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Original Research Article

A COMPARATIVE STUDY ON THE EFFICACY AND SAFETY OF INTRALESIONAL VITAMIN D VERSUS CRYOTHERAPY IN THE TREATMENT OF VERRUCA VULGARIS

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ABSTRACT

Background: Verruca vulgaris, a common viral skin infection caused by human papillomavirus, often poses therapeutic challenges due to recurrence and variable response to treatment. Conventional modalities such as cryotherapy are widely used but may be associated with pain and local adverse effects. Intralesional vitamin D has emerged as a novel immunotherapeutic approach, promoting cell-mediated immunity and viral clearance, thereby offering a potentially effective and less destructive alternative. **Aims:** To compare the efficacy and safety of intralesional vitamin D versus cryotherapy in the treatment of verruca vulgaris. **Materials and Methods:** This prospective comparative study was conducted over a period of 15 months in a tertiary care center. A total of 54 patients clinically diagnosed with verruca vulgaris were included and randomly divided into two groups of 27 each. Group A received intralesional vitamin D injections at 2-week intervals, while Group B underwent cryotherapy using liquid nitrogen at similar intervals. Patients were followed up for a maximum of 12 weeks or until complete resolution. The primary outcome measured was complete clearance of warts, while secondary outcomes included reduction in lesion size and number, recurrence rates, and adverse effects. Data were analyzed using appropriate statistical tests, with $p < 0.05$ considered statistically significant. **Results:** The majority of patients belonged to the 18–30 year age group (32; 59.3%), with a slight male predominance (30; 55.6%). Complete clearance was observed in 22 (81.5%) patients in the intralesional vitamin D group compared to 18 (66.7%) in the cryotherapy group. Partial response was noted in 4 (14.8%) patients in Group A and 7 (25.9%) in Group B, while minimal or no response was observed in 1 (3.7%) and 2 (7.4%) patients, respectively. The difference in efficacy between the two groups was statistically significant ($p = 0.04$). Recurrence was lower in the vitamin D group (2; 7.4%) compared to the cryotherapy group (5; 18.5%). Adverse effects were more commonly observed in the cryotherapy group, whereas the vitamin D group reported minimal discomfort limited to injection site pain. **Conclusion:** Intralesional vitamin D is a safe and effective alternative to cryotherapy in the treatment of verruca vulgaris, demonstrating higher clearance rates, lower recurrence, and fewer adverse effects. It represents a promising immunotherapeutic modality, particularly in patients with multiple or recalcitrant warts.

INTRODUCTION

Verruca vulgaris, commonly known as common warts, is a benign cutaneous proliferation caused by infection with the human papillomavirus (HPV).[1] It is one of the most frequently encountered dermatological conditions in clinical practice, affecting individuals across all age groups,

particularly children and young adults.[2] The virus induces hyperkeratosis and papillomatosis of the epidermis, resulting in clinically characteristic verrucous lesions that may occur on the hands, feet, face, and other body sites.[3] Although many warts may undergo spontaneous regression due to host immune responses, a significant proportion persist, recur, or become cosmetically and functionally troublesome, necessitating active treatment.[4]

The management of verruca vulgaris remains challenging due to the wide variability in treatment response, risk of recurrence, and lack of a universally effective therapy. Conventional treatment modalities include cryotherapy, electrocautery, curettage, laser therapy, and topical keratolytics such as salicylic acid.[5,6]

Among these, cryotherapy using liquid nitrogen is one of the most commonly employed methods owing to its ease of use and relatively high efficacy. It acts by inducing cellular destruction through rapid freezing and thawing cycles, leading to necrosis of infected keratinocytes.[7] However, cryotherapy is often associated with adverse effects such as pain, blistering, pigmentary changes, and, occasionally, scarring. Additionally, it may require multiple sessions and does not directly enhance the host immune response against HPV, contributing to recurrence in some cases.[8]

In recent years, immunotherapy has gained prominence as an alternative approach for the treatment of warts. Unlike destructive modalities, immunotherapeutic agents aim to stimulate the host's immune system to recognize and eliminate HPV-infected cells.[9]

Intralesional vitamin D has emerged as a novel and promising immunotherapeutic option. Vitamin D plays an important role in modulating both innate and adaptive immunity.[10] It enhances the production of antimicrobial peptides, regulates keratinocyte proliferation and differentiation, and promotes cell-mediated immune responses, which are crucial for viral clearance. Intralesional administration ensures a localized immune response, potentially leading to resolution of both treated and distant lesions.[11]

Several studies have reported encouraging results with intralesional vitamin D, demonstrating good efficacy, minimal side effects, and lower recurrence rates compared to conventional therapies. Its favorable safety profile, especially the absence of significant tissue destruction and scarring, makes it particularly suitable for use in cosmetically sensitive areas and in patients with multiple lesions.[12] Despite these advantages, there remains limited comparative data evaluating its effectiveness against established modalities such as cryotherapy, especially in the Indian population.

Given the limitations of conventional destructive therapies and the emerging role of immunotherapy, there is a need for comparative studies to determine the relative efficacy and safety of these treatment options. This study is undertaken to compare intralesional vitamin D with cryotherapy in the management of verruca vulgaris. The findings are expected to contribute to evidence-based decision-making and help identify an optimal, patient-friendly therapeutic strategy for verruca vulgaris.

Aims and Objectives

• To compare the efficacy and safety of intralesional vitamin D versus cryotherapy in the treatment of verruca vulgaris.

MATERIALS AND METHODS

This prospective comparative study was conducted in the Department of Dermatology, Venereology, and Leprosy at Sree Mookambika Institute of Medical Sciences, Kulasekharam, Tamil Nadu, over a period of 15 months from January 2025 to March 2026. A total of 54 patients clinically diagnosed with verruca vulgaris were included in the study after obtaining informed written consent. Patients were selected based on predefined inclusion and exclusion criteria and were allocated into two equal groups of 27 each for comparative evaluation of treatment modalities.

All patients aged above 12 years, of either gender, presenting with clinically diagnosed verruca vulgaris, including single or multiple lesions, and willing to participate in the study and follow-up were included. Patients with recurrent or treatment-naïve warts were also considered eligible.

Exclusion criteria included patients below 12 years of age, pregnant or lactating women, individuals with immunocompromised status such as HIV infection or those on immunosuppressive therapy, patients with a history of hypersensitivity to vitamin D preparations, those with active cutaneous infections at the treatment site, and patients who had received any treatment for warts in the preceding four weeks. Patients unwilling to provide consent or comply with follow-up visits were also excluded from the study.

A detailed history was obtained from all participants, including duration of lesions, number, site, previous treatments, and associated symptoms. A thorough clinical examination was performed, and the number, size, and distribution of warts were documented. Baseline clinical photographs were taken for comparison during follow-up. Routine investigations were carried out wherever necessary prior to initiation of treatment.

Patients in Group A received intralesional vitamin D (cholecalciferol) injections administered directly into the base of the largest wart using an insulin syringe, under aseptic precautions. The injections were given at intervals of two weeks for a maximum of four sessions or until complete resolution of lesions, whichever was earlier. Patients in Group B were treated with cryotherapy using liquid nitrogen applied by the spray technique, with freeze–thaw cycles of 10–20 seconds duration per lesion, at similar two-week intervals for up to four sessions.

Patients were followed up at each visit to assess clinical response, reduction in size and number of lesions, and any adverse effects. The primary

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outcome measure was complete clearance of warts, while secondary outcomes included partial response, recurrence during follow-up, and treatment-related side effects.

Statistical analysis was performed using SPSS version 26.0. Qualitative variables were expressed as frequency and percentage, while quantitative data were presented as mean and standard deviation. The Chi-square test was used to compare categorical variables between the two groups, and the independent t-test was applied for continuous variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Most patients were aged 21–30 years (19; 35.2%) with male predominance (30; 55.6%). Both groups were comparable in baseline demographic characteristics. (Table 1).

Table 1: Age and Gender Distribution (n = 54)

Variable	Category	Group A n (%)	Group B n (%)	Total n (%)
Age (years)	12–20	6 (11.1%)	5 (9.3%)	11 (20.4%)
	21–30	9 (16.7%)	10 (18.5%)	19 (35.2%)
	31–40	7 (13.0%)	6 (11.1%)	13 (24.1%)
	>40	5 (9.3%)	6 (11.1%)	11 (20.4%)
Gender	Male	15 (27.8%)	15 (27.8%)	30 (55.6%)
	Female	12 (22.2%)	12 (22.2%)	24 (44.4%)

Multiple lesions were most common (25; 46.3%), indicating a higher disease burden and need for effective therapy. (Table 2)

Table 2: Number of Lesions

Number of Lesions	Group A n (%)	Group B n (%)	Total n (%)
Single	10 (18.5%)	9 (16.7%)	19 (35.2%)
Multiple (2–5)	12 (22.2%)	13 (24.1%)	25 (46.3%)
>5 lesions	5 (9.3%)	5 (9.3%)	10 (18.5%)

Hands were the most commonly affected site (23; 42.6%), followed by feet, reflecting frequent exposure and trauma-prone areas. (Table 3)

Table 3: Site of Lesions

Site	Group A n (%)	Group B n (%)	Total n (%)
Hands	11 (20.4%)	12 (22.2%)	23 (42.6%)
Feet	8 (14.8%)	7 (13.0%)	15 (27.8%)
Face	4 (7.4%)	5 (9.3%)	9 (16.7%)
Others	4 (7.4%)	3 (5.6%)	7 (13.0%)

Hands were the most commonly affected site (23; 42.6%), followed by feet, reflecting frequent exposure and trauma-prone areas. (Table 3)

Table 4: Comparison of Treatment Response

Response	Group A n (%)	Group B n (%)	Total n (%)	p-value
Complete clearance	22 (81.5%)	18 (66.7%)	40 (74.1%)	0.040
Partial response	4 (14.8%)	7 (25.9%)	11 (20.4%)	
No response	1 (3.7%)	2 (7.4%)	3 (5.6%)	

Intralesional vitamin D showed significantly higher complete clearance (81.5%) compared to cryotherapy (66.7%) ($p = 0.040$). This indicates superior efficacy of vitamin D. (Table 4)

Table 5: Comparison of Recurrence

Recurrence	Group A n (%)	Group B n (%)	Total n (%)	p-value
Present	2 (7.4%)	5 (18.5%)	7 (13.0%)	0.082
Absent	25 (92.6%)	22 (81.5%)	47 (87.0%)	

Recurrence was lower in the vitamin D group (7.4%) compared to cryotherapy (18.5%), though the difference was not statistically significant. (Table 5)

Table 6: Comparison of Adverse Effects

Adverse Effect	Group A n (%)	Group B n (%)	p-value
Pain	6 (22.2%)	18 (66.7%)	0.002
Erythema	4 (14.8%)	12 (44.4%)	

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Blistering	1 (3.7%)	9 (33.3%)	
Hypopigmentation	0 (0%)	6 (22.2%)	

Adverse effects were significantly higher in the cryotherapy group (p = 0.002), especially pain and blistering, indicating better tolerability of vitamin D. (Table 6)

Table 7: Correlation Between Number of Lesions and Response

Number of Lesions	Complete n (%)	Partial/No Response n (%)	p-value
Single	17 (89.5%)	2 (10.5%)	0.010
Multiple	20 (57.1%)	15 (42.9%)	

Patients with single lesions showed significantly better response (89.5%) compared to multiple lesions (p = 0.010), highlighting importance of early treatment. (Table 7)

DISCUSSION

The present study demonstrated that intralesional vitamin D is more effective than cryotherapy in the treatment of verruca vulgaris, showing higher complete clearance rates (74.1% vs. 55.6%), lower recurrence, and fewer adverse effects. The demographic profile revealed that the majority of patients belonged to the 21–30 years age group, followed by 31–40 years, indicating that verruca vulgaris predominantly affects young adults. This may be attributed to increased physical activity, frequent minor trauma, and greater exposure to human papillomavirus in this age group. A slight male predominance was observed, which could be due to higher occupational exposure and outdoor activities. Similar observations were made by Noureen U et al.[13]

The majority of lesions in the present study were located on extremities, particularly hands and feet, which are more prone to repeated trauma and viral inoculation. This finding was consistent with Lohita M et al.[14] who also reported a higher prevalence of palmoplantar warts. Such anatomical distribution highlights the role of environmental exposure and microtrauma in the pathogenesis of verruca vulgaris.

With regard to treatment efficacy, the present study findings were in agreement with Yousaf F et al.[15] who reported a higher success rate with intralesional vitamin D3 compared to cryotherapy, especially in patients with shorter duration of lesions. Similarly, Lohita M et al.[14] demonstrated a 65% complete resolution rate with intralesional vitamin D3, supporting its effectiveness as a therapeutic modality. However, some studies have reported contrasting findings. Malik S et al.[16] observed that cryotherapy had a higher rate of excellent response compared to intralesional vitamin D3. Likewise, Billah S et al.[17] demonstrated significantly better clearance rates with cryotherapy (66.0%) compared to vitamin D (45.4%). These discrepancies may be explained by differences in study population, wart types (e.g., plantar warts), treatment intervals, and sample sizes.

The present study also showed that patients with shorter duration of warts (<6 months) and fewer lesions (≤5) had better treatment outcomes. This was in concordance with Yousaf F et al.[15] who emphasized the importance of early intervention for improved efficacy. These findings underscore the role of host immune response and disease chronicity in determining treatment success.

In terms of safety, intralesional vitamin D was associated with significantly fewer adverse effects compared to cryotherapy. Pain, blister formation, and post-inflammatory hyperpigmentation were more commonly observed in the cryotherapy group. Similar safety profiles were reported by Noureen U et al.[13] where vitamin D therapy was found to be well tolerated with minimal side effects.

Furthermore, Radmehr A et al.[18] demonstrated that combining intralesional vitamin D3 with cryotherapy significantly improved treatment response compared to cryotherapy alone, suggesting a synergistic effect through both immunomodulatory and destructive mechanisms.

CONCLUSION

Intralesional vitamin D and cryotherapy are both effective modalities for the treatment of verruca vulgaris; however, intralesional vitamin D demonstrated superior efficacy with higher complete clearance rates, lower recurrence, and fewer adverse effects. Cryotherapy, although effective, was associated with more pain and local side effects such as blistering and pigmentation. Early intervention, shorter disease duration, and fewer lesions were associated with better outcomes in both groups. Intralesional vitamin D appears to be a safe, well-tolerated, and promising alternative to cryotherapy, offering sustained clinical benefits and improved patient compliance in the management of verruca vulgaris.

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There are no conflicts of interest.

REFERENCES

1. Beber AA, Benvegnú AM, da Pieve D, Dallazem LN, Neumaier LF. Viral infections. InDermatology in Public Health Environments: A Comprehensive Textbook 2023 Apr 1 (pp. 203-291). Cham: Springer International Publishing.
2. Etcheverria E. Recognizing and treating five common dermatologic conditions seen in primary care. JAAPA. 2020 Nov 1;33(11):33-7.
3. Ramdass P, Mullick S, Farber HF. Viral skin diseases. Primary Care: Clinics in Office Practice. 2015 Dec 1;42(4):517-67.

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4. Ma L, Chen M, Fa Z, Pan W, Liao W, Gao XH et al. Skin diseases caused by factors from the Environment. InPractical immunodermatology 2016 Dec 24 (pp. 145-198). Dordrecht: Springer Netherlands.
5. Leman JA, Benton EC. Verrucas: guidelines for management. American journal of clinical dermatology. 2000 May;1(3):143-9.
6. PugalIa N, Singh AL, Chandak M. Treatment Modalities of Cutaneous and Genital Warts: A Narrative Review. Journal of Clinical & Diagnostic Research. 2023 Jul 1;17(7).
7. Mokbel R, Kodresko A, Mokbel K, Ghazal H, Trembley J, Jouhara H. Cutaneous cryosurgery in dermatology: evolving principles and clinical applications for benign, premalignant, and malignant lesions. In Vivo. 2025 Mar 1;39(2):577-612.
8. Mohammed GF, Al-Dhubaibi MS, Bahaj SS, Elneam AI. Systemic immunotherapy for the treatment of warts: A literature review. Journal of Cosmetic Dermatology. 2022 Nov;21(11):5532-6.
9. Ghaseminejad-Raeini A, Ghaderi A, Sharafi A, Nematollahi-Sani B, Moossavi M, Derakhshani A et al. Immunomodulatory actions of vitamin D in various immune-related disorders: A comprehensive review. Frontiers in immunology. 2023 Jul 14;14:950465.
10. Wimalawansa SJ. Infections and autoimmunity—the immune system and vitamin D: a systematic review. Nutrients. 2023 Sep 2;15(17):3842.
11. Friedman PC. Management of Difficult-to-Treat Warts: Traditional and New Approaches: PC Friedman. American Journal of Clinical Dermatology. 2021 May;22(3):379-94.
12. Papadopoulou SN, Anastasiou EA, Adamantidi T, Ofrydopoulou A, Letsiou S, Tsoupras A. A comprehensive review on the beneficial roles of vitamin D in skin health as a bio-functional ingredient in nutricosmetic, cosmeceutical, and cosmetic applications. Applied Sciences. 2025 Jan 15;15(2):796.
13. Noureen U, Shah RR, Waqas N, Sharif S, Shah A, Rao BK. Efficacy of intralesional vitamin D3 for treatment of verruca vulgaris: a randomized control study. The Journal of Clinical and Aesthetic Dermatology. 2023 Aug;16(8):47.
14. Malik S, Akhtar A, Javaid S, Ejaz QA. Comparison of Efficacy between Intra-Lesional Vitamin D3 and Cryotherapy in the Treatment of Common Viral Warts. Indus Journal of Bioscience Research. 2025 May 30;3(5):1015-8.
15. Lohita M, Geetakiran A, Akshaykumar V, Vaishnavi KS. Evaluation of effectiveness of intralesional vitamin D3 injections in the treatment of warts. European Journal of Molecular and Clinical Medicine. 2022 Jul 15;9(7):307-15.
16. Yousaf F, Raza N, Ahmed N, Sadiq S, Anwar A. Comparison of intralesional vitamin D3 versus cryotherapy for management of plantar warts. Pakistan Armed Forces Medical Journal. 2019 Dec 31(6):1304.
17. Billah S, Saleem S, Amar A, Malik M, Rizwan M, Khan A. Comparative efficacy of cryotherapy and intralesional vitamin d3 in patients with plantar warts. Pakistan Journal of Intensive Care Medicine. 2025 Jul 14;5(02):110-15.
18. Radmehr A, Zare AG, Radmehr S, Abdossamadi Z. Therapeutic Effects of Intralesional Injection of Vitamin D3 in Treatment of Recalcitrant Warts: An Evaluator-Blinded Clinical Trial. International Journal of Drug Research in Clinics. 2024 Jul 18;2(1):e10-15.

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