COMPARISON OF EFFICACY OF ORAL ZINC SULFATE VERSUS INTRALESIONAL VITAMIN D3 IN THE TREATMENT OF VIRAL WARTS

Shah Fiaz[1], Fahad Faiz Ullah[2], Fahad Khan[1], Khizer Hayat[1]

ABSTRACT

Objective: To compare the efficacy of oral zinc sulphate versus intralesional vitamin D3 in the treatment of viral warts.

Methods: This comparative quasi-experimental study was conducted at the Department of Dermatology, MTI-Hayatabad Medical Complex, Peshawar, from 01 July 2024 to 01 January 2025, after approval from the Institutional Research & Ethical Board (IREB) (Approval No: 1743). A total of 60 patients (12–70 years) with clinically diagnosed viral warts were enrolled through non-probability consecutive sampling. Participants were allocated into two groups based on treatment preference (non-randomised): Group A (n=30) received intralesional vitamin D3 injections (600,000 IU; 0.2 mL into the base of lesions) every two weeks for eight weeks, while Group B (n=30) received oral zinc sulphate (10 mg/kg/day) for eight weeks. Treatment response at week 8 was categorised as excellent (>90% clearance), good (75–90%), poor (50–74%), or no response (<50%). Patients were followed for three months to assess recurrence. Data were analysed using SPSS version 23.0; chi-square test was applied and $p<0.05$ was considered statistically significant.

Results: Mean age was 39.33±14.48 years in the vitamin D3 group and 37.50±13.75 years in the zinc sulphate group. Excellent response was observed in 60.0% (18/30) patients receiving vitamin D3 and 56.7% (17/30) receiving zinc sulphate ($p=0.840$). Recurrence at three months occurred in 33.3% (10/30) and 23.3% (7/30) patients, respectively ($p=0.390$).

Conclusion: Oral zinc sulphate and intralesional vitamin D3 showed comparable efficacy for viral warts, with no statistically significant difference in short-term recurrence.

Keywords: Viral warts; Zinc sulphate; Vitamin D3; Immunotherapy; Recurrence.

INTRODUCTION

Viral warts (verrucae) are benign epidermal proliferations caused by infection with human papillomavirus (HPV) and can involve the hands, feet, face, and other cutaneous sites.[1] They are common in clinical practice and, although some lesions may regress spontaneously, many persist and become symptomatic or cosmetically distressing, leading patients to seek active treatment.[2] A key challenge in wart management is variable treatment responsiveness and frequent relapse, which is influenced by host immunity, wart type, and HPV subtype.[3–4]

[1] Hayatabad Medical Complex, Peshawar
[2] Pak International Medical College, Peshawar

Address for Correspondence
Dr. Fahad Faiz Ullah
Assistant Professor Dermatology, Pak International Medical College, Peshawar
fahadsbp59@gmail.com

Conventional therapies such as topical keratolytics, cryotherapy, electrocautery, and other destructive modalities are widely used; however, these approaches may be painful, require multiple sessions, and still carry substantial recurrence.[5–6] Consequently, interest has increased in immunomodulatory options that enhance cell-mediated immunity against HPV-infected keratinocytes, with the aim of improving clearance and reducing recurrence rather than only destroying visible lesions.[7] Systemic zinc has been evaluated for its immunoregulatory effects and has shown benefit in some patients with recalcitrant warts, though outcomes vary across studies.[8] Similarly, intralesional vitamin D3 has been studied as an immunotherapy for cutaneous warts, with evidence suggesting clinically meaningful clearance in several trials and reviews.[9]

Despite growing international literature, comparative data between oral zinc sulphate and intralesional vitamin D3 remain limited, particularly in local settings where patterns of presentation and treatment practices may differ.[10] Therefore, this study aimed to compare the efficacy of oral zinc sulphate versus

intralesional vitamin D3 in the treatment of viral warts and to evaluate short-term recurrence following therapy.

MATERIALS AND METHODS

This comparative quasi-experimental study was conducted at the Department of Dermatology, MTI-Hayatabad Medical Complex, Peshawar, from 01 July 2024 to 01 January 2025, after approval from the Institutional Research & Ethical Board (IREB), MTI-HMC (Approval No: 1743). Written informed consent was obtained from all participants (and from guardians where applicable). Confidentiality was maintained by using coded data and restricting access to the dataset.

A total of 60 patients aged 12–70 years with clinically diagnosed viral warts (as per operational definitions) were enrolled through non-probability consecutive sampling. Pregnant or lactating women, patients with known hypersensitivity to vitamin D3 or zinc sulphate, those with immunosuppressive conditions, and individuals receiving any concurrent wart treatment during the study period were excluded. Sample size was calculated using the WHO sample size calculator by assuming efficacy of 90% for intralesional vitamin D3 and 50% for oral zinc sulphate, with 95% confidence level, 80% power, and 5% level of significance, resulting in 60 participants (30 per group).

Participants were allocated into two groups based on treatment preference; therefore, the study was non-randomised. Group A (n=30) received intralesional vitamin D3 injections, administered as 600,000 IU per session, with 0.2 mL injected into the base of lesions every two weeks for eight weeks. Group B (n=30) received oral zinc sulphate at a dose of 10 mg/kg/day for eight weeks. The primary outcome was wart clearance assessed at the end of the eight-week treatment period. Lesion size was measured using a vernier caliper, and treatment response was categorised as excellent (>90% clearance), good (75–90% clearance), poor (50–74% clearance), or no response (<50% clearance). After treatment completion, patients were followed for three months to document recurrence.

Data were recorded on a structured proforma and analysed using SPSS version 23.0. Quantitative variables including age, duration of lesions, number of lesions, and lesion size were summarised as mean ± standard deviation, while qualitative variables including gender, lesion location, treatment response categories, and recurrence were presented as frequencies and percentages. The chi-square test was applied to compare categorical outcomes between groups, and $p<0.05$ was considered statistically significant. To minimise the effect of confounding related to non-random allocation, stratification was performed for age, gender, and lesion location during analysis.

RESULTS

A total of 60 patients were included (30 in each group). Baseline characteristics were comparable between the intralesional vitamin D3 and oral zinc sulphate groups in terms of mean age, duration of lesions, number of lesions, and mean lesion size (Table 1). Overall, 47 (78.3%) participants were male and 13 (21.7%) were female. Lesions were most frequently located on the feet and hands, with no statistically significant difference in lesion-site distribution between the two groups (Table 2).

At the end of eight weeks, the distribution of treatment response (excellent, good, poor, and no response) did not differ significantly between the groups (p=0.840). An excellent response was observed in more than half of the patients in both arms, indicating that both interventions achieved clinically meaningful wart clearance within the study period (Table 2).

On three-month follow-up, recurrence was observed in 17 (28.3%) patients overall, and the recurrence rate did not differ significantly between the vitamin D3 and zinc sulphate groups (p=0.390), suggesting comparable short-term durability of response (Table 2).

Table 1: Descriptive Statistics of Study (n=60)

Group	Variable	Mean ± SD
Vitamin D3	Age (years)	39.33 ± 14.48
	Duration of Lesions (weeks)	13.00 ± 6.78
	Number of Lesions	4.93 ± 2.48
	Size of Lesions (mm)	5.93 ± 2.40
Zinc Sulfate	Age (years)	37.50 ± 13.75
	Duration of Lesions (weeks)	11.57 ± 7.01
	Number of Lesions	4.87 ± 2.80
	Size of Lesions (mm)	5.08 ± 2.53

Table 2: Demographic and Clinical Characteristics of Patients (n=60)

Variable	Groups		Total	P-value
Gender	**Vitamin D3**	**Zinc Sulfate**		
Male	24 (80.0%)	23 (76.7%)	47 (78.3%)	0.754
Female	6 (20.0%)	7 (23.3%)	13 (21.7%)	
Location of Lesions				
Feet	13 (43.3%)	11 (36.7%)	24 (40.0%)	0.554
Hands	9 (30.0%)	13 (43.3%)	22 (36.7%)	
Other areas	8 (26.7%)	6 (20.0%)	14 (23.3%)	
Treatment Response				
Excellent	18 (60.0%)	17 (56.7%)	35 (58.3%)	0.840
Good	6 (20.0%)	6 (20.0%)	12 (20.0%)	
No Response	4 (13.3%)	3 (10.0%)	7 (11.7%)	
Poor	2 (6.7%)	4 (13.3%)	6 (10.0%)	
Recurrence				
Yes	10 (33.3%)	7 (23.3%)	17 (28.3%)	0.390
No	20 (66.7%)	23 (76.7%)	43 (71.7%)	

DISCUSSION

The crux of our findings is that both intralesional vitamin D3 and oral zinc sulphate achieved clinically meaningful wart clearance with no statistically significant difference in overall response, indicating comparable effectiveness of these two immunomodulatory approaches in our setting.[11,12] This is important because conventional destructive therapies (e.g., cryotherapy, cautery) are often painful, require repeated visits, and may still be followed by relapse; hence, immunotherapy-based options are increasingly considered for patients seeking safer, less invasive alternatives.[12]

A key methodological result in our study is that the baseline clinical profile was broadly

comparable between groups (age distribution, lesion duration/number and lesion-site pattern), which strengthens the inference that the observed similarity in response is more likely attributable to comparable treatment performance rather than obvious baseline imbalance.[12] Nevertheless, viral wart outcomes are inherently heterogeneous and depend on host immunity, wart chronicity, and virological factors; therefore, even with similar baseline characteristics, differences may still arise due to unmeasured confounders such as HPV type, micronutrient status, or adherence.[16,18]

With respect to treatment response, the main message is that more than half of patients in both arms achieved an "excellent" response, and the distribution across response categories did not differ significantly. This aligns with clinical studies reporting favourable clearance rates with intralesional vitamin D3 for common cutaneous warts.[11–15] A plausible explanation is that intralesional vitamin D3 may exert immunomodulatory effects that enhance clearance of HPV-infected keratinocytes and can sometimes produce a response beyond the injected lesion.[13–15] In parallel, the efficacy observed with oral zinc sulphate is consistent with reports that zinc supplementation can support wart resolution through immune regulation and antioxidant pathways, although outcomes vary between studies.[16,17] The similarity between arms in our cohort can be reasonably explained by several factors: (i) both interventions work via immune modulation rather than direct tissue destruction; (ii) our follow-up window for assessing clearance was relatively short (8 weeks), potentially limiting separation between therapies that may differ in time-to-response; and (iii) response definitions and wart subtype mix (common vs plantar vs periungual) can influence apparent efficacy and comparability across studies.[13,14,18]

Regarding recurrence, the crux is that short-term recurrence at three months was not significantly different between groups, suggesting comparable durability of response in the early post-treatment period. Recurrence in warts is multifactorial and may reflect residual subclinical HPV, incomplete immune clearance, or reinoculation. Importantly, evidence indicates that HPV type may influence natural course and treatment response, which could also affect recurrence patterns; HPV typing was not performed in our study and may partly explain the numerical (but non-significant) differences observed.[18] The inference here is that while both therapies appear similarly effective in achieving short-term clearance, longer follow-up is required to determine whether either modality provides superior sustained remission beyond three months.[12]

Overall, this study contributes local comparative data suggesting that intralesional vitamin D3 and oral zinc sulphate are both reasonable immunotherapeutic options for viral warts, with similar short-term efficacy and recurrence. However, because allocation was based on patient preference, the study is not a true experimental/randomised trial, and selection bias cannot be excluded. Future work should use randomised allocation with allocation concealment, larger multicentre recruitment, measurement of baseline vitamin D/zinc status, wart subtype stratification, and longer follow-up to generate stronger causal inference and more definitive recurrence estimates.[13,16,18]

CONCLUSION

Oral zinc sulphate and intralesional vitamin D3 demonstrated comparable efficacy in the treatment of viral warts, with no statistically significant difference in short-term recurrence. Larger randomised controlled trials with longer follow-up are recommended to confirm comparative effectiveness and durability of response.

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