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Comparative Efficacy of Cryotherapy Versus Topical Trichloroacetic Acid 90% in Treatment of Common Warts

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ABSTRACT

Objective: To compare the efficacy of Cryotherapy using liquid Nitrogen versus Trichloroacetic acid 90% in treatment of common warts.

Study Design: Randomized Control Trial (ClinicalTrials.gov: NCT05712811).

Place and Duration of Study: Department of Dermatology, Combined Military Hospital Abbottabad, Pakistan from Jun to Nov 2022.

Methodology: Sixty patients with common warts (hard lesions, raised lumps with rough surfaces at the back of fingers, around nails and palm of hands) diagnosed by consultant dermatologist on clinical presentation were included in this study. The sample size was calculated by WHO Sample Size calculator. After randomization, patients were divided into two groups. Group-A was managed with Cryotherapy using liquid Nitrogen and Group-B was managed with topical Trichloroacetic acid 90%. Clinical evaluation was done at the end of twelfth week and then three months after the end of therapy to ascertain efficacy. Efficacy was established in terms of absence of all lesions with no recurrence/reappearance in both groups.

Results: Cryotherapy using liquid nitrogen was more efficacious (83.3%) in terms of absence of all lesions with no recurrence/reappearance of warts as compared to 90.0% topical Trichloroacetic acid (60.0%) (*p*-value 0.045).

Conclusion: This randomized controlled trial showed that Cryotherapy using liquid nitrogen was significantly more efficacious in treating common warts as compared to topical Trichloroacetic acid 90%.

Keywords: Common warts, Cryotherapy, Trichloroacetic Acid 90%.

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INTRODUCTION

Common warts are hyperkeratotic, benign cutaneous growths caused by Type 1, 2, and 7 Human papilloma viruses and approximately 10% of the population are affected worldwide. Different modalities are available to treat warts. Cryotherapy is one of the most common and effective treatments for common warts. Trichloroacetic acid (TCA) in high concentrations can be used as a therapeutic modality.[1] A study reported that cryotherapy achieved complete cure in 83.1% patients with common warts. Trichloroacetic acid (TCA) in higher concentration also has therapeutic potential but only 21.3% patients achieved complete cure (*p*-0.001).[1] HPV can cause epithelial neoplasms, which can be especially dangerous for people with weakened immune systems.[2] A total of 189 different types of HPVs have been identified.[3,4] Warts can appear at any age, though they are more common in children and teenagers.[5] Salicylic acid (SA) dressings, Cryotherapy, Bleomycin, 5-Fluorouracil (5-FU), Dinitrochlorobenzene (DNCB), Interferons (IFN), photodynamic therapy (PDT), pulsed-dye laser, duct tape, and combinational therapy using SA and Cryotherapy are all effective against warts.[5] Warts can be treated with a variety of methods, including Cryosurgery, Electrosurgery, Laser ablation, Surgical excision, and topical agents like Salicylic Acid (12%-26%) with Lactic acid paint, Podophyllotoxin, Trichloroacetic acid (TCA), 5-Fluorouracil, and Photodynamic therapy.[5]

Liquid nitrogen Cryotherapy is a highly effective treatment option for patients who can undergo treatment for common warts. Rapid freezing of cellular matrix under the extremely cold temperature of liquid Nitrogen (-20°C to -25°C) produces ice crystals and disrupts the cell membrane. As thawing occurs there is rapid input of water into cells which ultimately proves lethal for the cell.[6,7] The results found in the existing literature are inconsistent with one another. Despite being two of the most common treatments for viral warts, there is a lack of local data evaluating the efficacy of Trichloroacetic acid (TCA) 90% and Cryotherapy.[8]

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The current study was done to evaluate the efficacy of Cryotherapy with Trichloroacetic acid 90% in the treatment of common warts based on the existing literature, to enhance and improve existing treatment options and to find the better modality for improving patient care in today's era of evidence-based medical practices.

METHODOLOGY

This randomized controlled trial (ClinicalTrials.gov having ID: NCT05712811) was conducted at the Department of Dermatology, CMH Abbottabad, from June 2022 to November 2022. Ethical approval (file no: CMHAtd-ETH-16-Derm-22) was obtained from the Ethical Committee. The sample size was calculated by WHO Sample Size calculator with 83.1%[1] proportion of efficacy achieved with Cryotherapy as compared to 21.3% proportion efficacy of topical Trichloroacetic acid 90%, 80% power of test and 5% significance level. Non-probability consecutive sampling technique was used for data collection.

Inclusion Criteria: Patients of either gender, between 18 to 60 years, with common warts (hard lesions, raised lumps with rough surfaces at the back of their fingers, around nails and palm of their hands) diagnosed by consultant dermatologist on clinical presentation were included in the study.

Exclusion Criteria: Patients with warts on toes and tip of fingers, genital warts, mosaic warts, planter warts, cardiac, hepatic, and renal disease, hypercholesterolemia and those with hypersensitivity reactions were excluded.

Written informed consent was taken from all the study participants after a complete description. Common warts were diagnosed on clinical presentation by consultant dermatologist. To ensure randomization, the lottery method was used to allocate the patients to study groups. Group-A was managed with Cryotherapy once every two weeks for a total of twelve weeks, with liquid nitrogen using Cryoget method for 10 to 15 seconds on each lesion (depending on size, until a narrow white rim of around 1 mm developed around it for 15 seconds) and Group-B was managed with topical Trichloroacetic acid 90% by an applicator every two weeks for a total of twelve weeks. (Figure)

Patients were advised to remove the solution by washing their warts with water or regular saline after 20 minutes. Patients received treatment for a total of six sessions, or until the warts cleared up (which ever came earlier). Clinical evaluation was done at the end of therapy after twelve weeks 10 and three months after the end of therapy to look for any recurrence/reappearance of warts. Efficacy was labelled as "Yes" in cases with absence of all the lesions with no recurrence/reappearance while cases with persistent lesions and recurrence/reappearance of warts were regarded as cases of treatment failure and efficacy was labelled as "No".

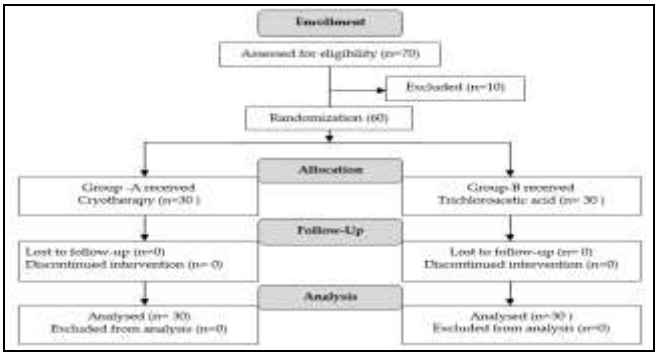

Figure: phases of study

The data was analyzed with Statistical Package for Social Sciences (SPSS) version 23.0. Mean+SD was calculated for quantitative variables such as age, duration of warts, and size of warts. Qualitative variables such as gender, site of warts, and efficacy were recorded as frequencies and percentages. The independent samples t test and chi-square test was applied on quantitative and qualitative variables respectively to compare efficacy in both groups keeping *p*-value <0.05 as significance level.

RESULTS

A total of sixty patients were recruited for the study. Out of 60 patients with common warts, 30 patients were managed by Cryotherapy using liquid Nitrogen, while 30 patients were managed by topical Trichloroacetic acid 90% after the randomization.

In Group-A, mean age was 33.97+10.53 years while in Group-B, mean age was 37.63+12.24 years (*p*-value 0.219). In Group-A mean duration of warts was 3.70+1.89 months while in Group-B mean duration of warts was 2.93+1.46 months (*p*-value 0.085). In Group-A mean size of warts was 2.93+1.46 mm while in Group-B, mean size of warts was 2.67+0.95 mm (*p*-value 0.033). In Group-A 16(53.3%) male and 14(46.7%) patients were recorded while in Group-B 08(40.0%) male and 12(60.0%) female patients were recorded (*p*-value 0.602). In Group-A 14(46.7%) patients had warts on the back of their figures,

11(36.7%) patients had warts around their nails while 05(16.7%) patients had warts on their palms. In Group-B, 14(46.7%) patients had warts on the back of their figures, 09(30.0%) patients had warts around nails while 07(23.3%) patients had warts on their palms (*p* 0.766). In Group-A, 20(66.7%) patients had solitary warts while 10(33.3%) patients had multiple warts. In Group-B 24(80.0%) patients had solitary warts while 06(20.0%) patients had multiple warts (*p*-value 0.243). (Table-I).

As per comparison of efficacy in both groups in terms of absence of all lesions with no recurrence/reappearance of warts, in Group-A, Cryotherapy showed effectiveness in 25(83.3%) patients, whereas in Group-B, TCA 90% was effective in 18(60.0%) patients. Statistically significant difference was observed between two groups in terms of efficacy of both treatment modalities (*p*-value 0.045) (Table-II).

Table-I: Demographic and Clinical Characteristics of Study Participants Among Groups (n=60)

Quantitative Variables	Study Groups		*p*-value
	Group-A (n=30)	Group-B (n=30)	
	Mean±SD	Mean±SD	
Age (Years)	33.97+10.53	37.63+12.24	0.219
Duration of Warts (Months)	3.70+1.89	2.93+1.46	0.085
Size of Warts (mm)	2.70+0.95	2.67+0.95	0.033
Qualitative Variables	Study Groups		*p*-value
	Group-A (n=30)	Group-B (n=30)	
Gender, n (%)			
Male	16(53.3%)	08(40.0%)	0.602
Female	14(46.7%)	12(60.0%)	
Site of Warts, n (%)			
Back of Figures	14(46.7%)	14(46.7%)	0.766
Around Nails	11(36.7%)	09(30.0%)	
Palms	05(16.7%)	07(23.3%)	
Number of Warts, n (%)			
Solitary	20(66.7%)	24(80.0%)	0.243
Multiple	10(33.3%)	06(20.0%)	

Table-II: Comparison of Efficacy in Both Groups (n=60)

Outcome Variable	Study Groups		*p*-value
	Group-A (n=30)	Group-B (n=30)	
Efficacy, n (%)			
Yes	25(83.3%)	18(60%)	0.045
No	05(16.7)	12(40%)	

DISCUSSION

Cryotherapy was a better treatment option amongst the two treatment modalities used in this study in terms of efficacy. While there is no universally effective therapy for common warts, several options exist each with its own success rate in eradicating the condition.[9]

Some of the treatments are oral Zinc Sulphate, intralesional injection of Antigens, Cryo-therapy, topical Immunotherapy, Electrosurgery, use of antimitotic medications, Carbon dioxide laser, Photodynamic therapy, and Topical immune response modifiers.[10]

While no randomized controlled studies have been conducted in the country comparing the two treatment techniques, the current study was done to evaluate the efficacy of cryotherapy with Trichloroacetic acid 90% in the treatment of common warts based on the existing literature.[11,12]

In our trial, 60% of patients saw improvement after therapy with Trichloroacetic acid 90%, while a study by Al-Ghurair *et al*.[13] using a similar dose of Trichloroacetic acid 90% delivered for two months found a significantly higher cure rate of 87%. Our findings were similar to those of Waqas *et al*.[14] in 2017 who used the same dosage of 90% Trichloroacetic acid for two months and reported a 62.22% cure rate, and to those of Hassan *et al*.[15] in 2013 who found a 60.97% cure rate. In 2010, Korean researchers Mun *et al*. reported a 50% cure rate with 90% Trichloroacetic acid.[16]

Our study showed a success rate of 83.3%, which is significantly higher than the meta-analysis by Kwok *et al*., which found a median cure rate of 49%,[17] for cryotherapy. Research by Bruggink *et al*.[18] in contrast, indicated that 37% of patients reacted favorably to Cryotherapy. In 2018, researchers Mahmoudi *et al*.[19] reported a 63.9% cure rate for cutaneous warts using Cryotherapy. However, we found an even higher rate of success (83.3%) in our research and therefore the results were quite encouraging. Hence based on our results, this study found that cryotherapy for common warts was superior to other treatment options, even though it had been reported to be painful and compliance to treatment with Cryotherapy was less due to the adverse effects profile ranging from hemorrhagic blisters formation, infection, dyspigmentation, recurrence, and erythema.[20]

Six doses of TCA resulted in a 70% clearance rate, as reported by Abdullah *et al*.[21] and a 96% clearance rate, as reported by Damstra *et al*.[22] Because of its speed, simplicity, safety, and low cost, cryotherapy is the treatment of choice for genital warts in pregnant women,[23] and patients who can withstand the pain

associated with it. Studies have shown that cryotherapy is more effective than TCA for treating cancer as TCA suppresses keratinocyte proliferation, collagen synthesis, protein synthesis, and fibroblast metalloproteinase activity. It has previously been shown that topical TCA 85% has good efficacy in treating grade I-III precancerous lesions of cervical cancer.[24-25]

Australian researchers Pirottaet 23 evaluated 489 people with external genital warts to assess the success rates of different treatments. They discovered that around half of patients were cured after the first session, and that there was no statistically significant difference between TCA and Cryotherapy. In contrast, our research revealed that Cryotherapy was substantially more effective than TCA in eradicating the lesions, with 90% in the treatment of common warts.

Lotfabadi *et al*.[24] studied 68 people with anogenital warts and found that those treated with Trichloroacetic acid had a higher cure rate after 6 sessions (94.1% vs 85.3%,p>0.05) than those treated with Cryotherapy (85.3%), however, we excluded patients with genital warts, but our results were different because we saw a statistically significant improvement in terms of absence of all lesions in patients treated with Cryotherapy (83.3% vs 60.0%, p-value 0.045).

LIMITATIONS OF STUDY

This study's limitations include its small sample size and the lack of a long-term follow-up. It is advised that in this age of evidence-based practices, more research procedures, such as randomized controlled trials and meta-analysis, be done in the local community to further evaluate the efficacy of various therapies for common warts.

CONCLUSION

This randomized controlled trial showed that cryotherapy using liquid nitrogen was significantly more efficacious in treating common warts as compared to topical Trichloroacetic acid 90%.

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Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

KG & BM: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

MAS & MH: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SI & HF: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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