

Efficacy of oral zinc sulphate versus cryotherapy in the treatment of palmoplantar warts

Sumreen Hafeez, Leena Hafeez*, Javaid Iqbal**, Ghulam Mujtaba†, Saima Illyas†

Tehsil Headquarter Hospital, Kabirwala.

* Department of Dermatology, Khawaja Fareed Social Security Hospital, Multan.

** Department of Dermatology, Independent Medical College, Faisalabad.

† Department of Dermatology, Jinnah Hospital, Lahore.

Abstract **Objective** To compare the efficacy of oral zinc sulphate versus cryotherapy in treatment of palmoplantar warts.

Methods This randomized control trial was conducted in Department of Dermatology Nishtar Hospital Multan for a period of 6 months. A total of 104 patients having palmoplantar warts of less than 3 months, 18-35 years of age and both genders were included. Patients with periungual warts and pregnancy were excluded. Patients were randomly allocated into two groups by lottery method. Group A patients were given oral zinc sulphate (10mg/kg/day) into two divided doses for 6 weeks. Group B patients were given cryotherapy at weekly intervals for maximum of 6 sessions. Patients were followed at 2nd, 3rd and 6th week. At the end of 6 weeks both the groups were evaluated for treatment efficacy.

Results The mean age of patients in group A was 24.58±5.32 years and in group B was 24.13±5.40 years. Out of 104 patients, 56 (53.85%) were females and 48 (48.15%) were males with female to male ratio of 1.2:1. Efficacy of Group A (oral zinc sulphate) was seen in 45 (86.54%) patients while in Group B (cryotherapy) was seen in 33 (63.46%) patients (p-value = 0.007).

Conclusion Oral zinc sulphate has more efficacy than cryotherapy in the treatment of palmoplantar wart.

Key words

Palmoplantar warts, zinc sulphate, cryotherapy.

Introduction

Warts are firm papules with rough surface, caused by *human papilloma virus* (HPV) infection. They range in size from less than 1mm to over 1 cm and can form large masses when confluent.¹ Different clinical forms of warts include common warts, palmoplantar warts, flat warts, filiform warts and anogenital warts.² HPV

is a small DNA virus that infects squamous epithelium and causes cell proliferation.¹ There are over 150 genotypically different types of HPV with classification based on defined variation of viral DNA. The majority of common warts are caused by HPV types 1, 2, 4, 27, 57 and plane warts by 3 and 10.³ Different methods of treatment of warts include occlusion, cryotherapy, electrocautery, and laser. Topical agents include salicylic acid, cantharidin, trichloroacetic acid, podophyllin, 5 fluorouracil, and tretinoin. Systemic therapies are oral zinc sulphate, cimetidine and retinoids.^{1,3,4} But no single therapy has been

Address for correspondence

Dr. Sumreen Hafeez
Consultant Dermatologist
Tehsil Headquarter Hospital, Kabirwala.
Ph: 03008717213
Email: drsumreen10@gmail.com

proven effective at achieving complete remission in every patient.

Cryotherapy is one of the most commonly used methods for treating warts. It involves freezing wart with the use of a very cold substance, usually liquid Nitrogen. The studies done previously on cryotherapy showed variable cure rates ranging from 39% to 76.5%.^{5,6}

Oral zinc sulphate is also an effective therapy in the treatment of warts. Zinc has an important effect on the immune system and it has been used as an immunomodulator to treat a variety of skin disorders.⁷ In one study the result showed 85.72% cure rate.⁸ Another study showed 82% cure rate.⁹

The aim of this study is to compare two common treatment modalities, oral zinc sulphate and cryotherapy in treatment of warts. Cryotherapy is considered a standard treatment for most warts² but different studies showed that oral zinc sulphate is safe and efficacious and there is no clear evidence that other therapies are better than this. The findings of this study will help clinicians to treat the warts effectively and find a better treatment modality for palmoplantar warts, considering the efficacy, availability, patient's visits, cost and side effects.

Methods

This randomized controlled trial was conducted in the department of Dermatology, Nishtar Hospital Multan for a period of six months from 02.01.2017 to 30.06.2017. The patients were selected via Non-Probability Consecutive Sampling. A total of 104 patients were enrolled meeting the inclusion criteria. Patients of both genders, aged between 18-35 years, having palmoplantar warts for less than 3 months, who have not taken any therapy for warts previously, with number of warts less than or equal to 5 and

size of warts less than 1.5 cm were included in the study. Pregnant and lactating women, patients with periungual warts and the patients not willing to participate were excluded from the study. Patients were randomly allocated in to two groups by lottery method. Group A, having 52 patients, was given oral zinc sulphate (10mg/kg/day) into two divided doses for 6 weeks. Group B, also having 52 patients, was given cryotherapy at weekly intervals for maximum of 6 sessions. Patients were followed at 2nd, 3rd and 6th week. Those who had cleared their warts on follow up visits were not given further treatment. Cryotherapy was performed in the hospital, by applying liquid nitrogen with a cotton tip applicator for 10 to 30 seconds, until the ice ball formation spread to involve 1 mm margin of surrounding normal skin. Oral zinc sulphate was given in the dose of 10 mg/kg/day. At the end of 6 weeks both the groups were evaluated for treatment efficacy.

Results

Age range in this study was from 18-35 years with mean age of 24.49±5.33years. The mean age of patients in group A was 24.58 ± 5.32 years and in group B was 24.13±5.40 years. Majority of the patients 67 (64.42%) were between 18 to 25 years of age. Out of 104 patients, 56 (53.85%) were females and 48 (48.15%) were males with female to male ratio of 1.2:1. Mean duration of disease was 7.81±2.77 weeks. Mean size of warts was 1.39±0.70 cm. Mean number of warts was 1.83±1.08. Efficacy of Group A (oral zinc sulphate) was seen in 45 (86.54%) patients while in Group B (cryotherapy) was seen in 33 (63.46%) patients as shown in **Figure 1** (p-value=0.007). Stratification of efficacy with respect to age groups, gender, duration of disease, size, number of warts, BMI and socioeconomic status of patient is shown in **Table 1**.

Table 1 Stratification of efficacy with respect to age groups, gender, duration of disease, size, number of warts, BMI and socioeconomic status of patient.

		<u>Group A</u>		<u>Group B</u>		<i>P Value</i>
		Yes	No	Yes	No	
With respect to age in both group	18-25 years	29(87.88%)	04(12.12%)	24(70.59%)	10(29.41%)	0.093
	26-35 years	16(84.21%)	03(15.79%)	09 (50.0%)	09 (50.0%)	0.026
With respect to gender	Male	24 (80.0%)	06 (20.0%)	18(69.23%)	08(30.77%)	0.353
	Female	21(95.45%)	01 (4.55%)	15(57.69%)	11(42.31%)	0.003
With respect to duration of disease	≤ 6 weeks	20(90.91%)	02 (9.09%)	14(66.67%)	07(33.33%)	0.051
	> 6 weeks	25(83.33%)	05(16.67%)	19(61.29%)	12(38.71%)	0.055
With respect to size of wart	≤ 1 cm	23(95.83%)	01 (4.17%)	20 (80.0%)	05 (20.0%)	0.091
	>1 cm	22(78.57%)	06(21.43%)	13(48.15%)	14(51.85%)	0.019
With respect to no. of wart	1-3	28(90.32%)	03 (9.68%)	22(66.67%)	11(33.33%)	0.022
	4-5	17(80.95%)	04(19.05%)	11(57.89%)	08(42.11%)	0.112
With respect to Socioeconomic status	Poor	17(80.95%)	04(19.05%)	14(63.64%)	08(36.36%)	0.206
	Middle	16(94.12%)	01 (5.88%)	11(61.11%)	07(38.89%)	0.020
	Upper	12(85.71%)	02(14.29%)	08(66.67%)	04(33.33%)	0.250

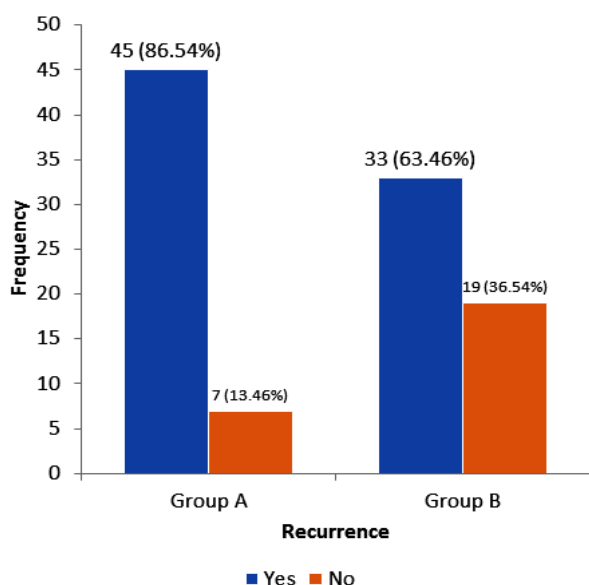


Figure 1 Comparison of efficacy in both groups.

Discussion

Zinc is perhaps the most important trace element for immune function and it has been used as an immunomodulator to treat a variety of skin disorders. Kitamura *et al.* proposed that toll-like receptor (TLR)-mediated regulation of zinc homeostasis influences dendritic cell function.¹⁰ Zinc deficiency has been shown to cause decreased immunity to cutaneous infections.^{11,12} It also has specific anti-viral activity; firstly, by cross-linking the double helix of viral DNA so

that it is unable to undergo the scission necessary for viral replication, and secondly, by inactivating the viral surface glycoproteins thus interfering with penetration into a susceptible host cell. Oral zinc sulphate is also an effective therapy in the treatment of warts Zinc sulfate is the most tolerated compound with highest bioavailability. Each 100 mg capsule of zinc sulfate contains 22.5 mg elemental zinc. Side effects are nausea, vomiting and mild epigastric distress.

Cryotherapy is one of the most commonly used methods for treating warts. It involves freezing wart with the use of a very cold substance, called cryogen. The most commonly used cryogen is liquid nitrogen with a temperature of -196°C.¹³ The effect on wart clearance may be through necrotic destruction of HPV-infected keratinocytes or by inducing local inflammation that triggers an effective cell-mediated response.¹³ Adverse effects with cryotherapy can include hypopigmentation or hyperpigmentation (especially in dark skin), tendon and/or nerve damage when therapy is too aggressive, and annular recurrence around the treated wart if blistering is excessive. Patients with poor circulation should also be treated with caution.¹³

In a study conducted in Pakistan in 2020 by Riaz *et al.* Oral zinc sulphate was found to be effective in 63.8% of the patients while cryotherapy was effective in 37.2% of the patients. They concluded that oral zinc sulphate was more effective than cryotherapy in the treatment of viral warts.¹⁴

Al Ghurair *et al.* treated 80 patients having recalcitrant warts with 10mg/kg of oral zinc sulphate and compared it with placebo. Complete clearance of warts was observed in 86.9% of the patients after two months of treatment which is similar to our study results.¹⁵

In another randomized double-blind placebo-controlled trial, oral zinc sulfate 10 mg/kg/d was given up to 2 months in patients with recalcitrant warts.¹⁶ After 2 months, complete clearance rate was 76.9% (10/13) in the treatment group versus 7.8% (1/13) in the placebo group. The regression of the warts was not asymptomatic as occurs in the natural evolution of the disease. Instead, it was associated with itching, increase in size and number of lesion for the first 2 weeks followed by subsidence.

Lopez-Garcia *et al.* in their study of 50 patients with ≥ 5 resistant warts¹⁷ found similar clearance rates with zinc sulfate and placebo (28% vs 24%) and pointed out that none of the patients in either group had low baseline zinc levels.

Stefani *et al.* conducted a randomized double-blind trial in 18 patients where they compared zinc sulfate (10 mg/kg/d) and cimetidine (35 mg/kg/d) for 3 months for resistant warts. They found zinc to be more effective than cimetidine.¹⁸

Regarding cryotherapy, our study results showed a clearance rate of 63.46% which is close to the results of big by M who demonstrated an efficacy of 65% in cryotherapy treated groups¹⁹

D Buckley in a study subjected 505 planter warts in 96 patients to open spray cryotherapy technique after debulking the warts with a surgical blade. 421 planter warts (83.5%) showed complete clearance rate with a single treatment. Clearance rate increased to 92.5% with three treatment sessions which is much higher than our findings.²⁰

Conclusion

This study concludes that oral zinc sulphate has more efficacy than cryotherapy in the treatment of palmoplantar wart. So, we recommend that oral zinc sulphate should be used routinely in these patients as it is more efficacious, easily available, less expensive with fewer side effects.

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