Original Article

Comparison Of The Efficacy Of 70% Trichloroacetic Acid Versus Cryotherapy In The Treatment Of Plantar Warts

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Abstract

Objective: To assess the efficacy of 70% Trichloroacetic acid and Cryotherapy as a treatment modality in the resolution of plantar warts.

Methods: This quasi-experimental study was conducted in the Dermatology department of a tertiary care hospital, from September 2024 to February 2025. 70 patients visiting the outpatient department meeting the inclusion criteria were enrolled in the study after approval from the hospital ethical committee. Informed written consent was taken from participants, and they were allocated into two groups. Group A was treated with Cryotherapy every two weeks, and those in Group B received a 70% Trichloroacetic acid application every week. All patients were followed for 8 weeks in order to assess the efficacy and to monitor the side effects of treatment.

Results: The mean age in the Cryotherapy group was 35.9 ±9.16 years, and in the Trichloroacetic acid group was 33.67 ±9.64 years. There were 44 (62.85%) male and 26 (37.14%) female participants in this study. Efficacy of therapy for plantar warts was observed in 14 (40%) patients in the 70% Trichloroacetic acid group, while in 9 (25.71%) patients in the Cryotherapy group, having a non-significant p value of 0.203.

Conclusion: 70% Trichloroacetic acid is equally effective as compared to Cryotherapy in the treatment of plantar warts, and it may be considered as a suitable alternative therapeutic option due to its comparable efficacy, easy availability, cost-effectiveness, and tolerability.

Keywords: Cryotherapy, Efficacy, Plantar Warts, Trichloroacetic Acid.

Introduction

Cutaneous warts are caused by infection of epidermal cells with Human Papillomavirus (HPV), resulting in benign skin growth. There are more than 200 species of HPV, and the prevalence of infection with HPV in school-going children is 2-20%.[1] However, only 3-5% develop warts, and among those, the incidence of palmoplantar warts is 14% per annum in the general population. Warts can manifest in all age groups; however, children and young adults are most commonly affected. [2]

Clinically, warts can involve any part of the body, and they are encountered in different morphological forms like common warts, filiform warts, anogenital warts, and palmoplantar warts.[2] Anogenital warts are transmitted through sexual contact and, if left untreated, can result in a significant increase in size, recognised as condyloma acuminata**.** Plantar warts involving the soles and heads of metatarsals usually result in pain, which forces the individual to seek treatment. Warts are benign lesions but cause social embarrassment, especially when they appear on exposed and sensitive parts of the body like the face, eyes and genitalia.[3] Inoculation of the virus could be secondary to direct or indirect contact and disruption in the epithelial barrier due to trauma, maceration, walking barefoot on public surfaces, and immunosuppression predispose to the development of warts. Inhalation of smoke during the ablation of warts with laser or electrocautery may also result in the development of warts in the airway tract.[4] Immunocompromised individuals are prone to develop recalcitrant warts, and malignant changes, such as verrucous carcinoma, may develop rarely.[5]

Warts are diagnosed clinically and confirmed on histology in doubtful cases. Multiple therapeutic options are being used for the treatment of warts, including local application of trichloroacetic acid (TCA), podophyllotoxin, 5-fluorouracil, electrocautery, autoinoculation, and C02 Laser ablation. Levamisole, zinc sulfate, and cimetidine have been used orally in past with limited effectiveness.[6] Intralesional injections of interferon, Candida albicans, BCG, MMR, and HPV vaccine are also used as immunomodulatory agents.[7,8] To date, no targeted anti-viral agent has been developed specifically for the treatment of warts.

Cryotherapy is the most frequently used method, and its advantages are rapid application and cost-effectiveness. Trichloroacetic acid (TCA) is a chemical cauterant that causes hydrolysis and destruction of keratinocytes infected with HPV, as well as stimulates the local immune response.[9] Efficacy of 40% trichloroacetic acid was reported as 86.67% as compared to 76.67% with cryotherapy by Karrabi M et al. in the resolution of plantar warts.[9] Whereas, Cengiz reported the efficacy of 40% trichloroacetic acid versus cryotherapy as (33.3% vs. 6.7%) in plantar warts.[10]

These studies showed that trichloroacetic acid has comparable effectiveness as compared to cryotherapy in plantar warts.

Because of the resistant and recurrent nature of warts, their treatment with conventional methods like cryotherapy and electrocautery often proves to be ineffective. Moreover, limitations of cryotherapy include the need for special equipment like cryo-cylinder, cryogun and its non-availability at different health centres. So, we conducted this comparative therapeutic trial to assess the efficacy of 70% trichloroacetic acid with cryotherapy to find out an alternate, easily available and cost-effective treatment modality for warts. This will

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help us to generate local data and improve the outcome in such patients by adopting the superior approach as the first choice of treatment in the future.

Materials And Methods

This quasi-experimental study was carried out in the dermatology department of CMH Hospital Malir, from 1st Sep 2024 to 28th Feb 2025. The sample size of 70 patients was determined by the WHO sample size calculator by using the efficacy of trichloroacetic acid (P1) and cryotherapy (P2) as 33.3% vs 6.7% [10], the power of the test was (1-β) =80% and the level of significance was 5%. Approval from the hospital's ethical and research committee (93/2024/trg/ERC) was obtained. Non-probability consecutive sampling was used, and patients were enrolled after their informed written consent.

Patients were diagnosed clinically, and the inclusion criteria included patients of both genders and all age groups, duration of warts 1-4 months, and patients who had not received any treatment so far. Pregnant, lactating females, and patients with keloidal tendency, history of Raynaud's disease, peripheral vascular disease, cold intolerance, or cold urticaria were excluded. Patient's information, including age, gender, number of warts, and disease duration, was noted on a predesigned proforma. The study was conducted in a single-blind fashion, and patients were split into two groups. Group A received Cryotherapy with liquid nitrogen gas, performing two freeze and thaw cycles (of 10 seconds each) every two weeks. Whereas in group B, 70% trichloroacetic acid solution was applied on warts with a cotton-tipped orange stick by the same physician for 5-10 seconds weekly for 8 weeks or till resolution of wart, whichever is earlier, and the patients were advised to wash that area 4 hours after the procedure. Patients were assessed and photographed regarding the resolution of warts and side effects (itching, local pain, ulceration, and scarring) related to treatment at each visit. Treatment was labelled as effective if complete clinical resolution of the warts was achieved 2 weeks after the last treatment.

Analysis of data was done by using SPSS version 25. Quantitative variables like age, duration and number of warts were expressed in terms of mean and standard deviation. Frequencies and percentages were calculated for qualitative variables like gender and efficacy. An Appropriate Chi-square / Fisher's Exact test was applied in both groups to assess effectiveness, using $p \leq 0.05$ as significant.

Results

70 patients were enrolled in this study, 35 patients in each 70% Trichloroacetic acid and Cryotherapy group. The mean age was 35.9±9.16 years in the Cryotherapy group and 33.67±9.64 years in the 70% TCA group. The mean duration of disease in the Cryotherapy and 70% TCA group was 2.6±0.78 and 2.3±0.81 months, respectively. The mean number of warts in the Cryotherapy group was 2.7±1.1, and in the 70% TCA group was 3.15 ±2.18. Distribution of quantitative variables was interpreted by the Shapiro-Wilk test for age (p=0.140), duration of warts (p=0.20) and number of warts (p=0.093) in the Cryotherapy group, while age (p=0.218), duration of warts (p=0.027) and number of wart (p=0.10) in 70%TCA group, as shown in table 1.

Table 1: Descriptive statistics of the Shapiro-Wilk test (n=70)

Groups	Variable	MEAN±SD	95% CI	P-VALUE
Cryotherapy	**Age** (years)	35.9±9.16	31.37±35.97	0.140
	Duration of warts (months)	2.6±0.78	2.17±2.56	0.200
	Number of warts	2.7±1.1	2.85±3.46	0.093
70% Trichloroacetic Acid	**Age** (years)	33.67±9.64	31.37±35.97	0.218
	Duration of warts (months)	2.3±0.81	2.17±2.56	0.027
	Number of warts	3.5±1.28	2.85±3.46	0.010

Gender distribution revealed 44 (62.85%) male and 26 (37.14%) female participants in total, and male predominance might be attributable to occupational exposure, outdoor activities, and sports. Frequencies of male and female patients in both groups are shown in Figure 1.

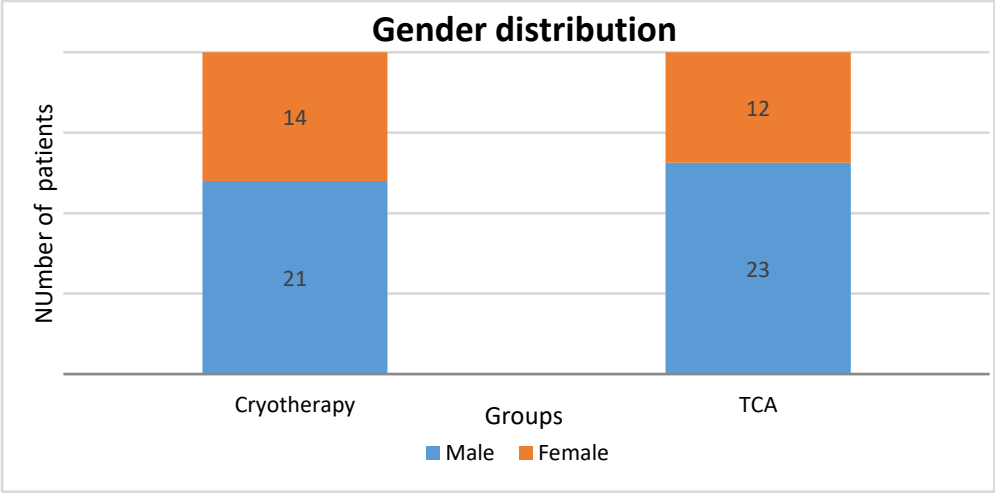

Figure: 1 Gender Distribution

Complete resolution of warts was observed in 14(40%) patients treated with 70% Trichloroacetic acid and 9(25.71%) patients treated with Cryotherapy (p= 0.203) as shown in Table 2. Although, difference in efficacy among the two groups was statistically non-significant, the number of patients cured in the 70% Trichloroacetic acid group was higher compared to the Cryotherapy group. Side effects observed during the procedures were mild burning pain in the TCA group as compared to moderate pain and blister formation in some patients in the Cryotherapy group; however, these unwanted effects were mild and self-resolving.

Table 2: Comparison of efficacy between groups (n=70)

Groups	Efficay		p-value
	Yes	No	
	No. of patients	No. of patients	
Cryotherapy	9 (25.7%)	26(74.3%)	0.203
70%Trichloroacetic acid	14 (40%)	21(60%)	

Discussion

HPV, a DNA virus, in plantar warts can remain dormant in epithelial cells for up to 12 months, and its continuous shedding via desquamated cells explains recurrence after treatment even in immunocompetent individuals.[2] Warts, which usually do not respond to standard treatment protocol, are called recalcitrant warts, and they may be associated with immunosuppression. Recalcitrant warts are a therapeutic challenge for health care providers, with high recurrence rates and have significant impact on quality of life. None of the treatments alone is 100% effective in warts, so different modalities are being used synergistically, and these frequently employed therapies are currently not supported by conclusive clinical trials as well.[6,10] Cryotherapy is an ablative procedure which is done with the use of various cryogens at a very low temperature, and liquid nitrogen is the most frequently used agent at -196 °C. It provokes intra- and extracellular ice formation, which causes necrosis of cellular organelles, ultimately leading to destruction of the targeted tissue.[11] Cryotherapy is considered as treatment of choice by most healthcare professionals, although discomfort, altered skin pigmentation, and vesicle formation are adverse effects related to this procedure.

Trichloroacetic acid (TCA) is a chemical substance that eradicates warts by causing coagulative necrosis and denaturation of the affected tissue.[12] TCA has been used in different concentrations ranging from 40% to 90% for plantar and genital warts.[13] The British Association of Dermatologists recommend the use of 50%–80% Trichloroacetic acid every week for the eradication of warts. We used 70% Trichloroacetic acid in this study and found it to be effective in 40% of patients, which is comparable with 33.3% efficacy as reported by Cengiz et al.[10]

Literature review varies regarding the effectiveness of TCA in warts, and varying concentrations of TCA have been compared in different studies. Abdul Megaid et al conducted a randomised control trial to compare 90% Trichloroacetic acid against Cryotherapy, and complete cure was seen in 21.3% of patients in comparison to 83.1% of patients treated with Cryotherapy (p<0.001); however, side effects were more common with Cryotherapy as compared to the TCA group.[13] Pezeshkpoor et al compared 80% and 35% TCA for treating warts, and they observed 46.7% improvement with higher concentration than 12% improvement with lower concentration (p = 0.017), which also supports our results.[14]

Cure rates of cryotherapy in warts treatment are also variable in different trials, as evident by the studies of Kerrabi, Cengiz, Muhaidat and Usman et al., who documented cure rates 76.67%, 6.7%, 39% and 34.7%, respectively.[9,10,15,16] Even different modes for delivery of Cryotherapy have also been assessed, as Albalat found intralesional Cryotherapy significantly more effective than use of cryospray (80.3% vs 50.8%, p <0.001 respectively) with a low recurrence rate in recalcitrant warts.[17]

Needling has gained attention as a potential treatment modality for warts as it creates microchannels in the skin, which facilitates deeper penetration of topically applied drugs in the virus-infected tissue. Bodar performed needling with the help of insulin syringes on recalcitrant warts, followed by the topical use of 100% Trichloroacetic acid and complete clearance was observed in 96.2% patients.[18] Mohta et al. carried out a comparative clinical trial in resistant warts by combining micro needling with 100% TCA versus microneedling with bleomycin. Needling with 100% TCA showed comparable efficacy against needling with bleomycin (63.5% vs 81.4%, p=0.13), respectively.[19]

As far as the efficacy of 70% trichloroacetic acid is concerned in our study, it is comparable to Cryotherapy in the resolution of planter warts, and our results of 70% TCA are comparable with those conducted by Cengiz, Abdul Megaid and Pazeshkapoor (40% vs 33.3%, 26% and 46.7% respectively), although there was a difference in concentration of TCA being used in these trials.[10,13,14] Easy availability, better safety profile, and simple application even at home make it a new addition to current treatment modalities, especially in resource-limited settings. The limitation of our study is that we did not follow the patients beyond 8 weeks to monitor sustained response and recurrence of plantar warts.

Conclusions

Topical application of 70% trichloroacetic acid in plantar warts is a relatively painless procedure with a better safety profile, and it could be considered as an alternative treatment modality, especially in kids, where inoculation, cryotherapy, or electrocautery is restricted secondary to discomfort associated with these procedures. However, more clinical trials with longer duration in multiple healthcare centres are required to validate our findings and to establish a standard treatment protocol.

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