

Evaluation of Different Concentrations of Hydrogen Peroxide Gel (10% and 20%) as a Potential New Therapeutic Option of Genital Warts

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Abstract

Background: Genital warts are a kind of sexually transmitted diseases caused by certain types of human papillomavirus (HPV). The main clinical manifestation of genital warts is benign hyperplasia of the skin and mucous membrane in the genitalia, anus and perineum. Genital warts not only affect physiological function but also cause psychological stress. HPV is the most common sexually transmitted infection globally, and most people are infected at some point in their lives. One major benefit of the H₂O₂ gel does not destroy healthy, uninfected tissues nor results in significant systemic side effects, local side effects such as irritation, necrosis of tissue surrounding the wart, allergic rashes, scarring, disfigurement or discomfort to the human treated there with. The aim of the present study was to assess the evaluation of different concentrations of hydrogen peroxide gel (10% and 20%) as a potential new therapeutic option of genital warts. **Methods:** This study is an interventional study which included 30 patients suffering from genital warts. All patients were selected from the outpatient clinic of dermatology and andrology department at Benha university hospitals. **Results:** There was no Statistical difference regarding age and gender between study groups. There was no statistical difference regarding disease duration. There was no statistical difference regarding Numbers and size of warts before treatment. Number of lesions decreased significantly in the three studied groups after 6 weeks of treatment. size of lesions decreased significantly in the three studied groups after 6 weeks of treatment. There is statistical difference regarding partial Treatment responses of study groups after 2 and 6 weeks. There is significant statistical difference regarding complete Treatment responses of study groups after 2 and 6 weeks. Size and number of lesions had negative impact on treatment responses. There was no statistical difference regarding Side effects recorded. **Conclusion:** Hydrogen Peroxide Gel (10% and 20%) was effective as treatment for genital warts with more efficacy of Hydrogen Peroxide Gel 20% than 10% with no severe side effects and more response rate. A once-daily application of topical H₂O₂ gel at bed time for 6 weeks can be considered a an effective, safe, cheap, and easy to use new topical treatment for genital warts with low recurrence rates.

Key words: Hydrogen Peroxide Gel, Concentrations, Therapeutic Option, Genital Warts.

1. Introduction

Mammalian tumor-inducing virus strains are common. Human papillomaviruses (HPVs) are DNA viruses, and there are more than 60 identified kinds. Tumors may be induced by these viruses. Several of these HPVs have been linked to the development of benign tumours, such as common warts, while others have been strongly linked to the development of dysplasia and carcinoma in the oral and genital mucosa of the infected mammal's oral and genital tracts [1]

There are both physical and psychological consequences of warts, which are a frequent skin illness. HPV (human papillomavirus) is the culprit (HPV). According to its kind, location, and immunological condition, HPV may produce a wide range of skin manifestations depending on the virus's type, location, and immune status. There are between 2.4 percent and 12.9 percent of people who have warts on their skin [2].

A cure for warts that is painless, without adverse effects, and without recurrence is still a goal for researchers. In the present day, patients may choose from a variety of therapy methods, including topical, intralesional, physical, and surgical. It's a shame that none of these options has worked out perfectly [3]

H₂O₂ is the chemical formula for hydrogen peroxide. HP is a short-lived result of several metabolic reactions in the human body. It is a reactive oxygen species (ROS) that has wide antiviral, antibacterial,

antiyeast, and antifungal sporicidal action. HP was previously explored and shown to be effective as a topical therapy for MC [4].

Hydrogen peroxide gel (10 percent and 20 percent) was used in this research to evaluate its potential as a novel treatment option for genital warts.

2. Patients and Methods

I.Study setting

This study was carried out at dermatology and andrology department, Benha university hospital during the period from December 2020 till November 2021.

II.Study type

This study was interventional study.

III.Ethical consideration:

- 1) Study protocol had been submitted for approval by ethical committee of Benha Faculty of Medicine.
- 2) An informed consent was taken from each patient before being enrolled in the study.
- 3) Personal privacy had been respected in all levels of this study. Collected data had not been used for any other purpose.

IV. Study population

This study included 30 patients suffering from genital warts. All patients were selected from the outpatient clinic of dermatology and andrology department at Benha university hospital.

The Patients were divided into three groups:

- **Group (A):** 10 patients received topical H₂O₂ gel 10%.
- **Group (B):** 10 patients received topical H₂O₂ gel 20%.
- **Group (C):** 10 patients received topical podophyllin.

2.1. Inclusion criteria:

All patients enrolled in the study had

- Clinically typical genital wart lesions.
- Different degrees of severity of genital warts.

2.2. Exclusion criteria:

- Patients with genital warts treated previously with any other topical treatment during the preceding two weeks.
- Presence of any other genital diseases.
- Pregnant and lactating females.

2.3. Methods

Every patient was subjected to the following:

❖ **Full History taking:**

A. Personal history, Including:

- Age, sex and occupation.

B. Medical history including:

- Onset
- Course
- Duration of the lesion

C. Family history of genital warts

D. Sexual history

E. History of other skin diseases

❖ **Examination:**

➤ **Complete genital examination to confirm the diagnosis of genital warts and assess the distribution and the extent of the lesion:**

• **Positioning**

- ✓ The supine position is most commonly used in genital exams.
- ✓ The supine lithotomy position is reserved for cooperative female adolescents. .

- ✓ The prone knee chest position is most commonly used for the perineal and anal examinations because it frequently affords an optimal view of the posterior hymen and/or the vagina, thus revealing the cervix and trauma or a foreign body.

❖ **Patients were subjected to:**

- Group (A): 10 patients received topical H₂O₂ gel 10%.
- Group (B): 10 patients received topical H₂O₂ gel 20%.
- Group(C);10 patient received podophyllin as regular treatment of genital warts.

2.4Gel composition:

- Our wart destroying gel was described as follows: combine 70% glycerin,5% carboxypolymethylene,10% and 20%hydrogen peroxide, and water adjusted to pH 6.5 with sodium hydroxide. Mix until homogenous.

2.5Method of application:

- The gel was applied by patients at home once daily at bed time at least for 6 hours.
- Treatment course 6 weeks, follow up every two weeks.

Data management and Statistical Analysis:

Data entry, processing and statistical analysis was carried out using Statistical package for social sciences (IBM-SPSS), version 24 (May 2016); IBM- Chicago, USA will be used for statistical data analysis. Tests of significance (Kruskal-Wallis, Wilcoxon's, Chi square, logistic regression analysis, and Spearman's correlation) were used. Data were presented and suitable analysis was done according to the type of data (parametric and non-parametric) obtained for each variable. P-values less than 0.05 (5%) was considered to be statistically significant.

- P- value: level of significance
- P > 0.05: Non-significant (NS).
- P < 0.05: Significant (S).
- P < 0.01: Highly significant (HS).

3. Results

Table (1) Number and size of lesions before and after 2 and 6 Wk of treatment

Group	Before treatment Mean ± SD	After 2 wk of treatment Mean ± SD	P value	After 6 wk of treatment Mean ± SD	P value
Number					
Group A	3.41 ± 3.78	3.40 ± 3.55	0.105	2.21 ± 3.712	<0.001
Group B	3.35 ± 3.74	3.26 ± 3.77	0.085	2.19 ± 3.813	<0.001
Group C	3.75 ± 0.98	3.65 ± 0.99	0.317	2.78 ± 0.86	0.009
Size					
Group A	6.06 ± 5.36	5.51±3.52	0.002	3.31±1.89	<0.001
Group B	6.94 ± 5.84	4.51±3.21	0.001	2.21±1.26	<0.001
Group C	6.54 ± 5.18	6.23±5.03	0.182	4.87±3.98	0.008

- the mean of number of lesions before treatment in subjects of group (A) was 3.41 with SD of 3.78 and the mean number of lesions after 2 weeks treatments in subjects of group (A) was 3.40 with SD of 3.55. Despite reduction in the number of lesions but there was no statistical difference regarding number of lesions before and after 2 weeks of treatment in group (A) as P-Value = 0.105.
- The mean of number of lesions after 6 weeks of treatment in subjects of group (A) was 2.21 with SD of 3.712. there was significant statistical difference regarding number of lesions before and after 6 weeks of treatment in group (A) as P-Value < 0.001.
- The mean of number of lesions before treatment in subjects of group (B) was 3.35 with SD of 3.74 and the mean of number of lesions after 2 weeks of treatment in subjects of group (B) was 3.26 with SD of 3.77. there was no statistical difference regarding number of lesions before and after 2 weeks of treatment in group (B) as P-Value = 0.085.
- The mean number of lesions after 6 weeks of treatments in subjects of group (B) was 2.19 with SD of 3.813. there was a significant statistical difference regarding number of lesions before and after 6 weeks of treatment in group (B) as P-Value < 0.001.
- The mean of number of lesions before treatment in subjects of group (C) was 3.75 with SD of 0.98 and the mean of number of lesions after 2 weeks of treatment in subjects of group (C) was 3.65 with SD of 0.99 and the mean number of lesions after 6 weeks treatment in subjects of group (C) was 2.78 with SD of 0.86. So there is no statistical difference regarding the number of lesions before and after 2 weeks of treatment in group (C) as P-Value = 0.317 but there was a statistical difference in the number of warts in group (C) after 6 weeks of treatment P value = 0.009.
- So in our study after 6 weeks of treatment there was marked decrease in number of lesions in group (B) who received 20% H2O2 and group (A) who received 10% H2O2 more than group (C)Who received Podophyllin.

Also

- the mean of size of lesions before treatment in subjects of group (A) was 6.06 with SD of 5.36 and

the mean of size of lesion after 2 weeks of treatment in subjects of group (A) was 5.51 with SD of 3.52. there is a statistical significance regarding size of lesions before and after 2 weeks of treatment as P-value = 0.002 .

- the mean of size of lesion after 6 weeks of treatment in subjects of group (A) was 3.31 with SD of 1.89. there is a significant statistical difference regarding size of lesions before and after 6 weeks of treatment as P-value < 0.001 .
- the mean size of lesions before treatment in subjects of group (B) was 6.94 with SD of 5.84 and the mean of size of lesion after 2 weeks of treatment in subjects of group (B) was 4.51 with SD of 3.21. there is a significant statistical difference regarding size of lesion before and after treatment as P-value 0.001 .
- the mean of size of lesion after 6 weeks of treatment in subjects of group (B) was 2.21 with SD of 1.26. there is high statistical significance regarding size of lesion before and after 6wk of treatment as P-value < 0.001 .
- The mean size of lesions before treatment in subjects of group (C) was 6.54 with SD of 5.18 and the mean size of lesions after 2 weeks of treatment in subjects of group (C) was 6.23 with SD of 5.03. there is no statistical significance regarding size of lesion before and after 2 weeks of treatment as P-value = 0.182.
- the mean size of lesions after 6 weeks of treatment in subjects of group (C) was 4.87 with SD of 3.98. there is a statistical significance regarding size of lesions before and after 6 weeks of treatment as P-value = 0.008.
- So after 2 weeks of treatment both groups (A) and (B) showed a statistical difference in the reduction of size of lesions but group (B) who treated with 20% H2O2 showed a better response in reduction the size of the lesions as compared with group (A) who treated with 10% H2O2 while there was no significant reduction in size in group (C) after 2 wk of treatment.
- After 6 weeks of treatment all groups showed significant decrease in size of lesions but both groups (A) and (B) showed more decrease in the size of lesions as compared to group (C).

Table (2) Treatment responses of study subjects after 2 weeks.

Variable	Group(A) No. (%)	Group (B) No. (%)	Group (C) No. (%)	P-value
Complete	1 (10%)	3(30%)	1(10%)	0.023
Partial	4 (40%)	5 (50%)	3 (30%)	0.034
No	5 (50%)	2 (20%)	6 (60%)	0.001

*P < 0.001 is considered High statistically significant.

According to table(2):

- The percentage of complete Treatment responses of study subjects after 2 weeks in groups A, B and C was 10%, 30% and 10% respectively. the percentage of partial Treatment responses of study subjects after 2 weeks in groups A, B and C was 40%, 50% and 30%

and the percentage of no Treatment responses of study subjects after 2 weeks in groups A, B and C was 50%, 20% and 60%.

- Also, the percentage of complete treatment response after 2 weeks of treatment was more in group (B) as

compared with group (A) and group (C) P value =0.023.

-While the percentage partial treatment response after 2 weeks of treatment was more in group (B) as compared with group (A) and both groups (A) and (B) had better partial treatment response than group (C) P value =0.034.

-The percentage of no Treatment responses of study subjects after 2 weeks in groups A, B and C was 50%, 20% and 60% respectively that means the percentage of no treatment response was more in group (C) as compared with group (A) and group (B) and the percentage of no response in group (A) more than group (B) P value = 0.001.

Table (3) Treatment responses of study subjects after 6 weeks

Variable	Group(A) No. (%)	Group (B) No. (%)	Group (C) No. (%)	P-value
Complete	5 (50%)	5 (50%)	2 (20%)	0.032
Partial	2 (20%)	5 (50%)	3(30%)	<0.001
No	3 (30%)	0	5 (50%)	<0.001

*P < 0.001 is considered High statistically significant.

Fisher exact test used.

According to table (3):

-the percentage of complete Treatment responses of study subjects after 6 weeks in groups A, B and C was 50%, 50% and 20% respectively. So, the percentage of complete treatment response after 6 weeks of treatment was more in group (B) and group (A) as compared with group (C) with a significant statistical difference P value = 0.032.

-The percentage of partial Treatment responses of study subjects after 6 weeks in groups A, B and C was 20%, 50% and 30%. So the percentage of partial treatment response after 6 weeks of treatment was more in group (B) as compared with both groups (A)

and (C) and group (C) more than group (A) with significant statistical difference P value < 0.001.

-the percentage of no Treatment responses of study subjects after 6 weeks in groups A, B and C was 30%, 0% and 50%.So the percentage of no treatment response after 6 weeks of treatment was more in group (C) than groups (A) and (B) and in group (A) more than group (B) with a significant statistical difference P value < 0.001.

-So the response after 6 weeks of treatment was better in groups A and B than group C and the response in group B better than group A.

Table (4) Effect of number and size of lesions on treatment response after 6 weeks.

Variable	Complete N=12 Mean ± SD	Partial N=10 Mean ± SD	No N=8 Mean ± SD	P-value
Number lesions before treatment	2.30 ± 2.43	4.18 ± 4.05	5.18 ± 3.66	0.03
Size of lesions before treatment (mm)	3.31±1.89	4.51±3.21	6.54 ± 5.18	0.03

ANOVA test used

According to Table (4):

-We found that the number of patients who had complete, partial and no treatment response after 6 weeks were 12,10 and 8 respectively.

-The mean number of lesions before treatment in patients with complete treatment response was 2.30 with SD 2.43. and the mean number of lesions before treatment in patients with partial treatment response was 4.18 with SD 4.05. and the mean number of lesions before treatment in patients with no treatment response was 5.18 with SD 3.66.

-We noticed that after 6 weeks of treatment, patients who had complete treatment response had lower number of lesions before treatment than patients whom had partial or no treatment response. And patients who had partial treatment response had lower number of lesions before treatment than patients with no treatment response with significant statistical difference P value = 0.03.

-The mean size of lesions (mm) before treatment in patients with complete treatment response after 6 weeks was 3.31 with SD 1.89. and the mean size of lesions (mm) before treatment in patients with partial treatment response was 4.51 with SD 3.21. and the mean size of lesions (mm) before treatment in patients with no treatment response was 6.54 with SD 5.18.

-We also observed that after 6 weeks of treatment patients who had complete treatment response had smaller size of lesions (mm) before treatment than patients whom had partial or no treatment response. And patients who had partial treatment response had smaller size of lesions (mm) before treatment than patients with no treatment response with significant statistical difference P value = 0.03.

-So, lesion`s number (P value = 0.03) and lesion`s size in (mm) (P value = 0.03) before treatment had significant negative impact on treatment responses.

Table(5) Side effects recorded

Group	Yes	No	P value
A	3 (30 %)	7 (70%)	0.32
B	2 (20%)	8 (80%)	
C	2 (20%)	8 (80%)	

Fisher exact test used.

According to Table (5):

- The percentage of patients who had side effects in group (A), (B) and (C) was 30%,20% and 20% respectively. While the percentage of patients who had no side effects in groups A, B and C were 70%,80% and 80% respectively. There was no statistical difference regarding side effects recorded between the three groups.

4. Discussion

We found a statistically significant difference in the number of lesions in group (A) before and after six weeks of treatment with HP (10 percent and 20 percent). Lesions in group (B) decreased significantly after six weeks of therapy compared to those in group (A).

H₂O₂ 3 percent and 6 percent was effective in decreasing the number of warts (non-genital warts) after six weeks, which is in keeping with our findings.

For plane warts, Nouh et al.,[6] found that HP 40% was effective.

After 8 weeks of therapy, Smith et al. [7] found that HP was 45 percent effective and safe in the treatment of common warts in 157 individuals.

One of the most recent studies to support the antiviral properties of HP is the one by Schianchi et al.,[8] who found an 85.7 percent reduction in the number of lesions in children who used 1.8 percent gel formulation for three-week treatment, while in our study the reduction in the number of warts occurred after six weeks of treatment with both 10% and 20% H₂O₂.

Stull et al.[10] reported that adding HP to sterile surgical preparation decolonizes Cutibacterium acnes, which is more support for HP's antibacterial action.

For the treatment of vaginal trichomoniasis, Cardone et al.[11] found that HP 3 percent vaginal irrigation was effective and cost-effective. Gonzalez Ramos [12] likewise found HP to be effective for the treatment of vaginal trichomoniasis.

Another study found that HP had an antibacterial impact by lowering the quantity of organisms (lactobacilli) and decreasing the duration of lesions in the short term (Hallen et al., 13).

Group (A) who utilised 10% H₂O₂ before and after treatment showed a statistically significant difference in the size of lesions compared to the other groups. In group B, which utilised 20% H₂O₂ before and after treatment, there was a statistically significant difference in the size of lesions. Similarly, Mahran et al. [5] found that warts (non-genital) decreased in size by 3 and 6 weeks in both treatment groups (3 percent) (6 percent).

However, only the size of the lesions had dropped dramatically after two weeks of therapy, but the number of lesions had not decreased much. Both the size and the number of warts in treatment groups (A) and (B) were significantly reduced after six weeks, however group (B) using a higher concentration of H₂O₂ saw the greatest decrease in size and quantity [20].

For the control group (C), we used Podophyllin, which showed a substantial decrease in both the size and quantity of warts after treatment for 6 weeks, while Mahran et al, [5] used regular water, which showed no change in size or number of lesions after the same period of time.

After two and six weeks of therapy, we found a substantial statistical difference between groups in terms of partial and total treatment responses.

After 2 and 6 weeks of treatment, partial and complete responses were better in group B (H₂O₂ 20%) than group A (H₂O₂ 10%) in agreement with our results, the study of Mahran et al., reported that the patients' complete responses were better in group B than in group A after 3 and 6 weeks of treatment, in accordance with our results.

There were fewer and smaller lesions (mm) in individuals who had a full therapy response compared with those who had partial or no treatment response. Prior to therapy, patients with partial treatment response had fewer and smaller lesions (mm) than patients who had no treatment response, with a statistically significant difference. It's statistically significant at a level of significance of 0.03.

Prior to therapy, the number and size of lesions had a substantial unfavourable influence on treatment outcomes. A research by Mahran et al., [5] shown that the number and size of warts may be utilised as a predictive indicator to predict treatment response.

There was no recurrence after 4 months of follow-up following treatment completion in either (H₂O₂ 10%) or (H₂O₂ 10%). (H₂O₂ 20 percent). After three months of therapy with H₂O₂, all patients had no recurrence of the disease, as reported by Nouh et al. [6]

Another study by Bigardi et al. [9] found no recurrence of MC six months after clearance of lesions after therapy with 1 percent H₂O₂.

Abstinence from sexual activity has been demonstrated to be a reasonably efficient technique of avoiding HPV infection, but it is not the only straightforward way to do so. It is possible for HPV to infect cells in the vaginal tract. , and may be spread by direct skin-to-skin contact. Even though birth control techniques such as barrier methods limit transmission, they do not completely remove the risk of infection. About a third of women say they use condoms to prevent the spread of genital warts, according to a new poll [15].

However, lesions that aren't covered by a condom pose a transmission danger [15]. It's not certain how infectious genital warts are, or whether the removal of the wart itself affects infectivity, as has been observed in the past [16].

The oxidative damage and oxygen generation caused by H₂O₂ may disturb the epidermis, resulting in vacuolar eruptions, as has been shown in the study [17].

According to Murphy & Friedman's retroactive study [17]. Low H₂O₂ concentrations have only produced temporary symptoms, such as paresthesia, blanching, and blistering, according to reports to a poison control centre. Diffuse reflectance spectroscopy investigations, which assess the skin's optical characteristics, have offered some insight into the process of blanching, albeit the exact mechanism is still unknown. Healthy volunteers' forearms were applied with 3% to 6% H₂O₂ and no changes in melanin concentrations were seen; however, temporary alterations in oxyhemoglobin were observed, showing that H₂O₂ had reached the epidermis and potentially the dermis, where capillaries are located. are situated [18].

Three patients in group A (10 percent H₂O₂) and two in group B (20 percent H₂O₂) had moderate and temporary erythema and mild burning sensations. No notable adverse effects were found with the use of H₂O₂, in accordance with Schianchi et al., [8], who reported only a burning sensation in one kid and a minor erythema in another child after using 1.8 percent H₂O₂ for 3 weeks in 21 children with MC.

After administering HP 3 percent and 6 percent for six weeks, Mahran et al. [5] found no significant local or systemic adverse effects in the groups they evaluated (non-genital warts). Topical H₂O₂ has been shown to be safe in these studies.

5. Conclusion

As a wart-curing therapy, a 20 percent solution of hydrogen peroxide gel was more successful than a 10% solution, with no harmful side effects and a higher response rate. New topical treatment for genital warts with low recurrence rates can be achieved by using topical H₂O₂ gel once a day at night for six weeks.

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