

Comparative Study of Topical 80% Trichloroacetic Acid With 35% Trichloroacetic Acid in the Treatment of the Common Wart

Fakhrozaman Pezeshkpoor MD,^a Mahnaz Banihashemi MD,^a Mohammad Javad Yazdanpanah MD,^a Hadis Yousefzadeh,^b Mohammad Sharghi MD,^c Hossein Hoseinzadeh^d

^aResearch Center for Cutaneous Leishmaniasis, Ghaem Hospital, Faculty of Medicine, Mashhad University of Medical Sciences (MUMS), Mashhad, Iran

^bImmunology PhD Student, Student Research Assembly of MUMS, MUMS, Mashhad, Iran

^cResident of Dermatology, Faculty of Medical Sciences, MUMS, Mashhad, Iran

^dGeneral Physician, Faculty of Medical Sciences, MUMS, Mashhad, Iran

ABSTRACT

Background: Common warts caused by the human papillomavirus (HPV) are considered to be the most common infectious skin disease. No individual treatment for common warts is effective as monotherapy in eradicating the lesions. The aim of this study is to evaluate the clinical efficacy of a 35% and an 80% trichloroacetic acid (TCA) solution in the treatment of the common wart.

Methods: In this single-blinded clinical trial, 62 eligible patients with common warts referred to the dermatology clinic of Ghaem Hospital in Mashhad, Iran. Patients were randomly divided into two groups, each treated with a TCA solution (group A, TCA 80%; group B, TCA 35%) once per week until complete clearance of the lesions or for a maximum duration of six weeks. Seven patients were excluded from the final analysis (one patient in group A and six patients in group B) for various reasons, including irregular follow-up, using physical tools such as razor blades to remove the lesion, and failure to complete treatment; and 55 patients were included in the final analysis.

Results: Improvement to treatment responses was classified as: no change (no changes in the number of warts), mild (clearing of less than 25% of warts), moderate (clearing of 25% to 75% of warts), and good (clearing of more than 75% of warts). At the end of follow-up, the clinical improvement of group A (n=30) was: 10 patients (33.3%) with a mild response, 6 patients (20%) with a moderate response, and 14 patients (46.7%) with a good response. In group B (n=25), 16 patients (64%) showed a mild response, 6 patients (24%) a moderate response, and 3 patients (12%) a good response. There was a statistically significant difference in improvement between the two treatment groups ($P=.017$). Improvement was greater with a higher concentration of TCA solution.

Conclusion: This study showed that a different concentration of TCA solution was an effective form of treatment for common warts. Trichloroacetic acid 80% is more effective, but this solution must be used only with careful consideration by a physician.

J Drugs Dermatol. 2012;11(11)e66-e69.

INTRODUCTION

Common warts are caused by the human papillomavirus (HPV). They affect 2% to 20% of school-aged children.¹ This infection can cause physical and emotional distress in patients.² There are different available treatments for the common wart, but in all cases, none of these treatments are individually effective in eradicating the lesions. Moreover, until now, there have not been any available specific antiviral therapies for HPV infection.³ The first line of therapy is salicylic acid resulting in regression of warts in two thirds of patients.^{4,5} In addition, cryotherapy, usually using liquid nitrogen, which freezes tissues and destroys the warts, is one of the most effective treatments. Chemical cauterization materials, such as monochloroacetic acid and trichloroacetic acid (TCA), have also been used as treatment.⁶ Trichloroacetic acid is a caustic and hemostatic agent. A saturated solution could be used alone for the treatment of many benign and dysplastic skin lesions. A solution of TCA with a concentration of 60% to 90% has been used for genital warts and for

vaginal and anal lesions.^{7,8} Trichloroacetic acid is applied topically and must be allowed to dry until a white frosting develops, and its application is accompanied by a burning sensation that lasts for two to five minutes.⁹ Studies using TCA 80% on genital warts have reported clearance rates of 70% to 81% after six applications.^{10,11} We hypothesized that applying a lower-concentration TCA solution could have different improvement results for the treatment of the common wart. This study was conducted to evaluate the clinical efficacy of TCA 80% and a lower concentration of TCA solution (35%) in the treatment of common warts. To date, this lower-concentration solution has not been used for treatment of the common wart.

METHODS AND MATERIALS

Patients and Study Procedures

This clinical trial study was approved by the Medical Ethics Committee of Mashhad University of Medical Sciences in Mashhad,

Iran. This study was single-blinded, where the dermatologist involved knew the prescription, but the patients did not, and was performed on 62 patients with common warts who were referred to the dermatology clinic of Ghaem Hospital in Mashhad, Iran. Patients were randomly divided into two groups: 31 patients were treated with TCA 80% (group A), and 31 patients with TCA 35% (group B). The division of participants was performed by a simple random-selection method: the patients who entered the study on odd days received TCA 80%, and the patients who entered the study on even days received TCA 35%.

Treatment and Follow-up

Exclusion criteria were patients younger than seven years, recent treatment of warts with another therapy, defects in wound healing such as diabetes, peripheral vascular disease, and distribution of the lesions anywhere except for the hands and feet. Before the procedure, the patients were advised to soak the lesions in tap water for two to five minutes until they become soft. After the lesions were dried, the TCA solution was applied with light pressure using a swab and allowed to dry until a white frosting developed. Treatment was continued for up to six weeks, and all patients were followed up each week. Any clinical improvement was evaluated by the same dermatologist at the end of week 7. After 12 weeks, the recurrence rate was evaluated.

Improvement to treatment responses was divided into four groups: no change (no changes in the number of warts), mild (clearing of less than 25% of warts), moderate (clearing of 25% to 75% of warts), and good (clearing of more than 75% of warts). Any side effects of treatment were recorded, such as erythema, itching, burning sensations, ulcers, scars, hyperpigmentation or hypopigmentation, infections, or edema.

Statistical Analysis

Data were collected and group comparisons involving categorical data made using chi-square analysis. Numerical data are expressed as mean \pm standard deviation (SD) or as proportions of the sample size.

Data were analyzed using SPSS for Windows (version 11.5; SPSS Inc, Chicago, IL). A *P* value less than .05 was considered significant.

RESULTS

Sixty-two patients with common warts were entered in our study. For various reasons, including irregular follow-up, using physical tools such as razor blades to remove the lesions, and failure to complete treatment, seven patients (one patient in group A and six patients in group B) were excluded, and 55 patients were included in the final analysis (Figure 1). Thirty patients (12 male and 18 female, aged 17.7 ± 9.6 years) were treated with TCA 80%, and 25 patients (5 male and 20 female, aged 20.4 ± 7.8 years) were treated with TCA 35%.

The weekly clinical improvement of the two groups is demonstrated in Table 1. In group A ($n=30$), clinical improvement after six weeks was: 10 patients (33.3%) with a mild response, 6 patients (20%) with a moderate response, and 14 patients (46.7%) with a good response. In group B ($n=25$), 16 patients (64%) had a mild response, 6 patients (24%) had a moderate response, and 3 patients (12%) had a good response. There was a statistically significant difference between the two treatment groups ($P=.017$), with group A showing a more favorable response.

Side effects such as burning sensations, tingling, local pain, scarring, and temporary hyperpigmentation were seen in 30% ($n=9$) of group A patients and in 20% ($n=5$) of group B patients.

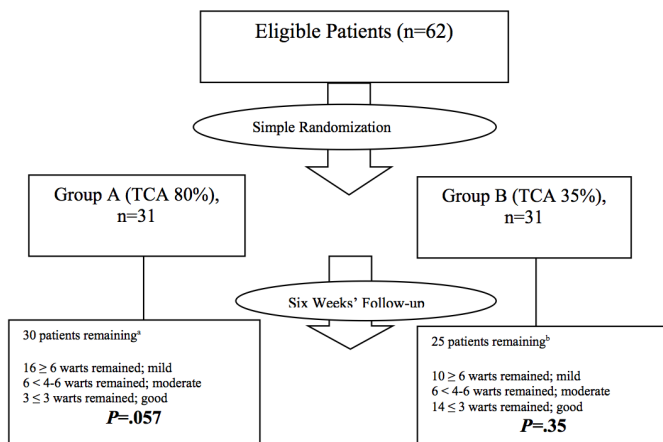
"Trichloroacetic acid has the advantage of a complete lack of systemic toxicity; it is not generally absorbed systemically, and its treatment is delivered in a controlled manner to provide limited local destruction, so it can be used during pregnancy."

Complications in group A were more severe than in group B, but there was no statistically significant difference between the two groups. In group A, the patients with 6 to 8 warts had a mild response, the patients with 6 warts had a moderate response, and the patients with 1 to 3 warts had a good response. In group B, the patients with 5 to 7 warts had a mild response, the patients with 3 to 5 warts had a moderate response, and the patients with 1 to 2 warts had a good response. (Figure 2).

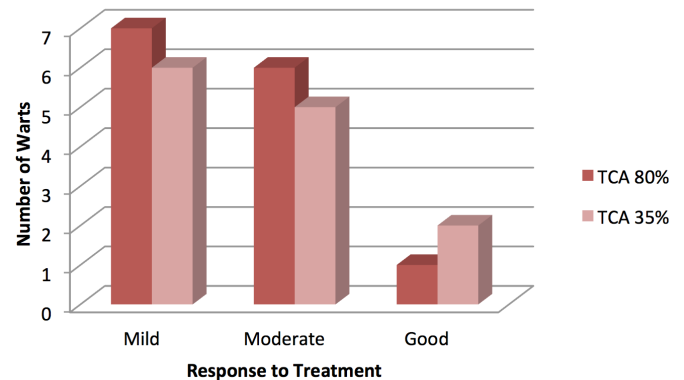
Twelve weeks after complete clearance, recurrence rates were 10% in group A, and 18.8% in group B.

DISCUSSION

There is no specific antiviral therapy available for curing HPV infections, and most treatments focus primarily on the destruction or removal of visible lesions or on the induction of cytotoxicity against the infected cell.² An extensive range of medications have been used to treat the common wart with different degrees of efficacy. These medications include keratolytic agents such as salicylic acid (67% efficacy), formic acid puncture (92% efficacy), glutaraldehyde (72% efficacy), silver nitrate (43% efficacy), imiquimod (70%-88% efficacy), oral zinc sulfate (86.9% efficacy), and oral cimetidine (32%-68% efficacy).¹²⁻²¹ In a previous study, our group found 82.6% efficacy using topical 80% phenol solution on the common wart.²² Cryotherapy has a similar efficacy to salicylic acid, and this method is inexpensive and available in every office. Trichlo-

FIGURE 1. CONSORT Flow Diagram of study patients.^aOne patient was excluded for irregular follow-up.^bTwo patients were excluded for using physical tools to remove lesions and four for irregular follow-up.

TCA, trichloroacetic acid.

FIGURE 2. Treatment response With TCA 80% and TCA 35% in patients with common warts.

TCA, trichloroacetic acid.

TABLE 1.**Frequency Distribution of Response to Treatment of Warts With TCA 35% and TCA 80%**

Response (P value)	TCA 80% (n=30)				TCA 35% (n=25)			
	No change	Mild	Moderate	Good	No change	Mild	Moderate	Good
End of week 1	16	14	–	–	22	3	–	–
		.76				.53		
End of week 2	12	18	–	–	18	7	–	–
		.36				.65		
End of week 3	4	16	10	–	7	18	–	–
		.024				.119		
End of week 4	–	14	16	–	1	19	5	–
		.76				.87		
End of week 5		10	18	2	–	19	5	1
		.03				.87		
End of week 6	–	10	6	14	–	16	6	3
		.057				.352		

TCA, trichloroacetic acid

roacetic acid 50% solution acts like phenol solution because of its destructive effects. Trichloroacetic acid works through the destruction of tissue by causing hydrolysis of cellular protein and, finally, cell death. All currently available published studies show that the effectiveness of TCA on genital warts is comparable with cryotherapy, having response rates between 70% and 81%.^{10,11} A few studies have shown that TCA was effective in treating cervical and anal warts.²³⁻²⁵ The effect of TCA on virus-infected cells is nonspecific. A low concentration of TCA (10%-30%) could be used for superficial peeling, and a higher concentration (50%-90%) for moderate to deep peeling. Trichloroacetic acid could also be helpful for skin diseases

such as xanthelasma palpebrarum and solar lentigines. Adequate application is achieved when the wart and surrounding area turn white. Trichloroacetic acid has the advantage of a complete lack of systemic toxicity; it is not generally absorbed systemically, and its treatment is delivered in a controlled manner to provide limited local destruction, so it can be used during pregnancy.³ Due to its rapid efficacy, TCA should be used with special care around the eyes because white frosting will appear after only a few minutes. The application of TCA is accompanied by a burning sensation that lasts for two to five minutes. Side effects are local pain, crust formation, infection, ulceration, and rarely, scar formation.²⁵

To the best of our knowledge, the current study is the first to evaluate the effectiveness of TCA in the treatment of the common wart. The clinical efficacy of different concentrations of TCA in our study was relatively similar to salicylic acid, but a higher concentration of TCA had a better response rate. Although this method is safe, simple to use, cost-effective, and readily available, care must be taken to prevent dermal injury and scar formation; therefore, we recommend that physicians use this method carefully.

DISCLOSURES

The authors have no relevant conflicts of interest to disclose.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the Research Council of Mashhad University of Medical Sciences, Mashhad, Iran, which financially supported the grant for this student thesis "Hossein Hoseinzadeh" with approval number 5106.

REFERENCES

- Kyriakis K, Pagana G, Michailides C, Emmanouelides S, Palamaras I, Terzoudi S. Lifetime prevalence fluctuations of common and plane viral warts. *J Eur Acad Dermatol Venereol.* 2007;21(2):260-262.
- Sterling JC. Virus infection. In: Burn T, Breathnach S, Cox N, Griffiths C, eds. *Rook's Textbook of Dermatology.* 8th ed. New York: Wiley Blackwell Ltd, 2010:37-52.
- Kirnbauer R, Lenz P, Okun M. Human papilloma virus. In: Bologna JL, Jorizzo JL, Rapini RP, eds. *Dermatology.* 2nd ed. New York: Mosby Elsevier; 2008:1180-1197.
- Ahmed I. Viral warts. In: Lebwohl M, Heymann WR, Berth-Jones J, Coulson J, eds. *Treatment of Skin Disease: Comprehensive Therapeutic Strategies.* 3rd ed. New York: Mosby; 2010:770-775.
- Bunney MH, Nolan MW, Williams DA. An assessment of methods of treating viral warts by comparative treatment trials based on a standard design. *Br J Dermatol.* 1976;94(6):667-679.
- Steele K, Shirodaria P, O'Hare M, et al. Monochloroacetic acid and 60% salicylic acid as a treatment for simple plantar warts: effectiveness and mode of action. *Br J Dermatol.* 1988;118(4):537-543.
- Scheinfeld N, Lehman DS. An evidence-based review of medical and surgical treatments of genital warts. *Dermatol Online J.* 2006;12(3):5.
- Kodner CM, Nasraty S. Management of genital warts. *Am Fam Physician.* 2004;70(12):2335-2342.
- Baker GE, Tying SK. Therapeutic approaches to papillomavirus infections. *Dermatol Clin.* 1997;15(2):331-340.
- Abdullah AN, Walzman M, Wade A. Treatment of external genital warts comparing cryotherapy (liquid nitrogen) and trichloroacetic acid. *Sex Transm Dis.* 1993;20(6):344-345.
- Damstra RJ, van Vloten WA. Cryotherapy in the treatment of condylomata acuminata: a controlled study of 64 patients. *J Dermatol Surg Oncol.* 1991;17(3):273-276.
- Berman A, Winkelmann RK. Involuting common warts. Clinical and histopathologic findings. *J Am Acad Dermatol.* 1980;3(4):356-362.
- Gibbs S, Harvey I, Sterling J, Stark R. Local treatments for cutaneous warts: systematic review. *BMJ.* 2002;325(7362):461.
- Bhat RM, Vidya K, Kamath G. Topical formic acid puncture technique for the treatment of common warts. *Int J Dermatol.* 2001;40(6):415-419.
- Hirose R, Hori M, Shukuwa T, et al. Topical treatment of resistant warts with glutaraldehyde. *J Dermatol.* 1994;21(4):248-253.
- Yazar S, Başaran E. Efficacy of silver nitrate pencils in the treatment of common warts. *J Dermatol.* 1994;21(5):329-333.
- Muzio G, Massone C, Rebora A. Treatment of non-genital warts with topical imiquimod 5% cream. *Eur J Dermatol.* 2002;12(4):347-349.
- Grussendorf-Conen EI, Jacobs S. Efficacy of imiquimod 5% cream in the treatment of recalcitrant warts in children. *Pediatr Dermatol.* 2002;19(3):263-266.
- Al-Gurairi FT, Al-Waiz M, Sharquie KE. Oral zinc sulphate in the treatment of recalcitrant viral warts: randomized placebo-controlled clinical trial. *Br J Dermatol.* 2002;146(3):423-431.
- Yilmaz E, Alpsoy E, Basaran E. Cimetidine therapy for warts: a placebo-controlled, double-blind study. *J Am Acad Dermatol.* 1996;34(6):1005-1007.
- Gooptu C, Higgins CR, James MP. Treatment of viral warts with cimetidine: an open-label study. *Clin Exp Dermatol.* 2000;25(3):183-185.
- Banihashemi M, Pezeshkpoor F, Yazdanpanah MJ, Family S. Efficacy of 80% phenol solution in comparison with cryotherapy in the treatment of common warts of hands. *Singapore Med J.* 2008;49(12):1035-1037.
- Boothby RA, Carlson JA, Rubin M, Morgan M, Mikuta JJ. Single application treatment of human papillomavirus infection of the cervix and vagina with trichloroacetic acid: a randomized trial. *Obstet Gynecol.* 1990;76(2):278-280.
- Malviya VK, Deppe G, Pluszczynski R, Boike G. Trichloroacetic acid in the treatment of human papillomavirus infection of the cervix without associated dysplasia. *Obstet Gynecol.* 1987;70(1):72-74.
- Taner ZM, Taskiran C, Onan AM, Gursay R, Himmetoglu O. Therapeutic value of trichloroacetic acid in the treatment of isolated genital warts on the external female genitalia. *J Reprod Med.* 2007;52(6):521-525.

AUTHOR CORRESPONDENCE

Mahnaz Banihashemi MD

E-mail:.....banihashemim@mums.ac.ir