

Efficacy and safety of topical application of 45% hydrogen peroxide solution in the treatment of common warts

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Abstract: Objective: The study aimed to evaluate the effectiveness and safety of hydrogen peroxide topical solution, 45% (HP45) for treatment common warts.

Patients and Methods: A Prospective study (Before & After) conducted for the period one year (January 2020- January 2021) at Tishreen University Hospital in Lattakia- Syria. 35 patients with common warts who received treatment with HP45 were included in the study.

Results: The median age was 21 years, 51.4% of patients were females. Most common sites of warts involvement were dorsum of the hands (44.6%), followed by palm of hands (41.3%). A statistically significant reduction in mean warts size was occurred at the end of treatment (0.2 ± 0.18 vs. 0.62 ± 0.6 , $p: 0.0001$). Complete clearance was achieved in 51.2% of patients, most of these cases were in the last session. The best response to the treatment was in warts located on the dorsum of hands, with size less than 1 cm and duration of disease less than one year. Regarding side effects, itching and stinging were more frequently seen, followed by edema.

Conclusion: Topical application of HP45 was effective in removal of common warts. Except of itching and stinging, serious side effects not occurred.

Keywords: Common warts, hydrogen peroxide

فعالية وأمان التطبيق الموضعي لمحلول بيروكسيد الهيدروجين بتركيز 45% في علاج الثآليل الشائعة

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المستخلص: هدفت الدراسة إلى تقييم فعالية وأمان محلول بيروكسيد الهيدروجين الموضعي 45% في علاج الثآليل الشائعة. طريقة البحث: كانت هذه دراسة مستقبلية (قبل، بعد) أجريت في مشفى تشرين الجامعي في اللاذقية- سوريا خلال عام واحد (كانون الثاني 2020- كانون الثاني 2021). شملت الدراسة 35 مريضاً مصاباً بالثآليل الشائعة تلقوا العلاج بمحلول بيروكسيد الهيدروجين 45%.

النتائج: بلغ معدل العمر 21 سنة، 51.4% من المرضى هم من الإناث. إن أكثر أماكن تواجد الثآليل شيوعاً هي ظهر اليدين (44.6%) تلاها راحة اليدين (41.3%). حدث تناقص هام إحصائياً في حجم الثؤلول في نهاية العلاج (0.18 ± 0.2 مقابل 0.6 ± 0.62 ، $p < 0.0001$)، مع تطور الشفاء التام لدى 51.2% من المرضى، ومعظم هذه الحالات كانت في الجلسة الأخيرة من العلاج. تم الحصول على الاستجابة الأفضل للعلاج في الثآليل المتوضعة على ظهر اليدين، ذات الحجم الأقل من 1 سم وبفترة زمنية أقل من سنة. بدراسة الآثار الجانبية للعلاج فإن الحكمة والوخز هي الأكثر تواتراً تلاها الودمة. الاستنتاج: يعتبر التطبيق الموضعي لمحلول بيروكسيد الهيدروجين (45%) علاجاً فعالاً في إزالة الثآليل الشائعة. باستثناء الحكمة والوخز لم يلاحظ حدوث آثار جانبية خطيرة.

الكلمات المفتاحية: الثآليل الشائعة، بيروكسيد الهيدروجين

Introduction.

Common warts are widespread benign epidermal neoplasms which occur in the mucosa and skin [1]. They are caused by different strains of human papillomavirus (HPV) group that produce different clinical types of warts, most commonly type 2, 4 followed by 1, 3, 27, 29, and 57 [2, 3].

Warts affects equally males and females. They occur most frequently in children and young adults, peak at 12 to 16 years and declining thereafter. The prevalence is estimated to be 10- 20% in school- aged children [4, 5].

They are spread via person to person contact or indirectly by fomites, showers and swimming pools that is carrying the virus. Common warts are usually located on the hands, feet, and appear either alone or in groups [6].

Spontaneous disappearing occurs approximately in 65% of warts, but most patients demand treatment because of the cosmetic disfigurement and tenderness. The available treatment options range from tissue keratolysis to immunotherapy to tissue destructive. Although there are a variety of treatment modalities, none is very effective in achieving complete response, and warts poses a therapeutic challenge [7, 8]. Thus, there is a significant need for a safe, effective, and cosmetically acceptable treatment.

Hydrogen peroxide (H_2O_2) is a reactive oxygen species which produced endogenously, and damage lipids, proteins, and nucleic acids oxidatively. High concentration of H_2O_2 solution (45%), is first approved by Food and Drug Administration (FDA) for treatment of raised seborrheic keratosis [9, 10].

Clinical trials showed that HP45 is effective in treating common warts. Although the exact mechanism of this effect is not fully understood, it may result from oxidative damage induced by H_2O_2 which cause death to abnormal cells [11]. Therefore, the objectives of the study were to: 1- determine the therapeutic efficacy and safety of HP45 in the treatment of common warts. 2- evaluate the association between the response to treatment and demographic characteristics of patients. 3- evaluate the association between the response to treatment and characteristics of lesions.

Patients and Methods.

This is a Prospective study (Before& After) of a group of patients older than one year with common warts attending the Dermatology Department's outpatient clinic at Tishreen University Hospital in Lattakia- Syria during a one year period (January 2020 to January 2021). The following data were recorded: demographic data (age, sex), size of warts, position and duration of disease. Exclusion criteria were patients with one of the following: immune suppression, warts on trunk and extremities, previous history of treatment with other modalities of therapy during the last two months, pregnancy, lactation, patients with common vitiligo, or constitutional eczema.

The position was cleaned by alcohol, then HP45 was applied on the lesion with the use of disposable applicator, and firm pressure for approximately 15 seconds, and then repeated in the same order up to three times. Every patient has received a session every week for a maximum of 8 sessions, and patients were followed for 3 months after the last session. Assessment was done by using clinical photograph at the beginning of the study and during each treatment session to record reduction in the size, number of warts, and side effects. The clinical response was graded into complete (complete cure) and no response (no change in size and number of warts).

Ethical consideration: All patients were provided a complete and clear informed consent after discussion about the study. This study was performed in accordance with the Declaration of Helsinki.

Statistical Analysis

Statistical analysis was performed by using IBM SPSS version20. Basic Descriptive statistics included means, standard deviations (SD), median, Frequency and percentages. The Wilcoxon test was used to compare two paired groups. Differences of distribution examined by using Fisher exact test. P value <0.05 was considered as statistically significant.

Results.

A total of 35 patients with common warts who presented to the Department of Dermatology from January 2020 to January 2021 were included in the study. The baseline characteristics of patients are as given in table (1). The median age of patients who enrolled in the study was 21 years, 35.3% of the patients were in the age group [10- 20[, and 51.40 % were female.

Table (1) Demographic characteristics of the study population

Variables	Result
Age (years)	21 (5- 55)

Variables	Result
<u>Age groups</u>	
<10	4 (11.8%)
[10- 20]	12 (35.3%)
[20- 30]	7 (20.6%)
[30- 40]	2 (5.9%)
≥40	10 (28.6%)
<u>Sex</u>	
Male	17 (48.60%)
Female	18 (51.40%)

As shown below (Table 2), the most common sites of warts involvement were dorsum of the hands (44.6%) followed by palm of hands (41.3%). The median duration of disease was 7 months. There was a significant reduction in lesion size at the end of the therapy (0.2 ± 0.18 vs. 0.62 ± 0.6) The response to the treatment was complete in 51.2%.

Table (2) Distribution of the study population according to different parameters of warts

Variables	
<u>Sites of warts</u>	
Dorsum of hands	54 (44.6%)
Palm of hands	50 (41.3%)
Face	7 (5.8%)
Dorsum of feet	6 (5%)
wrist	3 (2.5%)
Neck	1 (0.8%)
Duration of disease (month)	7 (2- 36)
<u>Warts size (cm)</u>	
Before treatment	0.62 ± 0.6 (0.30- 4.30)
After treatment	0.2 ± 0.18 (0- 2)
<u>Response to treatment</u>	
Complete response	62 (51.2%)
No response	59 (48.8%)

82.3% of the cases with complete clearance of the lesions were in the sessions (8) of the therapy, Figure (1)

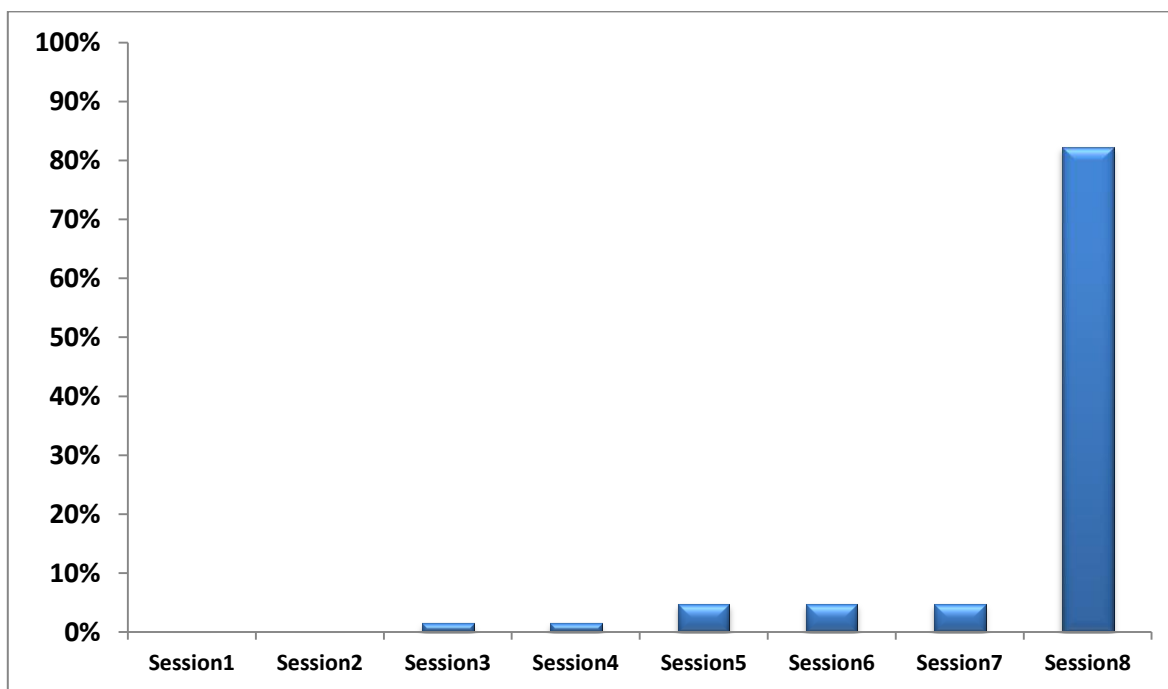


Figure (1) Distribution of the 62 warts with complete response according to the number of the sessions

Complete response to the treatment was more frequently in patients with duration of disease \leq 1 year (89.4% vs. 1.6%, $p:0.01$), size of warts <1 cm (96.8% vs. 3.2%, $p: 0.03$), and warts located on the dorsum of hands ($p:0.0001$), Table (3).

Table (3) Association between response to treatment and the demographic characteristics of the study population and parameters of warts

Variables	Response to treatment		p- value
	Complete response	No response	
<u>Sex</u>			
Male	10 (52.6%)	7 (43.8%)	0.6
Female	9 (47.4%)	9 (56.3%)	
<u>Age groups</u>			
<10	2 (11.1%)	2 (12.5%)	0.09
[10- 20]	7 (38.9%)	5 (31.3%)	
[20- 30]	2 (11.1%)	5 (31.3%)	
[30- 40]	1 (5.6%)	1 (6.3%)	
40 \geq	7 (36.8%)	3 (18.8%)	
<u>Duration of disease (years)</u>			
\leq 1	61 (98.4%)	47 (79.7%)	0.01
>1	1 (1.6%)	12 (20.3%)	
<u>Warts size (cm)</u>			
<1	60 (96.8%)	51 (86.4%)	0.03
1 \geq	2 (3.2%)	8 (13.6%)	

Variables	Response to treatment		p- value
	Complete response	No response	
Sites of warts			
Dorsum of hands	47 (75.8%)	7 (11.9%)	0.0001
Palm of hands	0 (0%)	50 (84.7%)	
Face	6 (9.7%)	1 (1.7%)	
Dorsum of feet	5 (8.1%)	1 (1.7%)	
wrist	3 (4.8%)	0 (0%)	
Neck	1 (1.6%)	0 (0%)	

As shown below (Table 4), most common side effects after each session were itching and stinging, followed by edema and hypopigmentation.

Table 4 Distribution of the study population according to the side effects after each session

Session number	Edema	Itching	Stinging	Hypopigmentation
1	8 (6.6%)	28 (23.1%)	27 (22.3%)	0 (0%)
2	12 (9.9%)	26 (21.5%)	29 (23.9%)	0 (0%)
3	9 (7.4%)	27 (22.3%)	26 (21.5%)	0 (0%)
4	10 (8.3%)	25 (20.7%)	26 (21.5%)	0 (0%)
5	11 (9.1%)	28 (23.1%)	27 (22.3%)	0 (0%)
6	7 (5.8%)	23 (19%)	24 (19.8%)	3 (2.5%)
7	9 (7.4%)	26 (21.5%)	25 (20.7%)	3 (2.5%)
8	5 (4.1%)	28 (23.1%)	22 (18.2%)	3 (2.5%)
Follow up- session	0 (0%)	0 (0%)	0 (0%)	3 (2.5%)

Discussion.

Common warts may be aesthetically bothersome as well as medically worrisome to patients and might affect the quality of life. Medical literature review revealed prior limited controlled clinical trials evaluating the efficacy of HP45 in removal common warts.

The current study demonstrated that common warts were more frequently in children and adulthood, and most common sites affected were dorsum and palm of the hands. The response to the treatment at the end of the treatment was complete in 51.2% depending on the location of warts, size of warts, and duration of the disease, without any correlation with age or sex of the patient. Improvement was more frequently in lesions located on the dorsum of the hands, small size, and with shorter duration of disease. Adverse effects were limited to local skin reactions, itching and stinging were the most observed effects of the treatment.

The exact mechanism of HP45 for treatment common warts has not been fully elucidated. It may be explained by the following: direct oxidation of organic tissues, generation of reactive oxygen species,

and generation of local concentrations of oxygen that are toxic to warts cells [12]. These results are comparable to the findings reported by previous studies.

Stephen et al., (2019) demonstrated the efficacy of HP45 topical solution in treatment common warts. Complete response was achieved in 19% of the cases, and most side effects were mild to moderate in severity. Hypopigmentation was the most common complications seen [13].

Aclaris therapeutics (2019), trial 1: This trial showed that complete clearance was achieved in 15.7%. Aclaris therapeutics (2019), trial 2: This trial also demonstrated that complete clearance was achieved in 13.1% [14].

Side effects of the previous trials were mild in 34.6%, moderate in 17.3%, and most of these adverse events were application site pain, scabbing, erythema, and erosion [14].

Complete cure rates attained by HP45 varied between trials; this can be attributed to many factors which include: age, wart type, durations of the warts.

In summary, treatment with topical HP45 solution provides noninvasive, safe and effective method in treating common warts.

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