

ORIGINAL ARTICLE

Comparative Study Between Treatment with Cryotherapy Alone Versus Cryotherapy Plus Salicylic Acid Dressing for Planter WartsMAHBOOB ALI¹, MUHAMMAD ADEEL SIDDIQUI², MAJID HUSSAIN³¹TMO Department Of Dermatology, Combined Military Hospital, Abbottabad^{2,3}Assistant Prof Department Of Dermatology, Combined Military Hospital, Abbottabad

Corresponding author: Mahboob Ali, Email: mehboobalisw89@gmail.com

ABSTRACT**Objective:** To compare cryotherapy alone versus cryotherapy plus salicylic acid dressing for planter warts.**Study Design:** Randomized Control Trial**Place and Duration of Study:** Department of Dermatology, Combined Military Hospital, Abbottabad from 01 Mar, 2022 to 01 Aug, 2022.**Methodology:** Seventy participants were enlisted using a non-probability sequential sampling method and then randomly assigned to one of two groups. SPSS Version 23.0 was used for data entry, data entry, and data analysis.**Results:** As per comparison of efficacy between both groups, 20 (57.1%) patients in Group A (Cryotherapy Alone) showed effective results while in Group B (Cryotherapy plus Salicylic Acid), 30 (85.7%) patients showed effective results. P Value = 0.008.**Conclusion:** This study demonstrated that treatment of planter warts with cryotherapy plus salicylic acid yielded significantly higher effective results in comparison to cryotherapy alone.**Keywords:** Planter Warts, Cryotherapy, Salicylic Acid**INTRODUCTION**

Human papillomavirus (HPV) causes verrucae plantaris, a common cutaneous lesion on the plantar aspect of the foot [1]. Although HPV is ubiquitous in our environment, cellular and humoral immune responses typically prevent it from spreading or eliminate it [2].

Warts can be painful and can lead to other difficulties, but there are some populations that are at a higher risk of getting HPV because they encounter the virus more frequently [3].

In addition to infecting other people, HPV can also spread to other locations in the area. While reducing exposure to risk factors can help prevent planter wart infection, HPV's widespread nature makes it difficult for such efforts to be effective [4]. It has been shown in research that planter warts can spread from person to person through just physical contact with the sores. Warts are more common in people with HPV because the virus disrupts the epithelial barrier [5]. There are over a hundred different forms of the HPV virus, so even though some warts go away on their own after a few years, others may need medical attention [6].

Warts, according to a number of studies, are extremely common (affecting around 10% of the population) all over the world [7]. More cases of HPV infection have been observed among people under the age of 30, compared to those beyond the age of 30. The estimated prevalence in the United States is between 10% and 20%. However, people with compromised immune systems and those who work with meat are disproportionately at risk [8]. The cancerous transformation of warts is quite rare. Even while verrucous carcinoma, a malignant form of wart development, is possible, it seldom spreads and only causes localised tissue loss [9]. Planter warts are treated in a manner that takes into account the patient's symptoms, personal preferences, and financial situation. Even though there are several therapy options, none of them are particularly effective, and relapses are common after any treatment. As a result, the most accessible and least distressing treatment option should be prioritised [10].

Salicylic acid is often considered a first-line therapy for the common wart because it can be used by the patient at home and does not necessitate a prescription. It has been shown to have a curative efficacy of up to 70% in some cases. Cryotherapy, retinoic acid, podophyllin, topical 5-fluorouracil, interferon, and imiquimod are some other effective treatments for planter warts [11].

In a single earlier trial, individuals with just foot warts were successfully treated with salicylic acid and cryotherapy. In this study, patients treated with cryotherapy had a 58% success rate at recovery, whereas those treated with salicylic acid had a 41%

success rate at recovery. On the whole, there is no statistically significant split [12].

Considering the frequency with which planter warts are treated and the absence of a well-established, practically applicable, and reliably preventative method in our local population, this study set out to compare the efficacy of cryotherapy alone to that of cryotherapy plus a salicylic acid dressing for planter warts.

METHODOLOGY

This was a randomized control trial carried out on 70 patients (35 patients in each group) through nonprobability consecutive sampling technique. This research study was carried out at the Department of Dermatology, Combined Military Hospital, Abbottabad from 01 Mar, 2022 to 01 Aug, 2022 after taking approval from Hospital's Ethical Review Board (Ref: CMHAtD-ETH-38-Derm-22). Patients presented to Skin OPD of our hospital with complaint of planter warts were assessed as per our inclusion criteria.

Inclusion Criteria: Patients having aged between 15 to 40 years and diagnosed with planter warts on toe foot based on clinical and physical examination with no history of treatment and patients of either gender was included in the study.

Exclusion Criteria: Patients with immunosuppressive conditions or using immunosuppressive medications (including oral corticosteroids); patients with neuropathy; and/or were on renal dialysis due to poor healing (caused by, for example, diabetes or peripheral vascular disease); patients unable to give informed consent. Selected patients were thoroughly briefed about the research purpose of this study prior to the start of study were excluded from the study.

Each of the participants was randomly assigned to one of two groups using a blocking procedure. Patients in Group A had Cryotherapy Alone, in which the researcher administered liquid nitrogen treatments at intervals of two to three weeks. It was either sprayed on or probed with liquid nitrogen. Patients in Group B were subjected to cryotherapy plus salicylic acid and therefore for salicylic acid, The researcher gave them advice on how to self-treat for up to eight weeks using 50 percent salicylic acid, applying it as directed by the manufacturer. Treatment-related planter wart clearance at 12 weeks post-randomization was considered the main outcome. Patients' self-reported results were collected at 12 weeks and verified by researcher examination of the afflicted region to indicate clearance of planter warts.

All the above data was recorded by the researcher himself under the supervision of a consultant dermatologist having at least seven years post fellowship experience.

RESULTS

In Group A (Cryotherapy Alone), mean and SDs for age was 22.97+5.39 years while mean and SDs for duration of warts was 3.91+1.54 months. In Group B (Cryotherapy plus Salicylic Acid), mean and SDs for age was 24.91+4.21 years while mean and SDs for duration of warts was 3.94+1.90 months. Group A (Cryotherapy Alone) included 27 patients aged 15–27 (77.1%) and 8 patients aged 28–40 (22.9%). Twenty-six patients (or 74.3% of the total) in Group B (Cryotherapy plus Salicylic Acid) were between the ages of 15 and 27, while nine patients (or 25.7% of the total) were between the ages of 28 and 40. The gender breakdown in Group A (Cryotherapy Alone) was 19 males (54.3% of total) and 16 females (45.7% of total). There were 19 male patients and 16 female patients in Group B (Cryotherapy plus Salicylic Acid).

As per comparison of efficacy between both groups, 20 (57.1%) patients in Group A (Cryotherapy Alone) showed effective results while in Group B (Cryotherapy plus Salicylic Acid) 30 (85.7%) patients showed effective results. P Value = 0.008. As per comparison of efficacy between both groups with respect to age, in

Group A (Cryotherapy Alone), 18 (66.7%) patients showed effective results in 15-27 years age group while 02 (25.0%) patients showed effective results in 28-40 years age group. P Value = 0.036. Similarly, in Group B (Cryotherapy plus Salicylic Acid), 24 (92.3%) patients showed effective results in 15-27 years age group while in 28-40 years age group, 06 (66.7%) patients showed effective results. P Value = 0.058.(Table No.1)

As per comparison of efficacy between both groups with respect to gender, in Group A (Cryotherapy Alone), 11 (57.9%) male patients showed effective results while 09 (56.3%) female patients showed effective results. P Value = 0.922. In Group B (Cryotherapy plus Salicylic Acid), 17 (89.5%) male patients showed effective results while 13 (81.3%) female patients showed effective results. P Value = 0.489. (Table No 2)

As per comparison of efficacy between both groups with respect to duration of warts, in Group A (Cryotherapy Alone), 19 (55.9%) patients in < 6 months duration of warts showed effective results while 01 (100%) with > 6-month duration of warts showed effective results. P Value = 0.380. Similarly, in Group B (Cryotherapy plus Salicylic Acid), 27 (84.4%) with duration of warts < 6 months showed effective results while 03 (100%) patients with > 6 months duration of warts showed effective results. P Value = 0.460.(Table No 3)

Table-1: Stratification of Efficacy with Age Groups (n=70)

Treatment Groups			Age Groups		Total	P Value
			15-27 Years	28-40 Years		
Group A (Cryotherapy Alone) (n=35)	Efficacy	Yes	18 66.7%	2 25.0%	20 57.1%	0.036
		No	9 33.3%	6 75.0%	15 42.9%	
	Total		27 100.0%	8 100.0%	35 100.0%	
Group B (Cryotherapy plus Salicylic Acid) (n=35)	Efficacy	Yes	24 92.3%	6 66.7%	30 85.7%	0.058
		No	2 7.7%	3 33.3%	5 14.3%	
	Total		26 100.0%	9 100.0%	35 100.0%	

Table-2: Stratification of Efficacy with Gender (n=70)

Treatment Groups			Gender		Total	P Value
			Male	Female		
Group A (Cryotherapy Alone) (n=35)	Efficacy	Yes	11 57.9%	9 56.3%	20 57.1%	0.922
		No	8 42.1%	7 43.8%	15 42.9%	
	Total		19 100.0%	16 100.0%	35 100.0%	
Group B (Cryotherapy plus Salicylic Acid) (n=35)	Efficacy	Yes	17 89.5%	13 81.3%	30 85.7%	0.489
		No	2 10.5%	3 18.8%	5 14.3%	
	Total		19 100.0%	16 100.0%	35 100.0%	

Table-3: Stratification of Efficacy with Duration of Warts (n=70)

Treatment Groups			Duration of Warts		Total	P Value
			< 6 Months	> 6 Months		
Group A (Cryotherapy Alone) (n=35)	Efficacy	Yes	19 55.9%	1 100.0%	20 57.1%	0.380
		No	15 44.1%	0 0.0%	15 42.9%	
	Total		34 100.0%	1 100.0%	35 100.0%	
Group B (Cryotherapy plus Salicylic Acid) (n=35)	Efficacy	Yes	27 84.4%	3 100.0%	30 85.7%	0.460
		No	5 15.6%	0 0.0%	5 14.3%	
	Total		32 100.0%	3 100.0%	35 100.0%	

DISCUSSION

In a clinical comparison of cryotherapy with liquid nitrogen alone and cryotherapy with 50% salicylic acid, we discovered that the combination treatment was much more successful than cryotherapy with liquid nitrogen alone in the treatment of planter warts. Patients were satisfied with both treatments; however, cost was greater for cryotherapy per cured patient.

Comparison with other studies: Planter and hand warts have been researched with varied degrees of effectiveness, and treatments include cryotherapy, salicylic acid, and a mixture of salicylic acid and lactic acid. Furthermore, no evidence favoring cryotherapy's efficacy over salicylic acid was discovered during these studies. Contrary to the findings of the aforementioned studies, our research indicated that cryotherapy paired with salicylic acid was substantially more effective than cryotherapy alone. Twenty patients in Group A (Cryotherapy Only) and thirty patients in Group B (Cryotherapy with Salicylic Acid) showed improvement, according our results. To rephrase: there is a 0.08% chance of anything occurring.

Differences in recovery rates across research groups can be due to the study's diverse sample of participants. Steele and Irwin omitted mosaic warts, which are thought to be more resistant to treatment, whereas Bunney et al.¹² only included persons with hand warts [13]. Patients who had self-treated, had more than five lesions, or had lesions greater than 9 mm in diameter were also not considered. It was also found that there were significant age differences among our sample populations. Twenty-seven patients (77.1%) between the ages of 15 and 27 were included in Group A (Cryotherapy Alone), while eight patients (22.9%) were included between the ages of 28 and 40. Patients aged 15–27 made up 74% of Group B (Cryotherapy plus Salicylic Acid) participants, while those aged 28–40 made up 25%. However, patients in the Bruggink et al. and Steele and Irwin trials were younger. Sixty-one percent of the study's subjects were children; among us, that number was just seventeen percent. Compared to our study's median age of 24, the trial conducted by Bruggink et al.¹³ included patients with a median age of 15 (interquartile range, 7-39) for cryotherapy and 13 (interquartile range, 7-31) for salicylic acid. We found that when comparing the effectiveness of Group, A (Cryotherapy Alone) with Group B (Cryotherapy with Salicylic Acid), Group A (Cryotherapy Alone) had better outcomes for 20 patients (57.1%). To rephrase: there is a 0.08% chance of anything occurring [14-17].

The results remained the same after controlling for age, whether or not the wart had been treated previously, the kind of planter wart, and patients' preferences at baseline. Group A (Cryotherapy Alone) had a 66% success rate among patients aged 15-27, and a 25% success rate among patients aged 28-40. This hypothesis has a P Value of 0.036. In a similar vein, 24 out of 27 patients in the 15-27 age range saw improvement with Group B (Cryotherapy plus Salicylic Acid), whereas 6 out of 10 patients aged 28-40 saw improvement. The probability of something happening is 0.058 [18-20].

Past research: Cryotherapy had a 45.61 percent success rate; salicylic acid had a 13.6 percent success rate; a cantharidin-podophyllin-salicylic acid formulation had a 97.82 percent success rate; laser had a 79.36 percent success rate; topical antivirals had a 72.45 percent success rate; intralesional bleomycin had an 83.37 percent success rate; and intralesional immunotherapy had a 68. (83.37 percent). Twenty (57.1%) participants participated in this research. To rephrase: there is a 0.08% chance of anything occurring.

Cryotherapy and salicylic acid were both ineffective against planter warts, so we combined them for even better results.

Acknowledgement: Brig Anjum anwar qadri

Strengths and Limitations of the Study: The many features of the trial, such as intention to treat analysis, blinded outcome assessment, and adequate randomization, collectively help to minimize bias. Planter warts that had been present for some times were self-treated by the vast majority of patients. Most experts agree that two months is a reasonable amount of time to wait before drawing any conclusions about the efficacy of a treatment for cutaneous warts. The human papillomavirus can hide in the body's epithelial cells for up to six months without presenting any outward symptoms, during which time the immune system can mount a reaction. In this research, we aimed to answer the clinical issue of whether or whether treating planter warts speeds up their natural healing process, given that we previously knew that many planter warts cure on their own. Our research shows that a treatment for planter warts has to last for at least 12 weeks before it can be considered successful. Although those in the salicylic acid group were instructed to self-treat for up to eight weeks, data on patient self-reported adherence to treatment was only collected at one- and three-weeks post-randomization. Despite the high rate of self-reported adherence, it may not have been successful against more deeply entrenched planter warts, as was reported by some patients.

CONCLUSION

This research was a high-quality comparison of two standard therapies for planter warts. When used together, cryotherapy and salicylic acid for planter warts were more efficient than either treatment alone. We found just one salicylic acid formulation, but its 50% concentration is much too high for clinical use. However, this study's findings provided unmistakable evidence that the two treatments had different success rates. Therefore, a combination of cryotherapy and salicylic acid is the best treatment for planter warts. The effectiveness of many of the alternative therapies for warts on the skin is questionable at best. More research into the efficacy of these treatments is required to inform their use in the future.

Conflict of interest: None

Authors contribution: MA: Design the study, MH: Analysis and interpreted result, BM: Data interpretation, manuscript writing, revision and approval of manuscript, NA: Coordinated, supervised data collection, and approval of final manuscript.

REFERENCES

- 1 Ray, A., Agrawal, I., & Kar, B. R. (2022). Intralesional MMR versus intralesional bleomycin in the treatment of digital warts: A randomized comparative study and review of the literature. *Turkish Journal of Dermatology*, 16(3), 73.
- 2 Witchev DJ, Witchev NB, Roth-Kauffman MM, Kauffman MK. Planter Warts: Epidemiology, Pathophysiology, and Clinical Management. *J Am Osteopath Assoc*. 2018 Feb 1;118(2):92-10.
- 3 Al About AM, Nigam PK. Wart. [Updated 2022 Jul 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK431047/>
- 4 Song HH, Soon HK, Dong IJ. Recurrent subungual viral warts. *J Wound Management Res* 2020;16(3):193-97.
- 5 Pongpanich F, Chaikasemsakun T, Boonsarn, N. Cryotherapy versus salicylic acid for planter warts: a systematic review. *Clin Acad*. 2019;43(2):54–64.
- 6 Das, S. Human Papillomavirus Infection: Management and Treatment. In: Rajkumar, R. editor. *Human Papillomavirus* [Internet]. London: Intech Open; 2020.
- 7 Oganessian A, Sivesind T, Dellavalle R. From the Cochrane Library: Topical Treatments for Cutaneous Warts *MIR Dermatol* 2021;4(2):e33900.
- 8 Farpratan P, Natchaya B. Cryotherapy versus salicylic acid for planter warts: a systematic review. 2019;43(2):
- 9 Kumar P et al. Therapeutic evaluation of efficacy of intralesional bleomycin in common warts including palmo-planter and periungual warts: a prospective study. *Int J Res Dermatol*. 2019 May;5(2):329-337.

- 10 Sara GO, Francisco JÁ, Afonso. Topical treatment for plantar warts: a systematic review. 2021;34(1)e4621.
- 11 Soo BS, Hyun KS, Hye LL. Treatment of recalcitrant plantar wart unresponsive to cryotherapy with acupuncture and moxibustion: a case report. *The Journal of Korean Medicine* 2021; 42(4): 238-243.
12. Bunney M, Nolan M, Williams D. An assessment of methods of treating viral warts by comparative treatment trials based on a standard design. *Br J Dermatol* 1976;94:667- 79.
- 13 Walczuk, I., Eertmans, F., Rossel, B., Cegielska, A., Stockfleth, E., Antunes, A., & Adriaens, E. (2018). Efficacy and safety of three cryotherapy devices for wart treatment: a randomized, controlled, investigator-blinded, comparative study. *Dermatology and therapy*, 8(2), 203-216.
- 14 Cockayne S, Hewitt C, Hicks K, Jayakody S, Kang'ombe AR, Stamuli E. Cryotherapy versus salicylic acid for the treatment of plantar warts (verrucae): a randomised controlled trial. *BMJ*. 2011;342:d3271.
- 15 Sara GO, Francisco JÁ, Yolanda GÁ, Esther G Morales, Irene SC. Topical treatment for plantar warts: a systematic review. 2021;34(1):e14621.
- 16 Zheng, K., Egawa, N., Shiraz, A., Katakuse, M., Okamura, M., Griffin, H. M., & Doorbar, J. (2022). The Reservoir of Persistent Human Papillomavirus Infection; Strategies for Elimination using Anti-Viral Therapies. *Viruses*, 14(2), 214.
- 17 Jaiswal, D. (2018). TO STUDY THE ROLE OF AUTO-IMPLANTATION THERAPY IN CUTANEOUS VIRAL WARTS (Doctoral dissertation).
- 18 Basavarajappa, S. J., Subramaniyan, R., Dabas, R., Lal, S. V., & Janney, M. S. (2021). A comparative study of topical 5% 5-fluorouracil with needling versus 30% trichloroacetic acid with needling in the treatment of plantar warts. *Indian Dermatology Online Journal*, 12(3), 412.
- 19 Mohta, A., Chand Ghiya, B., Dutt Mehta, R., Soni, P., Khokhar, R., Sharda, P., & Ranga, Z. (2022). Skin needling with 100% trichloroacetic acid vs. needling with bleomycin in the treatment of recalcitrant cutaneous warts. *Clinical and Experimental Dermatology*, 47(4), 730-734.
- 20 Mohta, A., Chand Ghiya, B., Dutt Mehta, R., Soni, P., Khokhar, R., Sharda, P., & Ranga, Z. (2022). Skin needling with 100% trichloroacetic acid vs. needling with bleomycin in the treatment of recalcitrant cutaneous warts. *Clinical and Experimental Dermatology*, 47(4), 730-734.