

Topical zinc sulphate solution for treatment of viral warts

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ABSTRACT

Objective: To assess the efficacy and safety of topical zinc sulphate solution in the treatment of plane and common warts.

Methods: This study consisted of a pilot and double blinded clinical trails. This was carried out in the Department of Dermatology and Venereology, Baghdad Teaching Hospital, Baghdad, Iraq during the period from December 2002 to October 2003. Ten patients with plane warts were enrolled in pilot-clinical trial, all patients used 10% w/v zinc sulphate solution topically, 3 times daily for 4 weeks while in the double blind trial, 90 patients were included (50 patients with common warts, 40 patients with plane warts). Patients were randomly used either topical 10% or 5% zinc sulphate solution or distilled water as a control topical therapy 3 times daily for 4 weeks. Full history and close clinical examination were performed to all patients before treatment.

Results: In the pilot trial, the full response for plane warts was 80%, while the full response for patients with plane warts in double blinded trial was 85.7%, 42.8% and 10% for those using 10% and 5% zinc sulphate solutions and distilled water subsequently. The difference was statistically significant ($p < 0.008$). The full response for patients with common warts were 11%, 5% and 0% for those who used 10% and 5% zinc sulphate solutions and distilled water respectively, the difference was statistically insignificant. No recurrence of warts occurred during follow up that ranged from 2-6 months after therapy.

Conclusion: Topical 10% zinc sulphate solution was a new effective and safe modality for treatment of plane warts.

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Viral warts are benign proliferation of skin and mucosa that result from infection with Human Papilloma viruses (HPVs).¹ Human Papilloma viruses are members of genus family Papovaviruses which are double stranded DNA viruses that replicate inside the nucleus.² Viral warts are a common skin problem encountered in daily practice,³ and there are many modalities for treatment such as electrocautery, chemical cautery and many intralesional therapies.^{1,2,4-7} Still there are no uniformly effective one and whatever method used there will be failure and recurrences.⁸ Zinc is an important trace element and essential nutrient, it is present in all organs, tissues and fluids of the body.⁴ The skin and its appendages are rich in zinc. At cellular level over 300 zinc metalloenzymes have been identified, in which zinc serving as either a cofactors or an essential component of these enzymes.⁸ Zinc used in treatment of many dermatological disorders which acts either as immunomodulator,⁹⁻¹¹ antiviral,^{12,13} antioxidant and help in wound healing^{9,14} or cytotoxic.¹⁵ Zinc sulphate has been used successfully in the treatment of common warts and genital warts orally,¹² and intralesionally in recalcitrant common warts.¹³ The aim of the present work is to assess the efficacy of topical zinc sulphate solution in the treatment of common and plane viral warts.

Methods. This study was conducted in the Department of Dermatology and Venereology, Baghdad Teaching Hospital from December 2002 to October 2003. Ten patients were enrolled in pilot trial as part one and 90 patients in double blinded study as a second part. Full history was taken from each patient regarding age, gender, duration of warts, family history of the same disease and any previous treatment used for warts. Also, physical examination was carried out to assess the number and location of warts. The treatment was explained to patients and their oral consents were taken for the treatment. We excluded all patients with diabetes mellitus, medical problems such as immunosuppressive

conditions, patients who recently received any mode of therapy (topical or systemic) for the last 2 months before beginning this study. Patients were instructed to use the treatment topically 3 times daily for 4 weeks. A solution of 10% w/v zinc sulphate was prepared by dissolving 100 grams of zinc sulphate ($ZnSO_4 \cdot 7H_2O$ from British Drug house, Pool, England) in one liter of distilled water. While 5% w/v zinc sulphate was prepared by dissolving 50 grams of zinc sulphate in one liter of distilled water. Control solution contains distilled water only. Ten patients with plane warts were included in the pilot clinical trial. All patients used a 10% zinc sulphate solution topically. Ninety patients were shared in the double-blinded trial (40 patients with plane warts and 50 patients with common warts). Each patient was given randomly a container of the solution which labeled by a third person while the treating doctor and patient kept blindly until the end of the study. When the key was opened, the patients distributed according to type of solution used into: 20 patients used 10% zinc sulphate solution, 36 patients used 5% zinc sulphate solution and 34 patients used distilled water. All patients were reexamined and evaluated at the end of second week and at the end of fourth week (end of therapy) to assess the response to treatment and to record any adverse effects. The response was considered a full response when there were complete clearances of the lesions, and no response when there was no change; otherwise the response was regarded partial. Each patient with full response followed up monthly to record any recurrence of warts up to 6 months from the end course of therapy.

Statistical analysis was carried out using SPSS (Statistical Package for Social Science) version 10. A Chi-square test was used to compare the percent of response, and t-test was used to compare the mean of number and duration of warts in different groups. Probability value of less than 0.05 was considered statistically significant.

Results. In the pilot clinical trial in which all 10 patients with the plane warts used 10% zinc sulphate solution (Table 1), at the end of second week of treatment 5 (50%) patients showed partial response, while other

Table 1 - Response rates of patients in the pilot trial.

Responses	After 2 weeks n (%)	After 4 weeks n (%)
Full response	0 (0)	8 (80)
Partial response	5 (50)	0 (0)
No response	5 (50)	2 (20)
Total response	10 (100)	10 (100)

5 (50%) patients showed no changes and at the end of therapy (end of 4th week). Thus, 8 (80%) patients get a full response at the end of treatment, while the other 2 (20%) patients revealed no response. Sixty percents of the patients had some itching or pain at the sites of the lesions, all these patients showed a full response at the end of therapy. Three patients with full response had post inflammatory hypo pigmentation at the sites of lesions that disappeared completely within one month after stopping the therapy. All patients with full response followed up monthly for 2-6 months with a mean of 3.7 months, no patient showed any recurrence of the warts. In the double blinded trial, 90 patients used the treatment, 23 of them did not complete the therapy and considered as default patients. Thus, the study groups included 67 patients only, 24 patients with plane warts and 43 patients with common warts. Patients with plane warts were 12 (50%) males and 12 (50%) females. Their age ranged from 4-27 years with a mean±SD of 7.37±24 years. The duration of the disease ranged from 1-48 months with a mean±SD of 11.04 ±4.39 months. The number of warts per patients ranged from 10-56 warts with a mean ±SD of 32± 15.28 warts. After opening the key at end of the study (Table 2), the patients were distributed according to the type of treatment used by patients as following: 7 patients used 10% zinc sulphate solution, 7 patients used 5% zinc sulphate solution, and 10 patients used distilled water. At the end of 2nd week of treatment, 5 patients with plane warts showed partial response (4 patients from group used 10% and one patient used 5%). At the end therapy (end of 4th week) 6 patients from those used 10% zinc sulphate solution showed a full response (85.7%), 3 patients from those who used 5% zinc sulphate solution showed

Table 2 - Response rates for patients with plane and common warts in double blinded trial.

Type of treatment	No. of Response		Total
	Full response	No response	
<i>Patients with plane warts</i>			
Ten percent zinc sulphate	6	1	7
Five percent zinc sulphate	3	4	7
Distilled water	1	9	10
Total	10	14	24
<i>Patients with common warts</i>			
Ten percent zinc sulphate	1	8	9
Five percent zinc sulphate	1	21	22
Distilled water	0	12	12
Total	2	41	43

a full response (42.8%) and only one patient from those who used distilled water showed a full response (10%). There was no partial response in all treatments. When these results with full response compared with each other, the findings were statistically significant $p < 0.008$. During the application of solution, 7 (50%) patients that used 10% and 5% zinc sulphate solution suffered from itching or pain at the sites of lesions (patients with 10% and with 5%). All these patients who suffered from itching or pain showed a full response at end of the study while patients with no response had no itching or pain during treatment. In patients with full response, 6 of them suffered post inflammatory hypo pigmentation (3 used 10%, 2 used 5%, one used distilled water) which disappeared completely within 1-2 months, while no patients showed any residual scar. When we compared between the mean of number of warts in patients with full response (40.2 ± 13.6) and patients with no response (34.3 ± 14.2) the p-value was 0.31 which was statistically not significant. And when we compared between the duration of disease between the patients with full response (14.7 months ± 14.1) and the patients with no response (8.4 months ± 1.5) the p-value was 0.149 which was statistically insignificant. This means that the number and duration of the disease played no role in response to topical zinc sulphate. Patients with full response were followed up monthly for 2 - 6 months (mean 3 months), no patient showed recurrence of lesions. The number of patients with common warts was 43 patients, 29 (67.4%) females and 14 (32.6%) males. Their ages ranged from 4-45 years with a mean \pm SD of 19.7 ± 8.5 years, while the duration of disease ranged from 1-48 months with a mean \pm SD of 13 ± 12.4 months. The number of lesions per patient was 1-27 warts with a mean \pm SD of 7.6 ± 6.4 warts. After opening the key, as showed in **Table 2**, the patients were distributed as following: 9 patients used 10% zinc sulphate solution, 22 used 5% zinc sulphate solution and 12 patients used distilled water. At the end of the second week of treatment, no patient showed any response to therapy, and at the end of 4th week, only 2 patients showed full response, one used 10% and other used 5%. Thus, the full response rates were 11.1% and 4.5% for patients with common warts used 10% and 5% solution respectively, the p-value was 0.489 which was statistically insignificant.

Discussion. Zinc is an important element for several human functions and included in all essential systems in the body, one of these is the immune system.^{10,11} Also zinc might have cytotoxic effect when used topically in high concentration.¹⁵ Serum zinc was found to be low in patients with viral warts when compared with healthy people.¹² Patients will be encouraged to use oral zinc sulphate in treatment of viral warts and was found

to be effective as oral therapy and as intralesionally (by injection).^{12,13} Viral warts especially plane type is a common dermatological problem among Iraqi children. Although there are many topical remedies that have been used such as retionic acid, salicylic acid, trichloroacetic acid, 5-flourouracil and podophylin, all had a much failure rates and associated with many side effects which might limit their uses.^{1,2,4} Topical zinc sulphate therapy proved to be effective in plane warts in both pilot and in double blind trials and the cure rates were 80% in pilot trial and 86% in the double blinded trial. The present work had shown that topical zinc sulphate solution was ineffective in patients with common warts, this probably due to thick hyperkeratotic surface that prevent penetration of drug. When compared with plane warts with thin surface while oral zinc sulphate has been effectively in the treatment common warts. Thus, we recommend using oral zinc sulphate in treatment of common warts.¹² The present therapy, using 10% zinc sulphate solution showed no important side effects apart from slight itching, pain and transient hypo pigmentation that seen in some cases which might occur even in spontaneous resolution of plane warts.^{1,2} The exact mechanism of action of topical zinc sulphate in plane warts is not fully understood but we can speculate that the beneficial effects might be attributed through many effects of zinc, like enhancement of immunity by its immunomodulating action,^{10,11} its direct antiviral effect^{12,13} or due to its cytotoxic effect.¹⁵

In conclusion, 10% topical zinc sulfate solution is an effective, non-costly, new therapy for treatment of plane warts.

We recommend further studies to evaluate topical zinc sulfate solution and in higher concentration in treatment of both plane warts and common warts in combination with keratolytic agent to increase its effectiveness and to shorten the duration of therapy.

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