

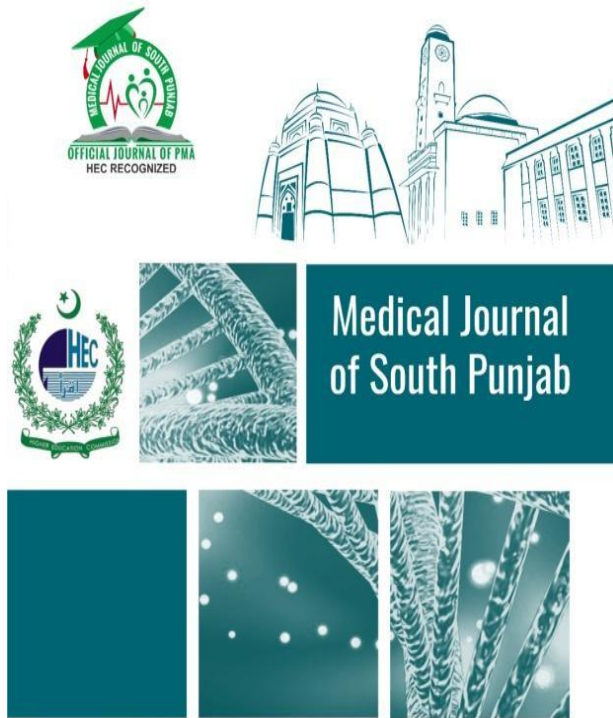
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Authors and Affiliation:

Shoaib Iqbal¹, Aliya Akhtar², Raheel Tahir³, Sidra Tahir⁴, Amra Batool⁵, Asma Batool⁶

¹⁻⁶Nishtar Hospital, Multan, Pakistan

***Corresponding Author Email:**

syadshoaibqbal@gmail.com

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Comparison of outcome with 50% salicylic acid versus cryotherapy in the treatment of plantar warts

Shoaib Iqbal¹, Aliya Akhtar², Raheel Tahir³, Sidra Tahir⁴, Amra Batool⁵, Asma Batool⁶

¹⁻⁶Nishtar Hospital, Multan, Pakistan

*Corresponding Author Email: syadshoaibiqbal@gmail.com

ABSTRACT:

Objective: To compare the outcome of 50% salicylic acid versus cryotherapy in treating plantar warts.

Methodology: An RCT was conducted at the dermatology department of Nishtar Hospital, Multan, from August 1st, 2024, to January 31st, 2025. A total of 656 patients with plantar warts were randomly allocated to Group A (cryotherapy) and Group B (50% salicylic acid). All patients were evaluated at the conclusion of week 12 following the commencement of therapy. The outcome was classified as complete response (absence of warts), partial response (decreased number of warts), and no response after 12 weeks of treatment. The outcome was compared using a 5% significance level chi-square test, and a p-value of ≤ 0.05 was considered significant.

Results: Both groups were comparable in terms of mean age, gender, duration of warts, and the number of warts. Group A had a higher complete response rate than Group B (30.8% vs. 24.7%; $p = 0.134$). No significant associations were found between patient response and study groups for age ($p = 0.180$), gender ($p = 0.120$), duration of warts ($p = 0.249$), or number of warts ($p = 0.458$).

Conclusion: Our study concludes that cryotherapy had a better complete response rate than 50% salicylic acid at 12 weeks of therapy in treating the plantar warts.

Keywords: Cold Therapy; Cryotherapy; Human Papillomavirus; Salicylic Acid; Plantar Warts; Verruca; Warts;

1. INTRODUCTION

Human papillomavirus (HPV) causes benign cutaneous lesions on the plantar surfaces of individuals, commonly referred to as plantar warts. There are over 100 recognized types. Plantar warts are primarily attributed to human papillomavirus types 1, 2, or 4¹. HPV frequently induces infections in the facial, palmar, plantar, and perineal regions.² Plantar warts typically exhibit self-limiting characteristics. They may occasionally cause discomfort, but they are highly contagious.^{3,4} The management of plantar warts frequently presents difficulties. Various therapeutic modalities have not consistently yielded successful outcomes. The modalities encompass topical acids, electrodesiccation, cryotherapy, and immunotherapy.^{5,6} Salicylic acid is one of the most frequently used topical treatments, which functions as a keratolytic agent, gradually eliminating virus-infected skin cells and potentially eliciting an immune response.⁷ Cryotherapy is another method that utilizes nitrogen in liquid form at a temperature of -196°C to induce inflammation through a cell-mediated response and facilitate cell eradication.⁸

Usman et al split 98 plantar wart patients evenly into two groups. Group A had cryotherapy, whereas Group B got 50% salicylic acid. The response rate was 26.5% in cryotherapy and 18.4% in 50% salicylic acid.⁹ After 12 weeks, 34.7% of group A and 30.6% of group B were effective. In another study, 40% topical salicylic acid was found to be superior to cryotherapy (66.7% vs 56.9%).¹⁰ This study aimed “to compare the effectiveness of 50% salicylic acid and cryotherapy in treating plantar warts”. Although a few studies have been conducted in Pakistan, this will not only help evaluate the outcomes of the proposed dual treatment modalities but also contribute to the local knowledge base. Analyzing the success rates of various treatments enables clinicians to identify the most effective therapies for patients, leading to improved cure rates and enhanced patient satisfaction. The Hypothesis of my study was “The frequency of complete response is higher in cryotherapy compared to 50% salicylic acid after 12 weeks of treatment.”

2. METHODOLOGY

A randomized controlled study was executed following the acquisition of institutional ethical permission (Ref # 21455/NMU; dated 09/12/2024). The procedure was conducted at the dermatology department of Nishtar Hospital, Multan, from August 1, 2024, until January 31, 2025. The sample size was determined with the method for two population proportions, with response rates of 18.4% for the 50% salicylic acid group and 26.5% for the cryotherapy group, at a power of 80% and a 95% confidence level.⁹ The minimum sample size was 656, with 328 participants in each category. Following the acquisition of informed consent, 656 patients of both sexes, aged 18 to 50 years, with either single or multiple warts on the plantar surface of their feet, were recruited using a non-probability sampling method. Individuals having a medical history indicating peripheral neuropathies, HIV, and diabetes mellitus were excluded from this investigation.

Following enrollment of 656 patients, their baseline parameters, including age, gender, duration, and number of warts, were recorded. Patients were randomly assigned to Group A (cryotherapy) and Group B (50% salicylic acid) using a lottery utilizing sealed, opaque envelopes. Group A had cryotherapy biweekly, with a minimum of four treatments. Group B received a 50% salicylic acid solution, which was to be applied daily to tissues with a cotton swab each morning for a duration of 8 weeks. All patients were evaluated at the conclusion of week 12 following the commencement of therapy. A consultant dermatologist will do an evaluation, uninformed of the designated treatment, and document the results about the resolution of the lesions from baseline. All data will be reported on a pro forma. The outcome was classified as complete response (absence of warts), partial response (decreased number of warts compared to baseline), and no response (unchanged or increased number of warts compared to baseline) following 12 weeks of treatment.

The analysis of data will be performed utilizing SPSS version 23. The Shapiro-Wilk test was used to evaluate the normality of the numerical data. Age, duration of warts, and quantity of warts were reported as mean and standard deviation. Gender and outcomes were presented as frequencies and

percentages. The group outcome was analyzed using a chi-square test at a 5% significance level. The data was categorized according to age, gender, and length to assess the impact on group outcomes. A post-stratification chi-square test was conducted, with a significance threshold set at a p-value of ≤ 0.05 .

3. RESULTS

A total of 356 patients were included in our study. The study patients were equally divided into two groups, Group A and Group B, each comprised of 328 participants (50.0%). The mean age was 34.77 ± 6.76 years in Group A and 36.40 ± 4.69 years in Group B, with a significant difference ($p < 0.001$). The age distribution showed that 26.5% of Group A and 11.9% of Group B were 18-30 years old, while 73.5% of Group A and 88.1% of Group B were 31-50 years old. The gender distribution was similar between the two groups (Male: 71.0% vs. 68.6%, Female: 29.0% vs. 31.4%, respectively, $p = 0.496$). The duration of warts was 26.41 ± 6.66 months in Group A and 28.56 ± 8.52 months in Group B, with an insignificant difference ($p = 0.176$). The number of warts was higher in Group A (3.88 ± 1.97) than in Group B (3.26 ± 1.43), with a significant difference ($p = 0.003$). (Table. I). In Group A, 30.8% achieved a complete response, 6.7% experienced a partial response, and 62.5% showed no response. In Group B, 24.7% had a complete response, 9.5% had a partial response, and 65.9% had no response. The difference was statistically insignificant between the groups ($\chi^2 = 4.01$, $p = 0.134$). (Table. II). No significant associations were found between patient response and study groups for age (18-30 years: $\chi^2 = 3.74$, $p = 0.154$; & 31-50 years: $\chi^2 = 3.42$, $p = 0.180$), gender (male: $\chi^2 = 5.39$, $p = 0.067$; & female: $\chi^2 = 4.24$, $p = 0.120$), duration of warts (<25 months: $\chi^2 = 2.10$, $p = 0.350$; & ≥ 25 months: $\chi^2 = 2.78$, $p = 0.249$), or number of warts (<3: $\chi^2 = 2.43$, $p = 0.297$; & ≥ 3 : $\chi^2 = 1.56$, $p = 0.458$). (Table. III).

Table 1:
Demographic and baseline variables

Variable	Group A 328 (50.0%)	Group B 328 (50.0%)	Test of sig.
Age (years)	34.77 ± 6.76	36.40 ± 4.69	
18-30	87 (26.5)	39 (11.9)	$\chi^2 = 22.63$, d.f=2, $p < 0.001$
31-50	241 (73.5)	289 (88.1)	
Gender			

Male	233 (71.0)	225 (68.6)	$\chi^2=0.46$, d.f=2, p=0.496
Female	95 (29.0)	103 (31.4)	
Duration of warts (months)	26.41±6.66	28.56±8.52	
<25	140 (42.7)	123 (37.5)	$\chi^2=1.83$, d.f=2, p=0.176
≥25	188 (57.3)	205 (62.5)	
Number of warts	3.88±1.97	3.26±1.43	
<3	153 (46.6)	191 (58.2)	$\chi^2=8.83$, d.f=2, p=0.003
≥3	175 (53.4)	137 (41.8)	
N (%), Mean±S.D			

Table 2:
Distribution of response rate between groups

Response	Group A 328 (50.0%)	Group B 328 (50.0%)	Test of sig.
Complete response	101 (30.8)	81 (24.7)	$\chi^2=4.01$, d.f=2, p=0.134
Partial response	22 (6.7)	31 (9.5)	
No response	205 (62.5)	216 (65.9)	
N (%)			

Table 3:
Association of patients' response and study groups with demographic and baseline profile

Variable	Response	Group A 328 (50.0%)	Group B 328 (50.0%)	Test of sig.
Age (years)				
18-30	Complete	30 (34.5)	7 (17.9)	$\chi^2=3.74$, d.f=2, p=0.154
	Partial	9 (10.3)	4 (10.3)	
	No	48 (55.2)	28 (71.8)	
31-50	Complete	71 (29.5)	74 (25.6)	$\chi^2=3.42$, d.f=2, p=0.180
	Partial	13 (5.4)	27 (9.3)	
	No	157 (65.1)	188 (65.1)	
Gender				
Male	Complete	73 (31.3)	61 (27.1)	$\chi^2=5.39$, d.f=2, p=0.067
	Partial	11 (4.7)	23 (10.2)	
	No	149 (63.9)	141 (62.7)	
Female	Complete	28 (29.5)	20 (19.4)	$\chi^2=4.24$, d.f=2, p=0.120
	Partial	11 (11.6)	8 (7.8)	
	No	56 (58.9)	75 (72.8)	
Duration of warts (months)				
<25	Complete	43 (30.7)	28 (22.8)	$\chi^2=2.10$, d.f=2, p=0.350
	Partial	11 (7.9)	11 (8.9)	
	No	86 (61.4)	84 (68.3)	
≥25	Complete	58 (30.9)	53 (25.9)	$\chi^2=2.78$, d.f=2, p=0.249
	Partial	11 (5.9)	20 (9.8)	
	No	119 (63.3)	132 (64.4)	
Number of warts				

<3	Complete	47 (30.7)	47 (24.6)	$\chi^2=2.43$, d.f=2, p=0.297
	Partial	10 (6.5)	19 (9.9)	
	No	96 (62.7)	125 (65.4)	
≥3	Complete	54 (30.9)	34 (24.8)	$\chi^2=1.56$, d.f=2, p=0.458
	Partial	12 (6.9)	12 (8.8)	
	No	109 (62.3)	91 (66.4)	
N (%)				

4. DISCUSSION

The majority of individuals will develop plantar warts at some point in their lives. Although plantar warts typically resolve on their own, individuals often seek treatment due to discomfort or the hindrance they pose to participating in sports and daily activities.^{11,12} Multiple methods, including cryotherapy, topical therapies, surgical curettage, and alternative remedies, can be addressed. A search for a safe and cost-effective treatment for plantar warts continues.^{3,13}

Regarding demographics, the mean age was approximately 35 years, with the majority of patients falling within the 31-50 years age range. The gender distribution was similar between the two groups (Male: 71.0% vs. 68.6%). A study indicated that 65.1% of patients were male, 77.6% resided in rural areas, and 37.5% were under 24 years of age.¹⁴ Males are more likely to engage in activities that increase the risk of exposure to human papillomavirus (HPV), such as walking barefoot in communal areas like locker rooms, gyms, or swimming pools.¹⁵ Regarding the features of warts, the mean duration until seeking treatment was around 26-28 months. The reasons for putting off treatment include the relatively harmless condition of warts, the possibility of self-resolution, and subtler forms of social discomfort or psychological distress. Treatment is sought after due to persistent troublesome symptoms and failed attempts at self-management.¹⁶

Group A (Cryotherapy) achieved a better complete response rate compared to topical 50% salicylic acid (30.8% vs 24.7%, p = 0.134), but the difference was statistically insignificant. A study conducted in Peshawar reported a better, but statistically insignificant, complete response for cryotherapy compared

to 50% salicylic acid (26.5% vs. 18.4%).¹⁷ Another study reported cryotherapy was effective for only 56.7%.¹⁸ In a study conducted by Brugginket *al.*, complete clearance was noted in 34% of those patients who were treated with cryotherapy and 31% in those treated with salicylic acid.¹⁹ In a recent network meta-analysis, cryotherapy was associated with the highest remission rate for treating palmoplantar warts, but at the cost of the highest pain scores and greater recurrences.²⁰

The current study found no significant relationships between treatment outcomes and patient-level characteristics, including age, gender, duration of treatment, or the presence of plantar warts. These clinical or demographic characteristics did not affect the treatment outcomes of 50% salicylic acid or cryotherapy. These findings support previous research indicating that individual factors do not significantly affect the efficacy of plantar wart treatment.²¹ The lack of connection with wart duration or number suggests that both treatments can be used regardless of disease duration or lesions.²² This study has a few limitations. First, the follow-up period was short, and this duration does not capture long-term efficacy or recurrence rates. Furthermore, the use of a non-probability sampling technique may limit the generalizability of the results. Lastly, crucial patient-centered outcomes, such as pain associated with treatment, cost-effectiveness, and overall satisfaction with the treatment regimen, were not evaluated, which are essential in influencing actual treatment adherence.

5. CONCLUSION

This study evaluated the efficacy of cryotherapy in comparison to 50% salicylic acid treatment for plantar warts. Though there was a greater response rate to cryotherapy, this difference did not reach statistical significance. Outcomes were independent of age, gender, duration, or the number of warts.

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