	74.2%
Diabetes	Yes	15	15.5%	17	17.5%
	No	82	84.5%	80	82.5%

Table 2: Comparison of efficacy in both groups

Efficacy	Groups				P value
	Group A (Cryotherapy)		Group B (Intralesional vitamin D3)		
	n	%	n	%	
Yes	64	66.0%	44	45.4%	0.004
No	33	34.0%	53	54.6%	

Table 3: Stratification of efficacy in both groups with demographics and comorbidities

Demographics and comorbidities			Groups				P value	
			Group A (Cryotherapy)		Group B (Intralesional vitamin D3)			
			n	%	n	%		
Gender	Male	Efficacy	Yes	27	64.3%	19	36.5%	0.007
			No	15	35.7%	33	63.5%	
	Female	Efficacy	Yes	37	67.3%	25	55.6%	0.23
			No	18	32.7%	20	44.4%	
Hypertension	Yes	Efficacy	Yes	13	65.0%	8	32.0%	0.02
			No	7	35.0%	17	68.0%	
	No	Efficacy	Yes	51	66.2%	36	50.0%	0.04
			No	26	33.8%	36	50.0%	
Diabetes	Yes	Efficacy	Yes	9	60.0%	3	17.6%	0.01
			No	6	40.0%	14	82.4%	
	No	Efficacy	Yes	55	67.1%	41	51.2%	0.04
			No					

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Education status	Educated	Efficacy	No	27	32.9%	39	48.8%	0.0001
			Yes	40	75.5%	18	39.1%	
	Uneducated	Efficacy	No	13	24.5%	28	60.9%	0.72
			Yes	24	54.5%	26	51.0%	
Employment status	Employed	Efficacy	No	20	45.5%	25	49.0%	0.001
			Yes	38	74.5%	17	40.5%	
	Unemployed	Efficacy	No	13	25.5%	25	59.5%	0.45
			Yes	26	56.5%	27	49.1%	
Living place	Urban	Efficacy	No	20	43.5%	28	50.9%	0.08
			Yes	27	65.9%	24	48.0%	
	Rural	Efficacy	No	14	34.1%	26	52.0%	0.01
			Yes	37	66.1%	20	42.6%	
Socioeconomic status	Lower class	Efficacy	No	19	70.4%	15	46.9%	0.06
			Yes	8	29.6%	17	53.1%	
	Middle class	Efficacy	No	41	64.1%	26	45.6%	0.04
			Yes	23	35.9%	31	54.4%	
	Upper class	Efficacy	No	4	66.7%	3	37.5%	0.28
			Yes	2	33.3%	5	62.5%	
Age distribution (Years)	15 to 30	Efficacy	No	26	61.9%	20	54.1%	0.48
			Yes	16	38.1%	17	45.9%	
	31 to 45	Efficacy	No	38	69.1%	24	40.0%	0.002
			Yes	17	30.9%	36	60.0%	
BMI (Kg/m2)	18 to 24.9	Efficacy	No	37	63.8%	27	48.2%	0.09
			Yes	21	36.2%	29	51.8%	
	> 24.9	Efficacy	No	27	69.2%	17	41.5%	0.01
			Yes	12	30.8%	24	58.5%	

DISCUSSION

Demographic variables such as age and BMI were comparable across studies. Our participants in Group A had a mean age of 31.55 ± 9.35 years, closely mirroring the 36.17 ± 11.84 years reported by Ilyas et al. for cryotherapy recipients (15). BMI values in our study (24.45 ± 1.39 for Group A and 24.53 ± 1.53 for Group B) were consistent with the generally healthy ranges (16). Gender distribution, however, showed slight disparities. Our study had 43.3% males in Group A and 53.6% in Group B, whereas Ilyas et al. reported a nearly equal split (46.7% males in both groups) (15). Comorbidities such as hypertension and diabetes were present in 20.6% and 15.5% of Group A patients, respectively, similar to the 25.8% and 17.5% reported in Group B.

Our study demonstrated that cryotherapy (Group A) achieved a potentially higher efficacy of 66.0% compared to 45.4% for intralesional vitamin D3 (Group B) ($P = 0.004$). This aligns with findings by Ilyas et al., who reported a 90% efficacy rate for cryotherapy compared to 76.7% for vitamin D3, although their results were not statistically significant ($p = 0.166$).¹⁵ Similarly, Amin et al. observed a 92% clearance rate with cryotherapy compared to 84% with vitamin D3, reinforcing cryotherapy's superior efficacy (17). These variations in significance may stem from differences in sample sizes, treatment protocols, or patient populations. For instance, our study involved 97 patients per group, Ilyas et al. studied 60 participants, whereas Amin et al. included 100 patients (15). Larger sample sizes often yield more robust statistical outcomes, which could explain the stronger significance in our results.

Abdel et al. compared duct tape occlusion with cryotherapy, documenting that cryotherapy exhibited better efficacy than duct tape therapy (18). Bhojwani et al compared cryotherapy with Salicylic Acid and found no notable difference in the effectiveness of both treatments (19). Similarly, Usman et al. (2024) reported no notable efficacy difference between salicylic acid (30.6%) and cryotherapy (34.7%), emphasising that treatment choice may hinge on patient preferences for speed versus convenience (20).

Recurrence rates are a key variable in assessing the treatment of planter warts. Amin et al. reported an 18% recurrence rate with vitamin D3 versus 14% with cryotherapy (17). Ilyas et al. observed no notable difference.¹⁵ This suggests that while cryotherapy may offer faster resolution, its long-term efficacy could be comparable to vitamin D3.

Our findings suggest that cryotherapy remained the most effective option for rapid wart resolution, particularly in clinical settings where time is a constraint. Intralesional vitamin D3 procedure is a painful procedure for the patients as each wart has to be injected separately, making the experience more uncomfortable than cryotherapy. Future research should explore combination therapies, such as cryotherapy followed by vitamin D3, to potentially merge the benefits of both approaches.

CONCLUSION

We conclude that cryotherapy is more effective than intralesional vitamin D3 in treating planter warts. Cryotherapy in our setting remains the most effective treatment option for planter warts.

DECLARATIONS

Data Availability Statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned.

Consent for publication

Approved

Funding

Not applicable

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTION

SANA MOHTASIM BILLAH (Resident Trainee)

Conception of Study, Data Collection, Data Analysis, Study Design, Review of manuscript, and Manuscript Drafting.

SUMMAYA SALEEM (Assistant Professor)

Critical Input, and Final Approval of Draft

ALI AMAR

Critical input.

MUHAMMAD FAROOQ MALIK

Literature Search

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Review of Literature.

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