

Comparative Efficacy of topical 5% Potassium Hydroxide and Liquid Nitrogen in the Treatment of Plane Warts

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ABSTRACT

Objective: To study the efficacy while comparing Potassium Hydroxide 5% with Liquid Nitrogen in treatment of plane warts.

Study Design: Randomized-controlled trial (ClinicalTrials.gov: NCT05895071)

Place and Duration of Study: Department of Dermatology, CMH-Abbottabad Pakistan, from Nov 2022 to April 2023.

Methodology: The sample size of 60 patients (aged 4 to 30 years was randomly assigned into two Groups i.e. from 60 patients, in Group-A 30 were advised topical 5%-Potassium Hydroxide solution on affected area once at night upto 4 weeks and in Group-B 30 patients were treated with cryotherapy using Liquid Nitrogen on cotton bud once every two weeks. Patients were reassessed at every two weeks and final assessment was done at 12th week whereas follow up was done every three months for recurrence. The treatment final outcome which categorized complete recovery on complete disappearance of warts with normalization of skin markings.

Results: In Group-A (mean age 15.70+7.35 years) 24 (80%) patients whereas IN Group-B (mean age 16.40+7.81years) 14 (46.7%) patients recovered completely. The 02 (6.7%) patients of Group A and 6(20.0%) patients of Group-B showed no response, rest of patients showed partial response to the treatment having significant p-value 0.003. There was no patient reported with recurrence of warts in Group A while in Group B 4(13.3%) patients. There is not any drop outs.

Conclusions: The Topical 5% KOH showed significant better response. Its treatment adherence is better as compared to the Liquid Nitrogen therapy and reporting lesser side effects.

Keywords: Cryotherapy Liquid nitrogen, Potassium Hydroxide, Warts.

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INTRODUCTION

Warts are one of the most frequent skin illnesses in the world. Human papillomavirus (HPV) types 3 and 10 produce plane warts¹. Lesions can be smooth, flat, or raised papules that are skin colour or pigmented. They are spherical or polygonal in form, with sizes ranging from 1 to 5 mm. Predilection sites include the face, dorsa of the hands, and forearms. Because the possibility of spontaneous relapse must be considered, the treatment approach should not be overly harsh².

Warts can be treated using a variety of methods, including chemical, physical, and destructive procedures, among others. The best one is determined by the location of the lesions, the patient's age, the side effects, and the patient's choice³. Due to subpar technique and reporting, the topical treatment of warts, particularly flat warts, is unreliable. As a result, investigating the effects of topical therapies is highly suggested⁴.

Potassium Hydroxide is a strong metallic base that is used in the detection of fungal infections, the treatment of male genital warts and the treatment of molluscum contagiosum in children⁵. The mode of action is through its keratolytic actions, which lead to the death of virus-infected cells, resulting in the removal of warts. It is less painful, causes fewer scars, is less irritating, and is suitable for youngsters. Itching, erythema, and dyspigmentation are side effects⁶. Cryotherapy i.e., Liquid Nitrogen is one of the most used methods for treating warts. It is a simple and successful method. It works by either simply by destroying HPV-infected keratinocytes or by generating local inflammation, which leads to the establishment of a cell-mediated response⁷⁻⁸. The final outcome was disappearance of skin warts and normalization of skin markings. Treatment was categorized effective by the following criteria; Complete response; complete disappearance of warts and normalization of skin markings. Partial response; decrease in number or size of warts but warts didn't clear completely, without normalization of skin markings. No response; no decrease in number or size of warts. It was also used in a study conducted by

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Reddy EM (2023) et al for treatment of Viral warts⁹. The rationale of this study is to compare effectiveness of topical 5% Potassium Hydroxide and Liquid Nitrogen in the management of plane warts. To the best of our knowledge, there is limited regional and national literature available focusing on our purpose of study.

METHODOLOGY

The randomized controlled trial study was conducted at dermatology unit of the CMH, Abbottabad from Nov-2022 to April-2023 after Ethical Review Board approval (Reg# CMHAtD-ETH-50-Derm-22) and RCT (Reg#ClinicalTrials.gov Identifier: NCT05895071). Sixty patients aged 4 to 30 years were enrolled by using a non-probability consecutive sampling technique after informed consent. The randomization process has been done to avoid selection bias and concealment of treatment allocation. The CONSORT flow diagram (2010) has been drawn to comprehensively presented randomization process¹⁰. A consent of minors was also taken from their parents. The sample size was calculated by using OpenAPI app sample size calculator for RCT taking 95% confidence interval, power of study as 80%, the expected cure rate of Potassium Hydroxide 5% as 80% and Liquid Nitrogen as <50%, estimated sample size was 46, but sample size of 60 was taken to increase the validity of study¹¹.

Inclusion Criteria: The patients 4-30 years of age, affected by more than 3 plane warts on face as well as hands, had duration of 3 to 6 months, including both males and females were included.

Exclusion Criteria: The pregnant or breastfeeding women, diabetic patients and those taking immune suppressive drugs, were excluded.

Patients were divided into 2 Groups. In Group-A 30 patients were given topical 5% Potassium Hydroxide solution on affected side of face and dorsal side of hands once at night for upto 4 weeks and in Group-B 30 patients treated with cotton bud method of cryotherapy with Liquid Nitrogen once every two weeks with two freeze thaw cycles in single sitting. Patients were reassessed at every two weeks. The treatment carried out upto 12 weeks or until complete recovery from warts. The patients who recovered completely still follow up for 3 months after complete recovery to monitor any recurrence.

All inspections and therapy evaluations were completed by me, under the supervision of a

consultant dermatologist. Treatment was categorized effective by the following criteria; 1) Complete response; complete disappearance of warts and normalisation of skin markings, 2) Partial response; decrease in number or size of warts but warts didn't clear completely, without normalisation of skin markings, 3) No response; no decrease in number or size of warts (Figure-1).

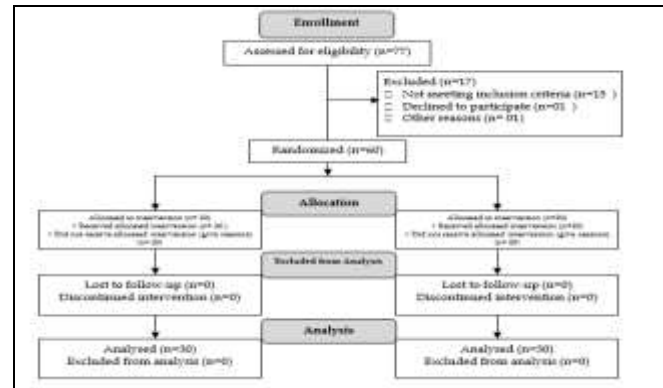


Figure-1: Patient Flow Diagram

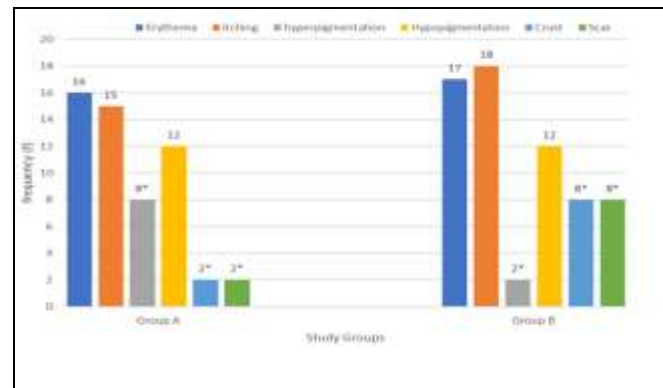


Figure-2: Side effects reported at after Treatment in Both Groups (n=60)

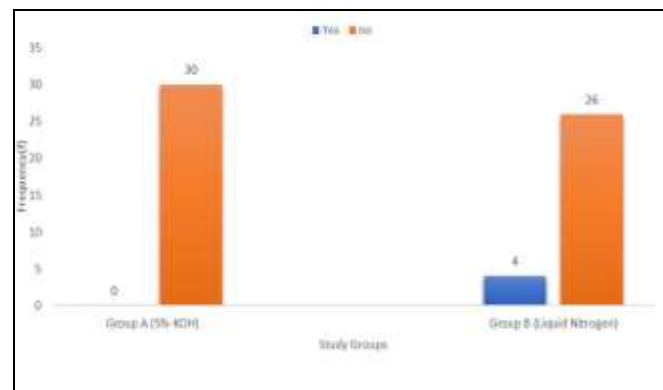


Figure-3: Recurrence of Warts at the end of Treatment on Follow-Up of Patients between Both Groups (n=60)

Data was analyzed using SPSS Statistical Package for the Social Sciences (SPSS) version 26. The quantitative variables like age and duration of illness were calculated by taking means and standard deviation. The qualitative variables like gender and the outcome or efficacy were calculated by taking frequency and percentages. Comparison of efficacy in two Groups was done by using Statistical Package for the social sciences (SPSS) version 26:00. To determine statistical significance taking p -value ≤ 0.05 as significant, and chi-square test was used.

RESULTS

Before trial begins baseline characteristics of both the Groups are compared. both the Groups are similar in characteristics at baseline. The Mean age of Group-A and Group-B was 15.70+7.35, 16.40+7.81years respectively. In Group-A, (56.6%) patients reported warts on Face but in Group B, 21(70%) patients had warts on Dorsal Hands. There is also statistically significant difference between site of warts and both treatment Group (p -value=0.037). The duration of warts ranges from 3 to 6 months (p -value=0.045). There are significant relations among site and duration of warts between both Groups ($p < 0.05$) (Table-I).

Table-I: Baseline Characteristics of Study Groups (n=60)

Variables		Potassium Hydroxide 5% (n=30)	Liquid Nitrogen (n=30)	p -value
Age (years)	5-9	6(20.0%)	7(23.3%)	0.945
	10-19	14(46.7%)	13(43.4%)	
	20-30	10(33.3%)	10(33.3%)	
	Mean+SD	15.70+7.35	16.40+7.81	
Site of Warts	Face	17(56.6%)	09(30.0%)	0.037
	Dorsal Hand	13(43.4%)	21(70.0%)	
Duration of warts (Months)	3 to 6	25(83.3%)	18(60.0%)	0.045
	>6	05(16.7%)	12(40.0%)	

While comparing treatment response at 12th week, in Group-A (5%-KOH) 24(80.0%) patients showed complete response as compared to the 11(46.7%) patients in Group-B. On the other hand, 02(6.7%) patients of Group-A showed no response which is lesser in number as compared to 06 (20.0%) patients in Group-B. Rest of the patients showed partial response to their respective treatment Group. There is also a statically significant between both

treatment Groups in terms of their efficacy or response as p -value is 0.003, but efficacy of 5%-KOH is significantly better than Liquid Nitrogen (Table-II).

Table-II: Treatment Response at 12th week (n=60)

Treatment response	5% Potassium Hydroxide (n=30)	Liquid Nitrogen (n=30)	p -value
Complete	24(80.0%)	11(46.7%)	0.003
Partial	04(13.3%)	13(33.3%)	
No response	02(6.7%)	06(20.0%)	

On following-up patients after treatment, both the treatment Groups showed side effects as illustrated in Figure-2. Side effects such as Hyper-pigmentation, crust and scar showed statistically significant difference (p -value<0.05). Moreover, Liquid Nitrogen showed more side effects are compared to the 5%-KOH. On the other hand, while observing recurrence of warts, 5%-KOH Group showed not any single recurrence of warts, but four patients who treated by Liquid Nitrogen complaint about recurrence of warts during follow-up (Figure-3).

DISCUSSION

Warts can be managed using a myriad of methods, including chemical, physical, and destructive methodologies; antiproliferative drugs; and immunotherapy.^{12,13} Cryotherapy targets HPV-infected keratinocytes by necrotic degradation¹⁴. KOH works by triggering the killing of virus-infected cells, resulting in the removal of warts¹⁵. Thus, randomized control trial was done to compare efficacy and safety of these two drugs as less literature work is available at provincial or national level to the best of our knowledge. In this study topical 5%-Potassium Hydroxide showed better response than liquid nitrogen. It was easier to apply by patient improving compliance with no recurrence and lesser side effects which is similar to the study conducted in 2012 by Al-Hamdi et al. in Iraq¹².

The determinants such as age, site and duration of warts reported statistically significant results between both Groups except age. In this study after applying Cryotherapy and Potassium Hydroxide on face and dorsal hand we observed significant better response of topical 5% potassium hydroxide. But on contrary, in the study conducted in 2001 by Ahmed et al.¹⁶, topical 5% Potassium Hydroxide and cryotherapy were equally effective in treatment of warts.

Patients were educated regarding appearance of any side effects and seeking medical advice for symptomatic treatment or cessation of the medication. Potassium Hydroxide caused lesser side effect which made it potentially safer than liquid nitrogen. There was statistically significant relationship among hyperpigmentation, crust and scars as p -value <0.05 . These findings were also reported by a previous study Galal *et al.*¹⁷ This study reported no recurrence case after treatment with Potassium Hydroxide as compared to Liquid Nitrogen 4(13.3%). These results are similar to the study conducted in 2016 by Jayaprasad *et al.* in India¹⁸. This study was done to analyze the efficacy as well as safety of these two drugs. Finding KOH as alternative to conventional treatments make it easier to use at home, decrease hospital burden and address compliance issues.

LIMITATION OF STUDY

The present study was conducted over a comparatively short period of time. Depending on the nature of the disease, large randomized multicenter trials with relatively long follow-ups are required to further confirm the results for assessing the efficacy of distinctive modes of treatment. The utmost goal of treatment was to improve individual life quality. The appropriate course of therapy should be individualized to each patient based on age and medication tolerance.

CONCLUSION

The Topical 5% KOH showed significant better response than liquid nitrogen. The topical 5% KOH was more compliant to apply by patient, no recurrence rate or less side effects as compared to the Liquid Nitrogen therapy.

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Authors' Contribution

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

SA & BM: Data acquisition, data analysis, 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.

ZN & SI: 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.

REFERENCES

- Ozaydin-Yavuz G, Bilgili S, Guducuoglu H, Yavuz I, Elibuyuk-Aksac S, Karadag A. Determinants of high-risk human papillomavirus infection in anogenital warts. *Postepy Dermatol Alergol* 2019; 36(1): 76-81. <https://doi.org/10.5114/ada.2019.82915>
- Nofal A, Elmonsef A, Ragab E, Elkholy BM. An Overview of Various Lines in The Treatment of Warts. *Egypt J Hosp Med* 2022; 86(1): 570-573. <https://doi.org/10.21608/ejhm.2022.215111>
- Abeck D, Tetsch L, Lüftl M, Biedermann T. Extragenital cutaneous warts—clinical presentation, diagnosis and treatment. *J Dtsch Dermatol Ges* 2019; 17(6): 613-634. <https://doi.org/10.1111/ddg.13878>
- Oganseyan A, Sivesind T, Dellavalle R. From the Cochrane Library: Topical Treatments for Cutaneous Warts. *J Med Internet Res* 2021 ; 4(2): e33900. <https://doi.org/10.2196/33900>
- Gerlero P, Hernández-Martín Á. Update on the treatment of molluscum contagiosum in children. *Actas Dermosifiliogr* 2018; 109(5): 408-415. <https://doi.org/10.1016/j.ad.2018.01.007>
- Makki MA, Abdel-Aleem H, Saddik M. Clinical Efficacy of Potassium Hydroxide 10% for the Treatment of Common Warts. *Int J Med* 2022 ; 4(7): 2503-2506. <https://doi.org/10.21608/IJMA.2022.147626.1478>
- Bharti AC, Singh T, Bhat A, Pande D, Jadli M. Therapeutic strategies for human papillomavirus infection and associated cancers. *Front Biosci* 2018; 10(1): 15-73. <https://doi.org/10.2741/e808>
- Singh S, Neema S. Comparison of electrosurgery by electrodesiccation versus cryotherapy by Liquid Nitrogen spray technique in the treatment of plantar warts. *Med J Armed Forces India* 2020; 76(2): 156-160. <https://doi.org/10.1016%2Fj.mjafi.2018.11.005>
- Reddy EM, Rajashekar TS, Kumar KS, Reddy ME, Rajashekar TS. A Comparative Study of Intralesional Acyclovir vs Immunotherapy for Treatment of Viral Warts. *Cureus* 2023; 15(5): e38781. <https://doi.org/10.7759%2Fcureus.38781>
- Shaikh AM, Mehta MM, Chawan VV. Evaluation of reporting of CONSORT flow diagrams in randomized controlled trials in a national and international pharmacology journal. *Perspect Clin Res* 2019; 10(4): 168. https://doi.org/10.4103/picr.picr_73_18
- Bruggink SC, Gussekloo J, Berger MY, Zaaier K, Assendelft WJ, de Waal MW, et al. Cryotherapy with Liquid Nitrogen versus topical salicylic acid application for cutaneous warts in primary care: randomized controlled trial. *Can Med Assoc J* 2010; 182(15): 1624-1630. <https://doi.org/10.1503/cmaj.092194>
- Al-Hamdi KI, Al-Rahmani MA. Evaluation of topical Potassium Hydroxide solution for treatment of plane warts. *Indian J Dermatol* 2012 ; 57(1): 38. <https://doi.org/10.4103/0019-5154.92675>
- Alamgir AN. Biotechnology, in vitro production of natural bioactive compounds, herbal preparation, and disease management (treatment and prevention). In *Therapeutic Use of Medicinal Plants and their Extracts*. Springer; 2018.
- Tripathi A, Sahu U. An overview of HPV: Causes, symptoms, and clinical manifestations. *Immunopathology, Diagnosis and Treatment of HPV Induced Malignancies*. Academic Press; 2022.
- Khattab FM, Khashaba SA. Evaluation of combined treatment with long-pulsed neodymium-doped yttrium aluminum garnet laser and Potassium Hydroxide for the treatment of recalcitrant wart: a prospective comparative study. *J Dermatolog Treat* 2020; 31(1): 56-60. <https://doi.org/10.1080/09546634.2019.1618436>
- Ahmed I, Agarwal S, Ilchyshyn A, Charles-Holmes S, Berth-Jones J. Liquid Nitrogen cryotherapy of common warts: cryo-spray vs. cotton wool bud. *Br J Dermatol* 2001; 144(5): 1006-1009. <https://doi.org/10.1046/j.1365-2133.2001.04190.x>
- Galal EA, Ali MM, Ali MS. Comparative study between Potassium Hydroxide 5% and Liquid Nitrogen in treatment of plane warts. *Sci J Al-Azhar Med* 2020; 4(4): 644. https://doi.org/10.4103/sjamf.sjamf_83_20
- Jayaprasad S, Subramanian R, Devgan S. Comparative evaluation of topical 10% Potassium Hydroxide and 30% trichloroacetic acid in the treatment of plane warts. *Indian J Dermatol* 2016 ; 61(6): 634. <https://doi.org/10.4103%2F0019-5154.193670>