ORIGINAL ARTICLE

Comparative short-term efficacy of 15% potassium hydroxide versus cryotherapy in treatment of viral warts

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ABSTRACT

Background: Viral warts are benign skin lesions, which are ascribed to human papillomavirus. There are several possible treatments options. The objective of this study is to evaluate the short-term effectiveness of 15% potassium hydroxide with cryotherapy in treating viral warts.

Methods: It was quasi-experimental study done in the Department of Dermatology, PNS Shifa Hospital, Karachi after getting ethical approval from September 2025 – April 2026. 260 patients with viral warts aged 10 years and above were enrolled with non-probability sequential sampling into two groups, Group A was treated to topical 15% potassium hydroxide (KOH) applied as a single application per day over four weeks, and Group B underwent a series of four weeks treatment based on the weekly use of cryotherapy. The analysis of data was done in SPSS 23; chi-square test was used and a p-value ≤0.05 was considered statistically significant.

Results: A total of 260 patients were enrolled, with 130 patients in each treatment group. After 4 weeks, treatment success (good/excellent response) was achieved in 99 (76.2%) patients receiving 15% potassium hydroxide compared with 73 (56.1%) receiving cryotherapy (p = 0.002). Pain (43.1% vs 13.8%), blistering (31.5% vs 4.6%), and pigmentary changes (20.8% vs 3.8%) were more frequent with cryotherapy (all p < 0.001). Potassium hydroxide independently predicted treatment success (AOR = 2.45, 95% CI: 1.42–4.21; p = 0.001).

Conclusion: Clinical response was better with topical 15% potassium hydroxide than with cryotherapy for viral warts, which was well tolerated.

Keywords: Cryotherapy, Potassium hydroxide, Treatment efficacy, Viral warts.

BACKGROUND

Viral warts are typical benign epidermal proliferations attributed to the infection with human papillomavirus (HPV) and are a common cause of dermatology visits in every country across the globe. Although warts are benign, they can be very physically uncomfortable, cosmetically troubling and psychosocially distressing especially when the lesions are numerous, painful and resistant to remedies.[1] A number of treatment practices have been used in the management of viral warts, either to kill infected tissue or to enhance the immune response of the host. One of the most common treatments, still in use, is cryotherapy with liquid nitrogen because it is widely available and perceived to work, despite its association with pain, skin blisters, pigmentary changes, and the necessity of recurring clinic visits.[2]

Palmoplantar warts are frequently reoccurring, thick warts caused by an infection with the HPV virus that can be hard to treat. A keratolytic agent, potassium hydroxide (KOH), has been identified as a relatively easy and inexpensive treatment option due to its ability to cause the destruction of HPV-infected tissue and to stimulate a local inflammatory response. A study showed that the use of topically 15% KOH for multiple palmoplantar warts was effective, and an alternative to other treatments like salicylic acid.[3] Genital and cutaneous warts management is still an evolving process with constant updates on why effective, safe, inexpensive and user-friendly treatments were required. Although the practice of cryotherapy has been accepted as a standard practice, its shortcomings have led to the consideration of topical agents that can deliver similar benefits with minimal side effects.[4]

Cutaneous warts treatment is advised according to clinical guidelines depending on efficacy, safety, patient

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tolerance and resource availability; no single treatment modality is superior.[5] This has resulted in growing interest in non-invasive topical treatments as a first line or adjunct therapy. Comparative data also indicate that the effects of various topical and physical modalities differ and that some topical agents lack direct head-to-head comparisons.[6] Comparative studies with the different treatment options are therefore important to help inform clinical decision-making for relative efficacy and safety.

Comparative research has shown that potassium hydroxide especially 10% concentration is effective in treating plane and palmoplantar warts and the safety profile is acceptable with limited systemic side effects.[7] Such results justify the consideration of greater doses of KOH in wart subtypes that are difficult to treat. The methods of cryotherapy are diverse and variations in the method of application and freezing-thaw can greatly affect the outcomes of treatment and the occurrence of adverse events. Future observational research has observed differences in efficacy and tolerability of cryotherapy studies.[8] Potassium hydroxide versus cryotherapy in other viral skin infections, like molluscum contagiosum have also received comparative clinical trials, with similar effectiveness to their counterpart as well as the benefit of being easier to administer and less painful to the procedure.[9,10]

Topical 15% potassium hydroxide has more recently been considered as an agent in the treatment of a variety of palmoplantar warts with promising results compared to other keratolytic agents.[3] Nevertheless, there is a scarcity of direct comparisons of 15% potassium hydroxide and cryotherapy and hence, an additional controlled study is necessary to inform the use of evidence-based clinical practice.

MATERIAL AND METHODS

It was quasi-experimental research carried out in the Department of Dermatology, PNS Shifa Hospital in Karachi, with the permission of the Institutional Ethics and Research Committee with approval no: ERC/2025/DERMA/34. The research was conducted in a span of eight months from 1st September 2025 – 30th April 2026 Informed consent was signed by all participants or their guardians before they enrolled in the study.

WHO sample size calculation software was used in calculating the sample size which gave a total of 260 patients. The estimation was on a perceived effectiveness of 76.3% of potassium hydroxide and 60% of cryotherapy with a power of 90% with a level of significance of 5%.[11] Two hundred and sixty patients were recruited and assigned to two groups where 130 subjects were in each group. Non-probability sequential sampling was used to recruit eligible participants.

A non-random (quasi-experimental) allocation method was applied to assign patients to two treatment groups, and was done based on clinical flow and availability of treatment. Group A was treated with topical 15% potassium hydroxide and Group B was treated with cryotherapy of liquid nitrogen.

Both male and female patients aged 10 years and above who reported warts (common, plantar, flat or genital) were considered. Eligible patients had a duration of warts of over one month, lesion size of 2 mm or more and had not been treated within the last two months. Patients who were known to be hypersensitive to potassium hydroxide or liquid nitrogen, have immunosuppression, have neurological or psychiatric disorders that affect compliance with treatment, or are pregnant or lactating, were excluded. Upon admission, a medical history was taken and a full physical examination done.

Group A patients were asked to apply topical 15% of potassium hydroxide one time a day at night over 4 weeks.[3] The researcher showed the application technique and the treatment was continued at home by the patient or the caregiver.

Liquid nitrogen cryotherapy to patients in the outpatient dermatology department was done in Group B. Cryotherapy was done under the use of cotton tipped applicator which was applied perpendicular to the wart up to a frozen halo of up to 1-2 mm. The process was continued every week to a total of four weeks. Patients in the potassium hydroxide group were instructed to apply a thin layer of petroleum jelly to the surrounding normal skin before application of 15% potassium hydroxide to minimize irritation of healthy tissue.

In this study, efficacy assessments for skin wart treatment were uniformly conducted 4 weeks after treatment. Only clinical examinations were used to observe the size and clearance status of warts. Treatment responses were divided into four grades based on the percentage reduction in lesion size. The response to treatment was assessed using percentage reduction in wart burden, categorized into graded response levels

(<50%, 50–79%, 80–99%, and 100% clearance), consistent with previously published clinical studies evaluating potassium hydroxide for the treatment of cutaneous warts, where response was similarly defined based on lesion reduction and complete clearance.[7] All assessments were completed by the same researcher; no dermoscopy or photographic assessment methods were adopted, which controlled for inter-assessor bias.

Structured proforma was used to record demographic data, such as age, gender, residence, socioeconomic status and education level. Adverse effects as a result of treatment were also observed in the patients during the study period.

The Statistical Package for the Social Sciences (IBM SPSS Statistics) version 23 was used to enter and analyze the data. Normality tests were first conducted for all continuous variables: continuous variables that conformed to a normal distribution were described as mean ± standard deviation; non-normal variables, including the duration of wart disease, were described using median and interquartile range; and Categorical variables such as gender, accommodation, socioeconomic status, education level, type of wart, treatment modality, treatment response, and adverse effects were summarized as frequencies and percentages. For between-group comparisons, the chi-square test was adopted, and effect size was calculated by deriving relative risk (RR) with 95% confidence interval. Stratified analysis was used to control for 5 effect modifiers, and binary logistic regression was applied to obtain adjusted odds ratio (AOR) with 95% CI to control for confounding. The threshold for determining statistical significance was set at $p \leq 0.05$.

RESULTS

A total of 260 patients were included in the final analysis, with 130 patients in each group. The baseline demographic and clinical characteristics of the study participants are summarized in Table-I. Both groups were comparable with respect to age, gender distribution, residence, socioeconomic status, education level, type of wart, duration of lesions, and lesion size. No statistically significant differences were observed between the two groups, indicating adequate baseline homogeneity.

Table-II presents treatment response after 4 weeks comparing 15% potassium hydroxide and cryotherapy. The chi-square test was used to assess association between treatment modality and categorical response outcomes. In addition, effect size was interpreted using relative comparison of success rates (Good + Excellent response).

The frequency and types of treatment-related adverse effects observed in both groups are outlined in Table-III. Pain, blister formation, and pigmentary changes were significantly more frequent in the cryotherapy group, whereas burning sensation was more common in the potassium hydroxide group.

Table-IV presents multivariable logistic regression analysis assessing the independent association between treatment modality and clinical outcome (complete or near-complete clearance). The model was adjusted for age, gender, socioeconomic status, education level, duration of warts, and lesion size. Results are presented as adjusted odds ratios (AOR) with 95% confidence intervals (CI).

Table 1. Baseline demographic and clinical characteristics of study participants

Variable	Group A (15% KOH) n=130	Group B (Cryotherapy) n=130	Test Applied	p-value
Age (years), mean ± SD	26.8 ± 9.4	27.2 ± 8.9	Independent t-test	0.72
Gender (Male/Female)	78 (60.0%) / 52 (40.0%)	81 (62.3%) / 49 (37.7%)	Chi-square test	0.68
Residence (Urban/Rural)	92 (70.8%) / 38 (29.2%)	89 (68.5%) / 41 (31.5%)	Chi-square test	0.64
Socioeconomic status (Low/Middle/High)	46 (35.4%) / 61 (46.9%) / 23 (17.7%)	49 (37.7%) / 58 (44.6%) / 23 (17.7%)	Chi-square test	0.89
Education (≤Secondary / >Secondary)	74 (56.9%) / 56 (43.1%)	77 (59.2%) / 53 (40.8%)	Chi-square test	0.71
Type of wart (Common/Plantar/Flat/Genital)	54 (41.5%) / 38 (29.2%) / 21 (16.2%) / 17 (13.1%)	57 (43.8%) / 35 (26.9%) / 20 (15.4%) / 18 (13.8%)	Chi-square test	0.97
Duration of warts (>3 months)	81 (62.3%)	84 (64.6%)	Chi-square test	0.69
Lesion size 2–5 mm	61 (46.9%)	58 (44.6%)	Chi-square test	0.70
Lesion size >5 mm	69 (53.1%)	72 (55.4%)	Chi-square test	0.70

Note: Data are presented as mean ± standard deviation or frequency n (%). Chi-square test/Fisher's exact test was applied for categorical variables and independent t-test for continuous variables. A p-value ≤0.05 was considered statistically significant.

Table-II: Comparison of treatment efficacy between 15% potassium hydroxide and cryotherapy after 4 weeks

Treatment response	Group A (15% KOH) n (%)	Group B (Cryotherapy) n (%)
Poor (<50%)	9 (6.9%)	21 (16.2%)
Fair (50–79%)	22 (16.9%)	36 (27.7%)
Good (80–99%)	31 (23.8%)	29 (22.3%)
Excellent (100%)	68 (52.3%)	44 (33.8%)
Total effective (Good + Excellent)	99 (76.2%)	73 (56.1%)
p-value (Chi-square test)		0.002

Table-III: Treatment-related adverse effects in both study groups.

Adverse effect	Group A (15% KOH) n (%)	Group B (Cryotherapy) n (%)	p-value
Pain	18 (13.8%)	56 (43.1%)	<0.001
Burning sensation	42 (32.3%)	19 (14.6%)	0.001
Erythema	29 (22.3%)	34 (26.2%)	0.47
Blister formation	6 (4.6%)	41 (31.5%)	<0.001
Pigmentary changes	5 (3.8%)	27 (20.8%)	<0.001
Infection	0 (0%)	2 (1.5%)	0.16

Table-IV: Multivariable logistic regression analysis for treatment success (Good + Excellent Response).

Variable	Adjusted Odds Ratio (AOR)	95% CI	p-value
Treatment modality (KOH vs Cryotherapy)	2.45	1.42 – 4.21	0.001*
Age (years)	0.98	0.95 – 1.01	0.18
Male gender	1.12	0.68 – 1.86	0.65
Socioeconomic status (low vs others)	0.89	0.52 – 1.53	0.67
Education (≤secondary)	0.91	0.54 – 1.55	0.73
Duration of warts (>3 months)	0.76	0.45 – 1.29	0.31
Lesion size ≥5 mm	0.81	0.49 – 1.35	0.42

Statistically significant at $p \leq 0.05$

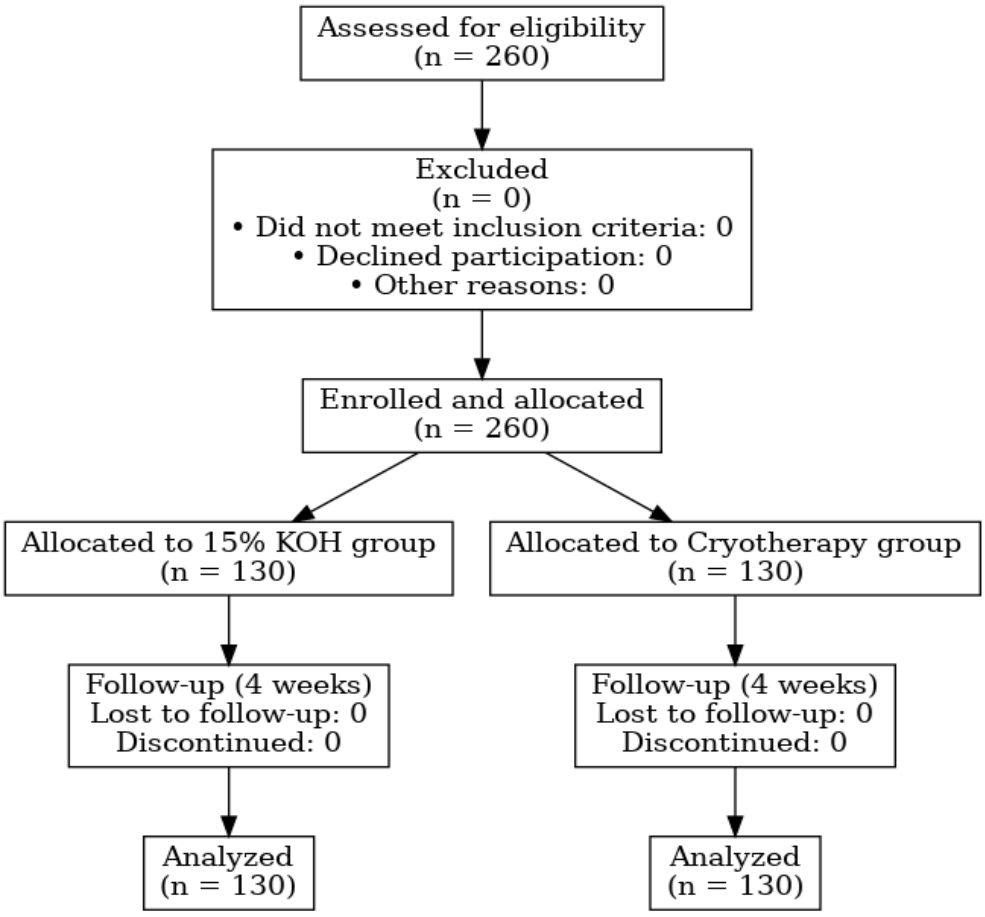

Figure-I: Participant flow diagram of patient enrollment, allocation, follow-up, and analysis.

DISCUSSION

This study found that after 4 weeks of treatment, the complete or near-complete clearance rate of topical 15% potassium hydroxide (KOH) was higher than that of liquid nitrogen cryotherapy, and this high-concentration preparation can serve as an effective and convenient treatment option for viral warts. Topical potassium hydroxide (KOH) has been explored as an alternative treatment for viral warts because of its keratolytic action and ability to induce local inflammation. In a comparative study, Jay prasad *et al*.[11] found that 10% KOH was effective in the treatment of plane warts, demonstrating outcomes comparable to 30% trichloroacetic acid while offering a simple and economical treatment option.

Alternative physical modalities have been explored to overcome limitations of cryotherapy, including thermotherapy, which shows similar efficacy but causes patient discomfort.[12] Recent research has also investigated combination therapies, such as topical methotrexate with micro needling, which have demonstrated improved results compared to cryotherapy alone.[13] These trends reflect a shift toward less destructive, targeted interventions for cutaneous warts.

Existing clinical recommendations for the treatment of cutaneous warts all concur that no one method is uniformly effective and that treatment choice should be made on a case-by-case basis, considering factors such as effectiveness, safety, and patient characteristics. This is consistent with the comparable results found in the present study regarding the use of both topical and destructive therapies as acceptable options.[14] Other modalities, such as intralesional immunotherapy, have shown promising clearance rates but require multiple clinic visits and trained personnel, limiting routine applicability.[15] In contrast, topical KOH is simple to apply, cost-effective, and suitable for resource-limited settings, making it a practical alternative. To minimize irritation to surrounding healthy skin, it is recommended that patients apply a thin layer of petroleum jelly around the wart before KOH application, ensuring the solution is confined to the lesion itself. This precaution contributes to the safety, tolerability, and ease of home use of topical KOH therapy.

Host-related factors, including immune response and lesion characteristics, play a crucial role in wart resolution.[16] KOH may enhance local immune activation via controlled tissue destruction and subsequent inflammatory response, which could contribute to its higher efficacy observed in this study.[17] Furthermore, previous studies evaluating lower concentrations of potassium hydroxide have demonstrated comparable clearance rates to cryotherapy with better tolerability, supporting the therapeutic potential of higher-strength formulations such as 15% KOH.[18]

Despite these promising results, certain limitations must be acknowledged. The follow-up period of four weeks was insufficient to assess long-term recurrence rates. The study was conducted at a single center, which may limit generalizability. Additionally, blinding was not feasible due to the nature of interventions, introducing potential observer bias. Patient-reported outcomes, such as pain and treatment satisfaction, were not quantitatively assessed and should be considered in future studies. Patients were allocated to the two treatment groups using a non-randomized (quasi-experimental) method, based on clinical flow and availability of treatment. This could have led to selection and allocation bias as group allocation was not random and may have affected baseline comparability and therapeutic results. This study also has another limitation: the present research on viral warts only evaluated two treatment approaches, topical 15% potassium hydroxide and cryotherapy, and did not include the other five established and emerging alternative therapies. The study's conclusions therefore cannot be generalized to comparative scenarios that involve these unincorporated treatment options.

Topical 15% KOH represents an effective, safe, and patient-friendly alternative to cryotherapy for the management of viral warts. Future studies with longer follow-up, multi-center design, inclusion of patient-reported outcomes, and assessment of recurrence rates are warranted to further validate these findings and guide clinical practice.

CONCLUSION

Topical 15% potassium hydroxide demonstrated better short-term efficacy than liquid nitrogen cryotherapy in achieving complete clearance of viral warts after four weeks of treatment. This medication has good overall tolerability, causes less pain, and is more convenient to use; it only has a higher incidence of burning sensations than cryotherapy. It can serve as a safe, low-cost, and

convenient alternative to cryotherapy. Future research needs to conduct multi-center studies with expanded sample sizes and extended follow-up periods to evaluate its recurrence rate and long-term outcomes.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Aroon Kumar: Conceptualization of the study, data collection, manuscript drafting, final approval of the manuscript

Atiya Rahman: Research supervision, methodological guidance, critical manuscript review, final approval of the manuscript

Madiha Hanif: Clinical supervision, patient management, contribution to manuscript revision

Janta Maheshwari: Data acquisition, patient follow-up, and literature review

Sidra Anwer: Data collection, statistical assistance, and manuscript preparation support

Izza Adnan: Literature search, data entry, assistance in manuscript formatting and preparation

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