Clinical Study

The Clinical Effectiveness of Intralesional Injection of 2% Zinc Sulfate Solution in the Treatment of Common Warts

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Objective. To investigate the clinical efficacy and safety of intralesional injection of 2% zinc sulfate solution in the treatment of common warts.

Patients and Methods. One hundred and twenty patients (78 females and 42 males) aged 5–55 years with 225 common warts participated in this prospective monocentric randomized study. All lesions were treated with intralesional injection of 2% zinc sulfate. Results. From 225 warts injected, 135 warts (60%) cured from the first session, 51 warts (22.67%) cured from the second session, and 12 warts (5.33%) cured from the third session. There is no significant relation between improvement and patient’s ages, duration, or number of warts (P > 0.05). All patients complained from pain during injection, and all treated lesions showed redness, tenderness, and swelling in the first 3 days after injection. Late complications were postinflammatory hyperpigmentation in 90 patients (75%), scaring in 9 patients (7.5%), and ulceration in 3 patients (2.5%). Recurrence occurred in 3 lesions (1.33%). Conclusion. The clinical data indicate that intralesional injection of 2% zinc sulfate is an effective maneuver in the treatment of common warts; however, its associated complications limit its use.

1. Introduction

Verrucae are benign proliferations seen in skin and mucosae due to infection with papillomaviruses [1]. Although they do not produce acute symptoms and regress spontaneously in two-thirds of lesions within 2 years, they often need treatment due to cosmetic concerns and the dread of autoinoculation [2].

Treatment strategies for warts could be categorized into ablative/cytodestructive (cryotherapy, CO2 laser, trichloroacetic acid, and electrothermal surgery) and topical treatments (podophyllin, podophyllotoxin, imiquimod, cryotherapy, and interferon) [3]. Studies comparing different wart treatments are few [4, 5].

These treatments are considered to be similar in terms of efficacy [5], yet they are different in terms of duration of treatment and cost-effectiveness [6].

Zinc sulfate has an immunomodulatory function and plays a role in enhancing cellular and humeral immunity [7, 8]. Hence, it is used in the treatment of different skin and systemic diseases [9].

Zinc sulfate has been used successfully in the treatment of common warts and genital warts orally [7] and topically in plane warts [10].

The aim of the present work is to assess the clinical efficacy and safety of intralesional 2% zinc sulfate solution in the treatment of common warts.

2. Patients and Methods

2.1. Recruitment of Patients. A total of 120 patients (42 males and 78 females) with 225 common warts, aged 5 to 55 years, from the attendants of outpatient’s clinics in the Department of Dermatology, Al Azhar University Hospital, Asyut, Egypt, between June 2013 and February 2015 were included. The study was approved by the Local Institutional Ethics Committee of Faculty of Medicine, Al Azhar University. The duration of disease ranged from 1 to 24 months (mean ± SD, 7.15 ± 5.04...
2. Results

One hundred and twenty patients with 225 common warts were enrolled in this study. 42 patients (35%) were males and 78 patients (65%) were females. The age of the patients ranged from 5 to 55 years with mean ages of $23.6 \pm 11.7$ years. 69 patients had single wart and 51 patients had multiple warts, with mean number of warts $1.88 \pm 1.4$. The duration of the lesions ranged from 1 month to 24 months with mean duration $7.15 \pm 5.041$ months. Sites of injected warts were 144 warts (64%) in the upper limb, 72 warts (32%) in the lower limb, and 9 warts (4%) in the face.

From 225 warts injected 135 warts (60%) cured from the first session, 51 warts (22.67%) cured from the second session, and 12 warts (5.33%) cured from the third session with a mean number of sessions of $1.63 \pm 0.774$. From the remaining 27 warts 18 warts (8%) showed moderate response, 3 warts (1.33%) showed mild response, and 6 warts (2.76%) showed no response (Table 1, Figure 1).

There was no significant relation between improvement of warts after treatment and patient's ages, duration of disease, or number of warts ($P > 0.05$) (Table 2).

As regards complications, all patients complained from pain during injection, and all treated lesions showed redness, tenderness, and swelling in the first few days after injection. Late complications were transient postinflammatory hyperpigmentation in 90 patients (75%) which disappeared spontaneously at the end of the study, persistent scarring in 9 patients (7.5%), and ulceration in 3 patients (2.5%). Recurrence occurred in 3 lesions after 6 weeks from the treatment (1.33%) (Table 3).
There is no antiviral treatment that is specific for HPV, but some of the available therapies interfere with the viral life cycle. The most common approach for treatment is to damage or destroy the infected epithelium. This can also induce cell death and antigen exposure and presentation, thereby potentially inducing an immune response [1].

Topical zinc sulfate had been used successfully in the treatment of a wide variety of skin disorders such as cutaneous leishmaniasis [9], leg ulcers [11,12], recurrent erythema nodosum leprosum [13], perifolliculitis capitis abscendens et suffodiens [14], and alopecia areata [8].

In this prospective study, intralvesional injection of 2% zinc sulfate solution was shown to be effective modality in treatment of common warts, as the cure rate was 88%, and most of them (60%) needed just a single injection. Pain during injection was the most common complication. Post-inflammatory hyperpigmentation and scarring were the most common late complications. Recurrence of wart at the same site occurred only in three lesions.

Little studies have utilized intralvesional injection of 2% zinc sulfate solution for the treatment of common wart. In Sharquine and Al-Nuaimy study [15], out of 173 warts in 53 patients subjected to intralvesional 2% zinc sulfate injection, the total number of warts showing complete cure was 170 warts with clearance rate of 98.2% of the treated lesions within 6 weeks of follow-up (80.92% of lesions needed a single injection and showed total clearance within 2 weeks). There are no reported cases of recurrence of wart at the same site previously injected.

The effect of intralvesional injection of 2% zinc sulfate was similar or more superior to the effect of topical zinc in previous studies. Topical zinc sulfate (10%) is effective in the treatment of common and plane warts, with 86% complete clearance achieved versus 10% clearance in the placebo group [10]. In double-blinded randomized clinical trials of zinc oxide (20%) versus an salicylic acid/lactic acid ointment, 50% of patients achieved clearance in the zinc oxide group compared with 42% in the salicylic acid/lactic acid group [16].

The mechanism of action of zinc sulfate in viral warts cannot be speculated but is probably similar to the action of zinc sulfate in cutaneous leishmaniasis and bleomycin in viral warts, as both induce necrosis and inflammation [17-20]. When zinc sulfate is injected intradermally, it causes a marked infiltration of inflammatory cells (first a wave of eosinophils then lymphocytes, and finally fibroblasts) towards the injection site [21].

We concluded from this study that intralvesional injection of 2% zinc sulfate should be considered as a therapeutic option in the treatment of common warts.

### Competing Interests

The authors declare that there are no competing interests.

### References

[1] J. C. Sterling, S. Gibbs, S. S. Haque Hussain, M. F. Mohd Mustapa, and S. E. Handfield-Jones, “British association of dermatologists’ guidelines for the management of cutaneous warts 2014,” *British Journal of Dermatology*, vol. 171, no. 4, pp. 696–712, 2014.

[2] J.-H. Mun, S.-H. Kim, D.-S. Jung et al., “Oral zinc sulfate treatment for viral warts: an open-label study,” *Journal of Dermatology*, vol. 38, no. 6, pp. 541–545, 2011.

[3] N. Scheinfeld and D. S. Lehman, “An evidence-based review of medical and surgical treatments of genital warts,” *Dermatology Online Journal*, vol. 12, no. 3, article 5, 2006.

[4] E. J. Mayeaux Jr. and C. Dunton, “Modern management of external genital warts,” *Journal of Lower Genital Tract Disease*, vol. 12, no. 3, pp. 185–192, 2008.

[5] P. Komercik, M. Akklic-Materna, T. Strimitzer, and W. Aberer, “Efficacy and safety of imiquimod versus podophyllotoxin in the treatment of anogenital warts,” *Sexually Transmitted Diseases*, vol. 38, no. 3, pp. 216–218, 2011.

[6] M. Alam and M. Stiller, “Direct medical costs for surgical and medical treatment of condylomata acuminata,” *Archives of Dermatology*, vol. 137, no. 3, pp. 337–341, 2001.

[7] F. T. Al-Gurairi, M. Al-Waiz, and K. E. Sharquie, “Oral zinc sulphate in the treatment of recalcitrant viral warts: randomized placebo-controlled clinical trial,” *British Journal of Dermatology*, vol. 146, no. 3, pp. 423–431, 2002.

[8] G. Lutz and H. W. Kreyssel, “Selective changes in lymphocytic differentiation antigens in the peripheral blood of patients with alopecia areata treated with oral zinc,” *Zeitschrift für Hautkrankheiten*, vol. 65, pp. 132–138, 1990 (German).

[9] K. E. Sharquie, R. A. Najim, I. B. Farjou, and D. J. Al-Timimi, “Oral zinc sulphate in the treatment of acute cutaneous leishmaniasis,” *Clinical and Experimental Dermatology*, vol. 26, no. 1, pp. 21–26, 2001.
[10] K. E. Sharquie, A. A. Khorsheed, and A. A. Al-Nuaimy, "Topical zinc sulphate solution for treatment of viral warts," Saudi Medical Journal, vol. 28, no. 9, pp. 1418–1421, 2007.

[11] M. M. Black, D. J. Gaw Kroger, C. A. Seymour, and K. Weismann, "Metabolic and nutritional disorders," in Textbook of Dermatology, R. H. Champion, J. L. Burton, D. A. Burns, and S. M. Breathnach, Eds., vol. 59, pp. 2577–2673, Blackwell Science Ltd, Oxford, UK, 6th edition, 1998.

[12] E. A. J. Wilkinson, "Does oral zinc aid the healing of chronic leg ulcer?" Archives of Dermatology, vol. 134, pp. 1556–1560, 1998.

[13] P. M. Mahajan, V. H. Jadhav, A. H. Patki, D. G. Jogaikar, and J. M. Mehta, "Oral zinc therapy in recurrent erythema nodosum leprosum: a clinical study," Indian Journal of Leprosy, vol. 66, no. 1, pp. 51–57, 1994.

[14] B. Berne, P. Venge, and S. Ohman, "Pericoliculitis capitis abscedens et suffodiens (Hoffman). Complete healing associated with oral zinc therapy," Archives of Dermatology, vol. 121, no. 8, pp. 1028–1030, 1985.

[15] K. A. Sharquie and A. A. Al-Nuaimy, "Treatment of viral warts by intraleisional injection of zinc sulphate," Annals of Saudi Medicine, vol. 22, no. 1-2, pp. 26–28, 2002.

[16] J. A. Khattar, U. M. Musharrafieh, H. Tamim, and G. N. Hamadeh, "Topical zinc oxide vs. salicylic acid-lactic acid combination in the treatment of warts," International Journal of Dermatology, vol. 46, no. 4, pp. 427–430, 2007.

[17] D. R. Lowry and E. J. Androphy, "Warts," in Dermatology in General Medicine, T. B. Fitzpatrick, A. Z. Eisen, I. M. Wolff, K. F. Austen, L. A. Goldsmith, and S. I. Katz, Eds., vol. 244, pp. 2484–2497, McGraw Hill Book, New York, NY, USA, 5th edition, 1999.

[18] M. A. Sobh, M. M. Abd El-Razic, R. A. Rizc, M. M. Eid, I. A. Abd El-Hamid, and M. A. Ghoneim, "IntraleSIONAL injection of bleomycin sulphate into resistant warts in renal transplant recipients versus non-transplant warty patients," Acta Dermato-Venereologica, vol. 71, no. 1, pp. 63–66, 1991.

[19] S. F. Templeton, A. R. Solomon, and R. A. Swerlick, "Intradermal bleomycin injections into normal human skin. A histopathologic and immunopathologic study," Archives of Dermatology, vol. 130, no. 5, pp. 577–583, 1994.

[20] M. P. James, P. M. Collier, W. Aherne, A. Hardcastle, and S. Lovegrove, "Histologic, pharmacologic, and immunocytochemical effects of injection of bleomycin into viral warts," Journal of the American Academy of Dermatology, vol. 28, no. 6, pp. 933–937, 1993.

[21] R. A. Najim, K. E. Sharquie, and S. A. Al-Zubaidy, "Possible mechanisms of action of the compounds injected intraleSIONally in the treatment of cutaneous leishmaniasis, in addition to their direct effects on the parasites," Annals of Tropical Medicine & Parasitology, vol. 100, no. 1, pp. 33–38, 2006.