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Research Article

Efficacy of oral zinc sulphate versus cryotherapy in the treatment of palmoplantar warts: a comparative interventional study

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Abstract

Objective: To compare the efficacy and safety of oral zinc sulphate versus cryotherapy in the treatment of palmoplantar warts.

Method: The comparative, interventional study was conducted at the Dermatology Department of Pakistan Navy Station Shifa Hospital, Karachi, from December 1, 2024, to May 31, 2025, and comprised patients of either gender aged 18-50 years presenting with clinically diagnosed palmoplantar warts. The patients were divided into Group A receiving oral zinc sulphate 10mg/kg/day for 8 weeks, and Group B undergoing cryotherapy every 2 weeks for up to 4 sessions. Outcomes included complete clearance, recurrence and adverse effects. Data was analysed using SPSS 26.

Results: Of the 60 patients, 30 (50%) were allocated to each treatment group. The mean age was 32.7±8.1 years in Group A and 33.4±7.8 years in Group B. Males constituted 17 (56.7%) patients in Group A and 16 (53.3%) in Group B, while females constituted 13 (43.3%) and 14 (46.7%), respectively. The baseline demographic and clinical characteristics were comparable between the two groups, with no statistically significant intergroup differences. Complete clearance was observed in 23 (76.6%) patients in Group A, followed by partial response in 6 (20.0%) and no response in 1 (3.3%). The

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corresponding values in Group B were 20 (66.6%), 7 (23.3%) and 3 (10.0%), respectively. Recurrence was significantly lower in Group A, 1 (4.3%), compared to Group B, 4 (20%) (p=0.04). Gastrointestinal adverse effects occurred in 4 (13.3%) patients in Group A, while pain in 19 (63.3%) and blistering in 11 (36.6%) were reported in Group B.

Conclusion: Oral zinc sulphate demonstrated comparable efficacy to cryotherapy in achieving complete clearance of palmoplantar warts.

Key Words: Palmoplantar warts, Zinc sulphate, Cryotherapy, HPV, Immunotherapy, Comparative treatment.

Introduction

Palmoplantar warts are benign hyperkeratotic lesions caused by infection with human papillomavirus (HPV), predominantly types 1, 2 and 4. These lesions commonly involve the palms and soles where they frequently cause pain, discomfort, cosmetic concerns, impairment of daily activities and reduced quality of life (QOL).[1-3]

Several treatment modalities are available for palmoplantar warts, including topical salicylic acid, cryotherapy, laser ablation, electrosurgery and immunotherapeutic agents. Current clinical guidelines recommend treatment selection in line with the wart size, anatomical location, patient preference and treatment tolerability.[1] Cryotherapy using liquid nitrogen remains one of the most commonly employed first-line treatment options because of its proven efficacy and widespread availability. However, treatment is often associated with pain, blister formation, multiple treatment sessions and recurrence, particularly in patients with recalcitrant or extensive lesions.[1,4-6]

Zinc is an essential trace element that plays a fundamental role in immune regulation, wound healing and antiviral defence through enhancement of both innate and cell-mediated immunity.[7] Oral zinc sulphate has, therefore, emerged as a potential systemic immunotherapeutic agent for the treatment of viral warts by facilitating immune-mediated clearance of HPV-infected keratinocytes.[8] Previous studies have demonstrated encouraging therapeutic outcomes with oral zinc sulphate, particularly in patients with

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recalcitrant, multiple, plane, common and genital warts.[9,10] Systemic therapy may offer particular advantages for palmoplantar warts, where destructive procedures can be painful and less well-tolerated.[11]

Although several clinical studies have evaluated oral zinc sulphate for the treatment of viral warts, their findings remain inconsistent. Some studies have reported clearance rates comparable to or better than conventional therapies together with lower recurrence rates, whereas others have demonstrated no significant advantage over standard treatment modalities.[12-18] Consequently, the comparative effectiveness of oral zinc sulphate and cryotherapy for palmoplantar warts remains uncertain.

The current study was planned to compare the efficacy and safety of oral zinc sulphate with cryotherapy in the treatment of palmoplantar warts.

Patients and Methods

The comparative, interventional study was conducted at the Department of Dermatology, Pakistan Navy Station (PNS) Shifa Hospital, Karachi, from December 1, 2024, to May 31, 2025. After approval from the institutional ethics review board, the sample size was calculated using the World Health Organization (WHO) sample-size calculator.[19] The calculation was based on a 95% confidence level, 80% study power, and an expected treatment efficacy of 70%. The expected efficacy was selected on the basis of previously published clinical evidence reporting a complete wart clearance rate of 68.4%, which was rounded to 70% for the sample-size estimation.[20] The sample was raised using a simple random sampling technique. The sample was raised using simple random sampling technique. Those included were adult patients of either gender aged 18-50 years presenting with clinically diagnosed palmoplantar warts. Eligible participants were recruited consecutively until the required sample size was achieved. Pregnant or lactating women, patients with immunosuppressive disorders, those with known hypersensitivity to zinc sulphate or cryotherapy, those having had systemic zinc supplementation or immunotherapy within the preceding three months, and patients

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with concomitant dermatological conditions that could interfere with treatment assessment were excluded.

After taking written informed consent from all the participants, demographic and baseline data was recorded on a standardised data collection form. Subsequently, the patients were randomised to oral zinc sulphate Group A and cryotherapy Group B using a computer-generated randomisation sequence. Allocation concealment was maintained using sequentially numbered, sealed opaque envelopes, which were opened only after participant enrolment.

Group A patients received oral zinc sulphate at a dose of 10mg/kg/day, divided into two daily doses, for eight weeks. Each tablet contained 220mg zinc sulphate, equivalent to 50mg elemental zinc. Treatment compliance and adverse events were assessed during each follow-up visit.

Group B patients underwent cryotherapy using liquid nitrogen applied by spray technique for 10-15 seconds until a frost halo developed around the lesion. Cryotherapy sessions were performed at two-week intervals, with a maximum of four treatment sessions or until complete wart clearance, whichever occurred first.

Clinical evaluation and standardized digital photographs were obtained at baseline and every two weeks throughout the treatment period. The primary outcome was complete clinical clearance of palmoplantar warts at the end of treatment. Secondary outcomes included time to complete clearance, recurrence during the 12-week post-treatment follow-up and treatment-related adverse effects.

Blinding could not be done because the nature of the interventions made either patient or physician blinding impractical. Clinical outcomes were assessed using predefined objective clinical criteria.

Data was analysed using SPSS 26. Continuous variables were summarised as mean ± standard deviation (SD) or median with interquartile range (IQR) as per data distribution, whereas categorical variables were expressed as frequencies and percentages. Comparisons between the treatment groups were performed using independent-samples t-test for continuous variables and the chi-square test or Fisher's

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exact test, where appropriate, for categorical variables. Two-tailed $p<0.05$ was considered statistically significant.

Results

Of the 60 patients enrolled in the study, 30 (50%) were allocated to each treatment group. The baseline demographic and clinical characteristics of the participants are presented in Table 1. There were no statistically significant differences between the two groups with respect to the recorded baseline demographic and clinical characteristics ($p>0.05$).

Complete clearance was observed in 23 (76.6%) patients in Group A, followed by partial response in 6 (20.0%) and no response in 1 (3.3%). The corresponding values in Group B were 20 (66.6%), 7 (23.3%) and 3 (10.0%), respectively ($p=0.32$) (Table 2).

During the 12-week follow-up period, recurrence was significantly lower in Group A, 1 (4.3%), compared to Group B, 4 (20%) ($p=0.04$) (Table 3).

The mean time to complete clearance was 6.0±1.3 weeks in Group A and 5.2±1.1 weeks in Group B ($p=0.07$) (Table 3).

Gastrointestinal adverse effects occurred in 4 (13.3%) patients in Group A, while pain in 19 (63.3%) and blistering in 11 (36.6%) were reported in Group B (Table 4). No serious adverse events were observed in either group.

Discussion

The present study compared the efficacy and safety of oral zinc sulphate with cryotherapy in the treatment of palmoplantar warts. Although oral zinc sulphate demonstrated a higher complete clearance rate than cryotherapy (76.6% vs. 66.6%), the difference was not statistically significant. However, patients treated with oral zinc sulphate experienced a significantly lower recurrence rate and fewer treatment-related adverse effects than those receiving cryotherapy. These findings suggest that oral zinc sulphate may represent a well-tolerated therapeutic alternative for selected patients with palmoplantar warts.

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Cryotherapy remains one of the most widely used first-line treatments for cutaneous warts because of its destructive effect on HPV-infected tissue. Nevertheless, pain during treatment, blister formation, repeated treatment sessions, and recurrence remain important limitations.[1–6] In the present study, cryotherapy produced a relatively high clearance rate, but recurrence occurred more frequently than in patients receiving oral zinc sulphate. These findings support the hypothesis that local tissue destruction alone may not eliminate latent viral infection completely, thereby predisposing some patients to recurrence.

Zinc plays an essential role in both innate and adaptive immune responses through regulation of lymphocyte proliferation, cytokine production and cell-mediated immunity. These immunomodulatory properties are believed to enhance the clearance of HPV-infected keratinocytes rather than simply destroying visible lesions.[7,8] This biological mechanism may explain the lower recurrence rate observed among patients treated with oral zinc sulphate in the present study.

Several studies have evaluated oral zinc sulphate for the treatment of viral warts with variable results. One study reported significantly higher clearance rates among patients receiving oral zinc sulphate, particularly in recalcitrant warts.[8] Another study observed favourable therapeutic responses following systemic zinc therapy.[9] Other investigators have also suggested that zinc supplementation may reduce recurrence by enhancing host immune function.[12,16,21] In contrast, some studies have reported little or no additional benefit compared to conventional therapies, indicating that treatment response may depend on factors such as wart subtype, lesion duration, baseline zinc status, and patient characteristics.[17,18]. The findings of the present study are consistent with this body of evidence, demonstrating comparable efficacy between oral zinc sulphate and cryotherapy while suggesting a potential advantage of zinc therapy in reducing recurrence.

The safety profile observed in the present study also favoured oral zinc sulphate. Only a small number of patients experienced mild gastrointestinal discomfort, which resolved without discontinuation of treatment. In contrast, post-procedural pain and blister

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formation were common among patients undergoing cryotherapy. Similar adverse effects have been consistently reported in studies evaluating cryotherapy for cutaneous warts.[18–20] These findings suggest that oral zinc sulphate may be particularly suitable for patients who have a low pain threshold, multiple lesions, or poor tolerance to destructive treatment modalities.

The present study has several clinical implications. Oral zinc sulphate is inexpensive, readily available, easy to administer, and associated with acceptable patient tolerability. Although complete clearance rates were comparable between the treatment groups, the lower recurrence rate observed with zinc therapy may provide an advantage in the long-term management of palmoplantar warts. Therefore, oral zinc sulphate may be considered an alternative treatment option, particularly for patients who decline or are unsuitable for repeated cryotherapy sessions.[22–24]

The current study has several limitations. It was conducted at a single centre with a relatively small sample size, which may have limited the statistical power to detect small differences in treatment efficacy. Follow-up was limited to 12 weeks, preventing the assessment of long-term recurrence. In addition, baseline serum zinc concentrations were not measured, therefore, the relationship between zinc deficiency and treatment response could not be evaluated. Future multicentre RCTs involving larger sample sizes, longer follow-up periods, and baseline assessment of serum zinc levels are recommended to further establish the role of oral zinc sulphate in the management of palmoplantar warts.

Conclusion

Oral zinc sulphate demonstrated comparable efficacy to cryotherapy in achieving complete clearance of palmoplantar warts, and was associated with a significantly lower recurrence rate and fewer treatment-related adverse effects, suggesting that oral zinc sulphate is a safe and well-tolerated treatment option and may serve as an alternative to cryotherapy, particularly for patients who are unable to tolerate painful destructive procedures or require systemic therapy.

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Table 1: Baseline demographic and clinical characteristics of study participants

Characteristic	Oral Zinc Sulphate (n=30)	Cryotherapy (n=30)	p-value
Age (years), mean ± SD	32.7 ± 8.1	33.4 ± 7.8	0.73
Male, n (%)	17 (56.7)	16 (53.3)	0.79
Female, n (%)	13 (43.3)	14 (46.7)	
Duration of warts (months), mean ± SD	8.4 ± 4.6	8.1 ± 4.3	0.80
Number of warts, median (IQR)	3 (2–5)	3 (2–5)	0.91
Palm involvement, n (%)	12 (40.0)	11 (36.7)	0.79
Sole involvement, n (%)	14 (46.7)	15 (50.0)	
Both palm and sole involvement, n (%)	4 (13.3)	4 (13.3)	

Table 2: Intergroup comparison of response to treatment.

Response	Oral Zinc Sulphate (n=30)	Cryotherapy (n=30)
Complete Clearance	23(76.6%)	20(66.6%)
Partial Response	6(20.0%)	7(23.3%)
No Response	1(3.3%)	3(10.0%)

Table 3: Intergroup comparison of recurrence and mean time to clearance.

Parameter	Oral Zinc Sulphate	Cryotherapy
Recurrence (12-week follow-up)	1(4.3%)	4(20%)
Mean Time to Clearance (weeks)	6.0 ± 1.3	5.2 ± 1.1

Table 4: Adverse effects observed in the two groups.

Adverse Effect	Oral Zinc Sulphate (n=30)	Cryotherapy (n=30)
Gastrointestinal Discomfort	4 (13.3%)	0 (0%)
Post-procedural Pain	0 (0%)	19 (63.3%)
Blistering	0 (0%)	11 (36.6%)

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JM: Design, data acquisition, analysis, interpretation and final approval.

SJ: Drafting, revision and final approval.

AR: Data interpretation, results and final approval.

SA: Abstract, writing, references and final approval.

NM: Provided resources, research work and final approval.

AK: Provides the patients data, follow up and final approval.

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