

## Treatment of Common Warts by Hydrogen Peroxide 50%

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### **ABSTRACT:**

#### **BACKGROUND:**

Common warts are common diseases encountered in daily dermatologic practice. They are caused by human papilloma virus which has about 200 genotypes. Although spontaneous resolution can occur in 65-78% after two years but disfigurement and social embarrassment necessitate treatment.

Hydrogen peroxide has damaging effects on nucleic acids, proteins and lipids. It is currently used for debridement of wounds and has healing promotion and antimicrobial effects. It was recently approved for the treatment of seborrheic keratosis.

#### **OBJECTIVE:**

To evaluate topical 50% hydrogen peroxide use in the treatment of common warts regarding the safety and efficacy.

#### **PATIENTS AND METHODS:**

This interventional study was carried out during the period from April 2019 to July 2020 at Dermatology Center / Baghdad Medical city. Thirty patients were enrolled in this study; 9 of them were defaulted for unknown reasons and 21 patients completed the study.

Each patient was fully assessed to determine the clinical type, sites, size and number of warts. All patients did not receive any treatment for warts in the last month before enrollment in the study. A layer of 50% hydrogen peroxide solution was applied to each wart and allowed to dry for 2 minutes and the application was repeated 2 to 3 times till the appearance of white frost or bubbling or the patient feels stinging sensation. If the warts had thick hyperkeratotic surfaces, a simple paring with scalpel was done. The solution was applied once weekly for 3 weeks. A total number of 57 lesions were treated.

#### **RESULTS:**

Twenty-one patients completed the study. The total number of lesions was 57. Regarding lesions response to treatment; 51(89.5%) lesions were cured, 6 (10.5%) lesions showed partial response and no lesion was recorded to show no response. Regarding the number of weeks needed to achieve cure; 18 (31.6%) lesions achieved cure in the first week, 22(38.5%) patients in the second week and 8(14%) in the third week. On follow up one month later, a further 3 (5%) lesions were also cured. Regarding relapse, 2 lesions (3.5%) were seen as relapse during the follow up visit, one month after stopping the treatment. Regarding the side effects for treatment; the following were noted; 16 (76.2%) patients had pruritus, 16(76.2%) patients had erythema, 12(57.1%) had stinging, and 9(42.9%) patients had pain.

#### **CONCLUSION:**

Hydrogen peroxide 50% solution is an effective topical therapy for common warts. It is non-costly, available, does not need local anesthesia with temporary and tolerable side effects.

**KEY WORDS:** Viral wart hydrogen peroxide

### **INTRODUCTION:**

Viral warts are caused by infection of the skin or the mucous membrane by human papillomavirus (HPV)<sup>(1)</sup>. They manifest as papillomas. They are associated with social embarrassment, anxiety and depression. People with increased risk include patients with immunosuppression, people in close contact with infected patients and nail biting<sup>(2)</sup>.

Subtypes of HPV are oncogenic, such as HPV-16 and -HPV-18<sup>(3)</sup>.

In an Iraqi study, the following proportions regarding the types of warts were noted; 63% common wart, 15% plane wart, 10.5% filiform wart, 7.5% palmoplantar wart, 3.5% genital wart and 0.5% epidermodysplasia verruciformis<sup>(4)</sup>. HPV infection most likely results in either subclinical or latent infection<sup>(5)</sup>. Clinical infection can be seen on the skin or mucous membranes<sup>(6)</sup>.

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The average reported spontaneous resolution rate was reported to be 30% within 10 weeks<sup>(7)</sup>. It is also estimated that 50% of disappeared spontaneously within one year, and about two-thirds within two years. However, most of patients need treatment due to embarrassment or anxiety. Typically, management should be simple and cheap with few side effects. There is no specific treatment that is 100% curative for warts<sup>(8)</sup>.

Topical Treatments commonly used include salicylic acid, glutaraldehyde, formalin, Occlusion, topical 5-fluorouracil, caustics, retinoic acids, vitamin D analogues, podophyllin, imiquimod, contact sensitization and topical antiviral therapy<sup>(9)</sup>. Intralesional therapy is also used in treatment and includes: intralesional immunotherapy, interferon (IFN), 5-Fluorouracil, Bleomycin, zinc sulfate and antiviral drugs<sup>(10)</sup>. Systemic agents have been used and include interferon, isotretinoin, zinc sulfate and H2 receptor antagonist<sup>(11)</sup>. Ablative measures are also used in wart management and include cryotherapy<sup>(12)</sup>, curettage/electrodessication, lasers, excision and hyperthermia<sup>(13)</sup>.

Hydrogen peroxide is a reactive oxygen species (ROS) that can damage lipids by oxidative damage, proteins, and nucleic acids. It is used for debridement of wounds, for promoting healing and as antimicrobial agent. It was approved recently for the treatment of seborrheic keratosis by the FDA<sup>(14)</sup>.

### PATIENTS AND METHODS:

This interventional study was carried out during the period from April 2019 to July 2020 at Dermatology Center/ Baghdad Medical city. The Scientific Council of Dermatology, Arab Board for Health Specializations gave the ethical approval. The study included 30 patients of whom 9 defaulted for unknown reasons and 21 completed the study.

The exclusion criteria for this study were the following; pregnancy, chronic illness, peripheral neuropathy, poor peripheral circulation, prolonged corticosteroid therapy, lesions with surface area more than 10 cm<sup>2</sup> and lesions close to eyes. Only common warts were included while other types of warts were excluded. None of the patients received warts' treatment in one month prior to the study. After full explanation to the patient and addressing their concerns about the disease regarding its course and prognosis, treatment modalities and their complications, a formal consent was taken from each patient.

Each patient was fully assessed by taking a full history regarding age, sex, address, family history, duration of warts, associated illness, any previous treatment used for warts. Also, each patient was fully examined to determine the clinical type, sites, size and number of warts. A solution of 50% hydrogen peroxide preserved in one liter bottle manufactured by (Panreac) company, made in Spain was used in the study.

### METHOD OF APPLICATION:

Wooden sticks were used to apply the solution. A layer was applied to each wart and allowed to dry for 2 minutes and the procedure was repeated 2 or 3 times till the appearance of white frost or bubbling or the patient felt a stinging sensation. No local anesthesia was used before the treatment.

If the warts were covered with a thick hyperkeratotic scale, a simple paring with scalpel was done. The solution was applied once weekly for 3 weeks. A total number of 57 lesions were treated. At each visit, the degree of response for each lesion was noted and patients were asked about side effects. A tape measure was used to determine the surface area of the lesions in millimeters.

The response was rated as the following; cure when the lesion disappeared completely, partial when the wart decreased in size but did not disappear completely and no response when the wart had no decrease in size. The lesions were also assessed one month after the last session. Statistical was done using Statistical package for social science version 26.

### RESULTS:

Twenty-one patients completed the study, 11 (52.4%) were females and 10 (47.6%) were males. Their ages ranged from 5-50 years with mean  $\pm$  SD 25.67 $\pm$  13.98 years. Patients  $\leq$  18 years constituted 38.1% of and patients  $>$  18 years old constituted 61.9% of the total number. The duration of warts ranged from 1-48 months with mean 8.1  $\pm$  12.07 months, the number of the lesions in each patient ranged from 1-7 with mean  $\pm$  SD 2.86 $\pm$ 1.49 lesions.

Regarding the previous treatment (more than one month prior to the study); 12 (42.9%) patients were treated before and 12 (57.1%) did not receive any treatment.

The total number of lesions was 57. The distribution of warts in on different body sites is shown in table 1.

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**Table 1: Site of lesions.**

Site	number of lesions	Percent
Hands	42	73.7%
Arm	8	14%
Feet	4	7%
Face	3	5.3%
Total	57	100%

Regarding lesions response to treatment; 51(89.5%) lesions achieved cure Figure 1 and 2), 6 (10.5%) lesions showed partial response and no lesions were recorded to show no response. The number of weeks needed to achieve cure were; 18 (31.6%) patients in the first week, while 22 (38.5%) patients in the second week and in

the third week 8 (14%) achieved cure. On follow up, one month after the last session three (5%) lesions also achieved cure. Regarding relapse, two lesions (3.5%) were seen to relapse during the follow up visit. Side effects are shown on table 2.

**Table 2: Side effects of treatment.**

Side effects	No. (%)
Pruritus	16 (76.2%)
Erythema	16 (76.2%)
Stinging	12 (57.1%)
Pain	9 (42.9%)
Edema	2 (9.5%)
Hyperpigmentation	2 (9.5%)
Hypopigmentation	2 (9.5%)
Ulceration	1 (4.8%)

### DISCUSSION:

Despite the large number of persons having warts, high-quality trials of treatment are limited and therapy is often selected on the basis of cost, convenience and tradition. Some studies included only adults<sup>(8)</sup>. In the present study, both adults and pediatric patients were included.

The most common sites in the current study, for the warts were the hands, followed by the arms, feet, and face. Zandi et al. also reported that the most common sites were the hands<sup>(15)</sup>. While Abdel Meguid et al.<sup>(16)</sup> recorded that most of their patients had lesions on the upper limbs. However warts can occur on any skin site<sup>(17)</sup>.

In the current study, 89.5% of the lesions were completely cured and another 10.5% showed partial response. While a clinical-trial sponsored by Aclaris Therapeutics in 2019 reported that hydrogen peroxide 45% topically applied to the warts twice weekly resulted in cure of 15.7% of lesions compared to spontaneous cure of 5.2% controls (received a combination of alcohol and water) after 60 days. After 137 days 28.6% of all warts were cured compared to 14.5%

spontaneously cured warts in controls<sup>(18)</sup>. In another clinical trial done by Smith et al. in 2020 on 79 patients who received twice weekly hydrogen peroxide for eight weeks and 78 patients who received a vehicle, and reported that cure rate was 25.3% after 8 weeks while they observed 2.6% spontaneous resolution in the control group<sup>(19)</sup>. The high cure rate in the current study could be related to the method of application; a layer of 50% hydrogen peroxide solution was applied to each wart and allowed to dry for 2 minutes and the application was repeated two to three times until the appearance of white frost or bubbling or feeling of stinging sensation. If the warts had thick hyperkeratotic surfaces, a simple paring with scalpel was done before application. While in the previously mentioned clinical trials, the patients were instructed to apply the solution at home (unsupervised) in a single layer. The difference in concentration could also be important; 50% in the current study compared to 45% in the previous clinical trials.

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Other modes of therapy were associated with different cure rates. In a study carried out in Egypt in 2019 by Abdel Meguid et al. studied 414 patients with common warts and treated them with either cryotherapy or trichloroacetic acid 90% <sup>(16)</sup>. The highest cure rates were for cryotherapy (83.1%) <sup>(16)</sup>. Other studies recorded lower cure rates for example phenol (82%) by Banihashimim et al. <sup>(20)</sup>, intralesional bleomycin (80%) by Mehta et al. <sup>(21)</sup> and intralesional vitamin D (80%) by Abdel El-Magid <sup>(22)</sup>.

The mechanism of action of hydrogen peroxide could be multifactorial, as there is evidence that it has antiviral activity <sup>(23?)</sup>. Its use in treating seborrheic keratoses was explained by that in high concentrations (>40%) it leads to oxidative damage to keratotic cells leading to their death <sup>(23)</sup>. It is possible that cells infected with HPV are directly damaged by the solution.

The present study does not include a control group because of the difficulty in recruiting patients in the circumstances of the covid19 pandemic; however, we can compare the cure rate with the spontaneous cure rate stated by previous studies. Aclaris mentioned a spontaneous cure rate of 5.2% after 60 days and 14.5% after 137 days of follow up <sup>(18)</sup>. Smith et al observed a spontaneous cure rate of 2.6% after 8 weeks <sup>(19)</sup>. These are much lower than the cure rate observed in the present study.

In the current study, the most frequent adverse effects were pruritus (76.2%), erythema (76.2%), stinging (57.1%), pain (42.9%), edema, hyperpigmentation, and hypopigmentation (9.5%) for each, and (4.8%) ulceration. These were higher than the results of the clinical-trial sponsored by Aclaris Therapeutics, as the adverse events reported included 10.24% pruritus, 17.32% erythema, 1.18% irritation, 31.50% pain, 3.94% edema, 0.39% discoloration, 0.79% ulceration <sup>(18)</sup>. These differences may be due to method of application and the higher concentration used in the present study.

The other modalities were also associated with significant side effects. For example cryotherapy was reported to cause hypopigmentation (53.8%), blistering (21.2%), scarring (13.2%), pain (12.7%), infection (3.3%), and erythema (0.5%). Local anesthesia was required before the treatment. While richloroaceticacid caused hyperpigmentation (34.7%)<sup>(20)</sup>. In a study bleomycin induced mild injection-site erythema, induration and pain in all treated patients <sup>(21)</sup>.

Zinc sulfate caused more local side adverse events in comparison to vitamin D that included pain, erythema, and hyperpigmentation <sup>(22)</sup>. Phenol is caustic and may cause systemic side effects.

### CONCLUSION:

Hydrogen peroxide achieved a cure rate higher than the aforementioned studies. It is available, non-costly and free from systemic side effects; local side effects are mild and temporary. Local anesthesia was not required before application.

### REFERENCES:

1. Hay RJ, Johns NE, Williams HC, Bolliger IW, Dellavalle RP, Margolis DJ, et al. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. *Journal of Investigative Dermatology*. 2014;134:1527-34.
2. Sterling JC. Human Papillomavirus Infection. In: Kang S, editor. *Fitzpatrick's Dermatology*. USA: McGraw-Hill Education; 2019. p. 3095-106.
3. World Health Organization. Human papillomavirus (HPV) and cervical cancer 11 November 2020 [cited 2020 Dec 2]. Available from: [https://www.who.int/news-room/fact-sheets/detail/human-papillomavirus-\(hpv\)-and-cervical-cancer](https://www.who.int/news-room/fact-sheets/detail/human-papillomavirus-(hpv)-and-cervical-cancer).
4. Mohammed B. Survey of cutaneous viral warts in Iraqi patients. A diploma thesis. College of Medicine, Baghdad University. 1989.
5. Cardoso JC, Calonje E. Cutaneous manifestations of human papillomaviruses: a review. *Acta dermatovenerologica Alpina, Pannonica, et Adriatica*. 2011;20:145-54.
6. Kirnbauer R, Lenz P. Human Papillomaviruses. In: Bolognia JL, Schaffer JV, Cerroni L, editors. *Dermatology E-Book: Elsevier Health Sciences*; 2017: 1383-98.
7. Gibbs S, Harvey I, Sterling J, Stark R. Local treatments for cutaneous warts: systematic review. *British Medical Journal*. 2002;325:461.
8. Sterling JC, Gibbs S, Haque Hussain SS, Mohd Mustapa MF, Handfield-Jones SE, Hughes JR, et al. British Association of Dermatologists' guidelines for the management of cutaneous warts 2014. *British Journal of Dermatology*. 2014;171:696-712.
9. Mulhem E, Pinelis S. Treatment of nongenital cutaneous warts. *American family physician*. 2011;84:288-93.

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10. Salman S, Ahmed MS, Ibrahim AM, Mattar OM, El-Shirbiny H, Sarsik S, et al. Intralesional immunotherapy for the treatment of warts: a network meta-analysis. *Journal of the American Academy of Dermatology*. 2019;80:922-30.
11. Al-Hamamy HR, Salman HA, Abdulsattar NA. Treatment of plane warts with a low-dose oral isotretinoin. *International Scholarly Research Notices Dermatology*. 2012; Article 163929, 3pages
12. Uyar B, Sacar H. Comparison of cryotherapy session intervals in the treatment of external genital warts. *Dermatologica Sinica*. 2014;32:154-56.
13. Dalimunthe DA, Siregar R, Tanjung C. Comparative clinical efficacy between electrodesiccation with curettage and application of 80% phenol solution in treatment of common warts. *Open access Macedonian journal of medical sciences*. 2018;6:326.
14. Balasubramaniam D, Burkhart CG. Hydrogen Peroxide Use for Chemical Destruction in Seborrheic Keratosis: A Review. *The Open Dermatology Journal*. 2019;13.
15. Zandi S, Ahmad Zadeh R, Yousefi SR, Gharibi F. Promising New Wart Treatment: A Randomized, Placebo-Controlled, Clinical Trial. *Iran Red Crescent Med J*. 2016;18:e19650-e.
16. Abdel Meguid AM, Abdel Motaleb AA, Abdel Sadek AMI. Cryotherapy vs trichloroacetic acid 90% in treatment of common warts. *Journal of cosmetic dermatology*. 2019;18:608-13.
17. Institute for Quality and Efficiency in Health Care. Warts: Overview. Cologne, Germany: InformedHealth.org; 2019 [cited 2020 10/28]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK279586/>.
18. ClinicalTrials.gov[internet]. United States: National Library of Medicine. Identifier: NCT03687372: Topical Solution for the Treatment of Common Warts. September 6, 2019 [cited 2020 10/28]. Available from: <https://clinicaltrials.gov/ct2/show/study/NCT03687372>.
19. Smith SR, Tyring SK, Grande KK, Schlessinger J, Gold MH, Shanier SD. Hydrogen Peroxide Topical Solution, 45% for Common Warts: Phase 2 Efficacy and Safety Trial Results. *Journal of drugs in dermatology : Journal of Drugs in dermatology*. 2020;19:969-76.
20. Banihashemi M, Pezeshkpoor F, Yazdanapanah MJ, Family S. Efficacy of 80% solution in comparison with cryotherapy in the treatment of common warts of hands. *Singapore Medical Journal* 2008;49:1035
21. Mehta KIS, Mahajan VK, Chauhan PS, Chauhan S, Sharma V, Rawat R. Evaluation of efficacy and safety of intralesional bleomycin in the treatment of common warts: Results of a pilot study. *Indian Journal of Dermatology, Venereology, and Leprology*. 2019;85:397.
22. Abd El-Magid WM, Nada EEA, Mossa RA. Intralesional injection of vitamin D3 versus zinc sulfate 2% in treatment of plantar warts: a comparative study. *Journal of Dermatological Treatment*. 2019:1-6.
23. DuBois J, Grande K, Bradshaw M, Schnyder J. Safety of hydrogen peroxide topical solution 40% and 45%(w/w) in patients with seborrheic keratoses on the trunk, extremities, and face: Results of a phase 2, randomized, double-blind, vehicle-controlled, parallel-group study: 10513. *Journal of the American Academy of Dermatology*. 2019;81.