



ROLE OF ORAL ZINC SULPHATE IN THE TREATMENT OF RECALCITRANT COMMON WARTS

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ABSTRACT

Objective: To determine the efficacy of oral Zinc Sulphate in treatment of recalcitrant common warts.

Methods: In this randomized control trial 60 patients with recalcitrant warts were randomly allocated into two groups named Group A (Oral Zinc sulphate) and Group B (Placebo). Group A 30 patients were given oral zinc sulphate in a dose of 10mg/kg to a maximum dose of 600mg/day for two months. Group B 30 patients received glucose tablets as placebo.

Results: Out of 30 patients in oral zinc sulphate group, 20 (66.7%) patients had complete eradication or at least 75% reduction in number of warts noted at presentation. On the other hand in the placebo group only 2 (6.8%) patients had > 75% reduction in number of warts. In oral zinc sulphate group it was noted that only 3 (10.0%) patients had less than 50% reduction in no. of warts. 7 (23.3%) had 50-75% efficacy and majority 20 (66.7%) patients had > 75 % reduction in number of warts. In contrast, in the placebo group 23 patients (76.6%) had less than 50% reduction, followed by 5 (16.6%) patients having 50-75% reduction and only 2 (6.8%) patients had > 75% reduction in no. of warts

Conclusion: Warts are common viral infection of skin caused by Human Papilloma Virus. Despite various treatment options available at times warts become recalcitrant. Oral zinc sulphate is an effective treatment option for recalcitrant multiple viral warts. Being oral therapy it is easy to take with less frequent follow up visits required.

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INTRODUCTION

Verrucae (synonym: warts) are one of the most common viral infections of humans. These are caused by humanpapillomavirus (HPV). Warts are common, benign and usually self limiting lesions. ¹ HPV can cause disease at any site in stratified squamous epithelium either keratinized (skin) or nonkeratinized (mucosa). Warts are broadly classified as cutaneous, oral, genital and laryngeal warts. Among cutaneous warts are common warts, plane warts, plantar warts, periungual and filiform warts. ² Not all warts need treatment as many give little inconvenience and will resolve spontaneously. ^{3,4,5} Different treatment options are available for warts which include duct tape occlusion, topical salicylic acid, glutaraldehyde, podophyllin and podophyllotoxin, 5-fluorouracil, cryotherapy, electrocautery and curettage, imiquimod, photodynamic therapy, lasers and many others. ^{6,7} Among the systemic treatments documented are Cimetidine, Levamisol and Zinc sulphate. ⁸ Of the available treatment options none is uniformly effective or virucidal. Their safety and efficacy have not been assessed in double blind controlled clinical trials. Cryotherapy, electrocautery and topical

salicylic acid are most commonly used treatment options but none without side effects. Electrocautery carries a risk of scarring, cryotherapy causes pain and salicylic acid is irritant on facial skin and may cause contact dermatitis. ^{5,10} HPV infection does not induce inflammatory cytokines and therefore options aimed at modulating immune system and facilitating production of cytokines have been proposed ¹¹. One immunomodulatory approach involves prescribing oral zinc, a micronutrient that is necessary for normal functioning of cells. ¹² Mun JH, *et al* showed complete resolution of warts in 50% of patients with no serious side effects. ¹¹ Sadighha A in 2009 conducted a study showing a remarkable clearance rate of 76.9% in zinc sulphate treated patients versus 7.8% in placebo group. ¹³ Raza N demonstrated that serum zinc levels were low in patients with persistent, progressive and recurrent viral warts. According to their study zinc levels were low in 56% of patients compared to 32% of control with a significant p value of 0.003. ¹⁴ Oral zinc sulphate is not being used locally for the treatment of recurrent viral warts. It is speculated that being an oral therapy it would be more convenient for patients, requiring lesser clinic visits as are required for other available treatment options

PATIENTS AND METHODS

This comparative study was conducted in Department of Skin and V.D S.N Medical College Agra, from Jun 2018 to Dec 18. Sample size (n) 60 patients ,30 in each group. Patients of either gender between 18 and 65 years of age having single or multiple common warts on extragenital skin that are resistant to salicylic acid , electrocautery and cryotherapy used for at least six months(recalcitrant) were included.

Immuno compromised patients and those having comorbidities like hypertension, diabetes or any other known chronic illness were not included in the study. Pregnant and lactating women were also not included. Number and site of warts were noted. Patients were randomly allocated to Group A and Group B by lottery method. Oral zinc sulphate in a dose of 10 mg/kg body weight upto maximum of 600 mg/kg per day were given to group A for a period of two months. Group B received glucose tablets as placebo. Patients were reviewed after 4 weeks. Final outcome was seen at 8 th week. Confounding factors like age, gender and duration of warts were controlled by stratification. Comparison of efficacy in two groups was calculated by Chi-Square test. p value of < 0.05 was considered as significant.

RESULTS

Majority (33.3%) of the patients were from the age interval of 20 – 30 years (Table 1). Mean age of Group A was 26.32 ± 4.642 years having minimum age of 18 and maximum of 48 years. The mean age of placebo group was 24.68 years ±5.492 years having range of 18 to 46years .According to gender distribution of the patients there were 18 (60.0%) males in group A (experimental group) and 16 (53.3%) in placebo group having almost equal distribution (Table 2). There was no main difference in average number of warts on presentation before treatment. The mean number of warts in Oral Zinc Sulphate group was 7.63±1.721 with a range of 3 to 15 warts and in placebo group it was 6.41±1.672 ranging from 2 to 12. After 4 weeks of treatment total number of warts reduced to 3.68±1.561 warts on average with a range of 1 to 7 warts in group A and in group B the number of warts reduced to 4.89±1.632 warts on average ranging from 3 to 8 warts After 8 weeks of treatment the average number of warts reduced very significantly in oral zinc sulphate group to 1.43±1.284 warts with a range of 0 to 5 warts and in placebo group the average number of warts were noted to 4.62±1.280 warts with a range of 1 to 6warts . The efficacy of the treatment was defined as at least 75% reduction in number of warts and it was noted that in oral zinc sulphate group majority of the patients had > 75% reduction in number of warts i.e. 20 (66.7%) . In the placebo group majority of the patients 23 (76.6%) had less than 50% reduction (Table 3).The cross tabulation with respect to gender shows that there was no significant (p-value > 0.05) association between gender and efficacy of drug

Table 1 Age distribution (n=60)

Categorized age	Frequency	Percent	Cumulative Percent
< 20	14	23.3	23.3
20 – 30	20	33.3	56.6
30 – 40	16	26.6	83.2
> 40	10	16.8	100

Table 2 Distribution of gender in both groups

Group	Gender	Frequency	Percent	Cumulative Percent
Group A	Male	18	60	60

(Oral Zinc Sulphate)	Female	12	40	100
	Total	30	100	
Group B (Placebo)	Male	16	53.3	53.3
	Female	14	46.7	100
	Total	30	100	

Table 3 Distribution of Efficacy percentage in both groups

Group	Efficacy Percentage	Frequency	Percent	Cumulative Percent
Group A (Oral Zinc Sulphate)	<50%	3	10	10
	50-75%	7	23.3	33.3
	>75%	20	66.7	100
Group B (Placebo)	<50%	23	76.6	76.6
	50-75%	5	16.6	93.2
	>75%	2	6.8	100

DISCUSSION

More than 150 types of HPV have been recognized.¹⁵ warts are benign epithelial proliferations caused by human papillomavirus (HPV). Common warts are the commonest type of warts in children and adults. ¹ HPV is efficient at evading recognition. The virus can globally down regulate keratinocyte innate immune sensors and suppress the type I interferon response, which is critical for the control of viral infection. There is no viremia and no virus-induced cell death; hence, there is no inflammation or danger signal to the immune system. ¹⁷ Therefore, methods aim at modulating and enabling the immune system to detect and defend against this virus, can be a therapeutic option. One such option is oral zinc sulphate. Zinc is required for multiple cellular tasks, and especially the immune system depends on a sufficient availability of this essential trace element. ¹⁸Thymulin which is a Thymus specific hormone binds to highly specific binding receptors on T cells, induces several T cell markers and promotes T cell functions including allogenic cytotoxicity, suppressor function and IL-2 production. Levels of Thymulin are significantly decreased in minor zinc deficiency. INF- γ is a major component of Th1 response and it upregulates MHC I antigen expression. INF γ is decreased in zinc deficiency. ¹⁹ There are several other mechanisms by which zinc acts in boosting the immune system and enabling to counteract various bacterial and viral infections. ¹⁹ Al Gurairi *et al* first conducted a randomized placebo controlled trial. He administered oral zinc sulphate in a dose of 10mg/Kg body weight for two months in patients with recalcitrant warts and showed a clearance rate of 87% versus no response in placebo group. ^{20,21} Two placebo controlled RCTs showed remarkable CR rates:76.9% and 78.1% in the zinc sulphate treated group compared with 7.8% and 13% in the placebo group after 2 months of treatment. ^{13,22} Another randomized double-blind prospective study comparing the efficacy of oral zinc sulfate and cimetidine revealed a 62.5% CR in the zinc-treated group versus 0% in the cimetidine group. ²³ Mun JH, *et al* showed complete resolution of warts in 50% of patients treated with oral zinc sulphate with no serious side effects. ¹¹

CONCLUSION

This study confirms the role of oral zinc sulphate as a systemic treatment modality for viral warts with the advantage of being non-invasive, non scarring, and having the potential of preventing recurrences. Being oral therapy it is easy to take with less frequent follow up visits required.

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