Comparative evaluation of carbon dioxide laser and cryotherapy by dermoscopy in treatment of warts

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Background
Viral warts are common pores and skin manifestations visible in each youngster and adults owing to the human papillomavirus. Human papillomavirus is transmitted at once with the aid of touch or in a roundabout way via the surroundings.

Aim and objective
The aim of our study was to compare the results of two therapeutic modalities, carbon dioxide (CO2) laser and cryotherapy, in the treatment of warts collectively with the dermoscopic assessment of viral warts before and after applying treatment.

Methods
A total of 50 patients were clinically recognized as having common warts and were recruited from the Dermatology Outpatient Clinics of Assiut University and Luxor preferred Hospitals. All patients were subjected to history taking and scientific and dermoscopic evaluations. In our study, we examined the efficacy of treatment of common warts using cryotherapy and CO2 laser according to improvement in size and width of warts, using dermoscopy, which helped us in our observation to attain a medical diagnosis of warts easily and correctly.

Results and conclusion
CO2 laser can be an effective and time-saving modality for warts and is a better modality than cryotherapy. However, studies with larger sample sizes and longer follow-up durations are suggested, which will verify the veracity of these results.

Keywords:
cryotherapy, dermoscopy, human papillomavirus

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Introduction

Human papillomavirus (HPV), a DNA virus, is associated with verrucae [1]. Cutaneous manifestations of HPV are extremely commonplace, especially on the fingers and toes. Warts can set off difficult, thickened pores and skin, black pinpoints, aches, or tenderness with considerable morbidity for the patients [2].

Many types of warts have been identified, which vary in form and site affected, in addition to the kind of HPV concerned. These include common warts (verruca vulgaris), flat warts (verruca plana), filiform or digitate warts, genital warts (venereal warts, condyloma acuminatum, and verruca acuminata), mosaic warts, periungual warts, and plantar warts (verruca plantaris) [3].

Treatment of warts can present a challenge, as treatment options are not uniformly effective. Viral warts regularly disappear without treatment [2]. In case of pain, pain, and lengthy duration, they can be treated. Treatment options include cryotherapy, electrocautery, salicylic acid, immune therapy, minor surgical treatment, or laser surgical procedure [4].

Cryotherapy is mentioned to be the most usually used treatment for warts. However, the treatment outcome of using cryotherapy as compared with topical salicylic acid is significant, and higher morbidity discourages the use of cryotherapy [5].

The current primary laser that is used for warts is carbon dioxide (CO_2) laser, followed by pulsed dye laser and Erbium: YAG laser. CO_2 laser has been used for recalcitrant warts, with remission costs starting from 50 to 100%, as stated in only some studies [5].

Dermoscopy is a noninvasive diagnostic approach that allows the visualization of morphologic features that are not visible to the bare eye, as a result representing a link between macroscopic scientific dermatology and microscopic dermatopathology [6]. Besides its relevance for evaluating pigmented structures, dermoscopy allows the recognition of vascular structures and different diffused features that generally are less visible to the bare eye [7].

The stated dermoscopic features of common warts include a frogspawn sample, mosaic sample, and dotted, linear, globular, or coiled vessels [8]. The mosaic pattern consists of enormously flattened, rounded structures of comparable

length, comparable to a jigsaw puzzle. Frogspawn sample includes densely packed papillae, each containing a red dot or loop, surrounded by a whitish halo [9].

Vascular structures are visible dermoscopically in commonplace warts as purple or black dotted, linear, globular, and coiled vessels. Hemorrhages are viable additional features, with black dots similar to thrombosed vessels. Hairpin vessels were generally seen in nonwart lesions.

Patients and methods (IRB17100050)

Inclusion criteria

Patients complaining of common warts older than 10 years and patients who stopped topical treatment in the preceding month were included after taking their concent.

Exclusion criteria

Patients less than 10 years of age, patients on other lines of treatment for common warts, pregnant and lactating women, presence of secondary bacterial infection, and noncooperative patients were excluded.

A total of 60 patients who fulfilled the aforementioned criteria were enrolled in the study after informed oral consent. Each patient was subjected to the following: personal history such as name, age, sex, occupation, residence, and marital status; disease history such as onset, course, duration, and previous treatment; history of previous treatment; and family history of warts.

A general clinical examination was carried out to detect any associated clinical systemic diseases.

The dermatological examination was carried out to determine the number, size, and size of warts, which were recorded in millimeters using a ruler in every visit, and the detection of the presence of inflammation at the site of the lesion.

Group A patients were treated by CO_2 laser. After routine sterilization and local anesthetic application, the lesions and a 2-mm surrounding margin of normal tissue were evaporated with a CO_2 laser. Each session consisted of one to two passes of laser light using a CO_2 laser unit, with a power of 15–25 W, according to the depth of the lesion, estimated on physical examination.

Group B: cryotherapy was performed by the same physician with a liquid nitrogen spray with a temperature of – 196°C and was applied with a spray gun. Patients were treated by two freeze-thaw cycles every 15 s with an interval of 5 s.

Postprocedure care for all patients in this study

Topical, systemic, and analgesic anti-inflammatory were prescribed. Patients were asked to come back every 3 weeks and 3 weeks after the third session to evaluate the therapeutic response of the two lines of therapy (number and size of warts) as well as the development of any complications.

Photographs of the lesions were taken at the time of the enrollment and every session and 3 weeks after the third session. All photographs were taken with Lumix digital camera (DMC–FH2) 14 megapixels.

The dermoscopic examination was done before treatment and 3 weeks after the third session for both treatment groups of warts using Dermlite DL4 (Fig. 1). Photographs were taken using a digital camera attached by an adaptor to the dermoscopy at the baseline and 3 weeks after the third session.

Criteria for dermoscopic evaluation were based on that mentioned in the literature. Dermoscopic features of common warts include frogspawn pattern, mosaic pattern, exophytic keratotic projection, knob, daisy flower, and nonspecific patterns. The vascular structures were classified as dotted, linear, hairpin, and coiled vessels [10].

In every visit, lesions were assessed for the number of the lesion, the size of the lesion, and complications like erythema, scar, hyperpigmentation, or hypopigmentation.

$$\text{Percentage reducition} = \frac{\text{Size before treatment - Size after treatment}}{\text{Size before treatment}} \times 100$$

A dermoscopic examination that was performed before and after the treatment of warts helped in the assessment of the cure of warts regarding the residual dermoscopic features, for example, red dots.

Dermoscopic evaluation of warts was done in every visit, as complete cure (total clearance of warts, with no evidence of residual warts), partial improvement (improvement in the size of warts, but without complete eradication

Figure 1

Dermlite IV, DL; 3 Gen.

of warts), and no improvement (no reduction in size or worsened with treatment) [11].

The statistical analysis was performed with the statistical package for the social science (SPSS), version 22.0 software, IBM, Assuit, Egypt. Data were presented as a number, percentage, mean, median, and SD. The χ^2 test and Fisher exact test were used to compare qualitative variables. Sensitivity, specificity, and positive and negative predictive values of dermoscopy were calculated. For all data, the *P* value was considered significant if less than 0.05.

Results

The age of the studied patients ranged from 16 to 41 years. Of the patients studied, 32 (53.3%) were males and 28 (46.7%) were females (Fig. 2 and Table 1).

Clinical characteristics of the patients in both groups are shown in Table 2.

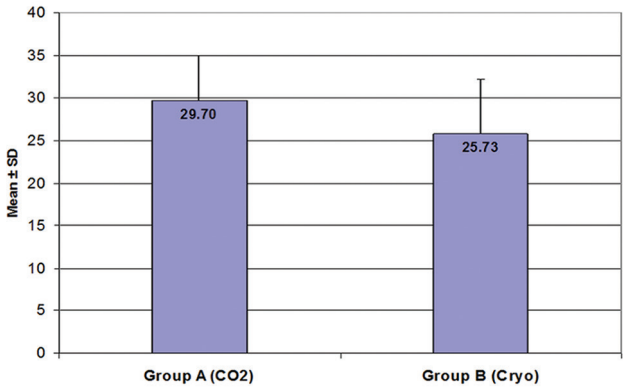
Among 52 patients, the most common sites of warts were the hands in both groups, followed by the face, legs, scalp, and foot, whereas the least affected sites were the arms, elbows, and neck (Table 3).

A significant reduction in the number of lesions was observed more in group A in comparison with group B at the third visit ($P = 0.007$) (Table 4).

The percent reduction of the number of warts in group A was significantly higher than that in group B (83.33 ± 35.36 vs. 65.34 ± 44.26, $P = 0.074$) (Table 5).

Regarding the size of treated warts, a decrease in the size of treated lesions was observed in both groups at different visits. A marked decrease in the size of treated warts at fourth visit was observed in group A (Table 6).

Figure 2



Age of patients.

The percent reduction in size of warts in group A was insignificantly higher than that in group B (87.44 ± 25.33 vs. 84.75 ± 28.65) (Tables 7 and 8).

Discussion

In this study, the efficacy of CO_2 laser and cryotherapy in the treatment of common warts was compared.

A total of 52 patients clinically recognized with viral common warts were enrolled and finished the study for

Table 1 Personal data of the studied groups

Personal data	Group A (CO_2 laser) [*n* (%)] *N*=25	Group B (cryotherapy) [*n* (%)] *N*=27	*P*
Sex			
Male	13 (52)	14 (51.9)	1.000
Female	12 (48)	13 (48.1)	
Age (years)			
Mean±SD	29.70±5.23	25.73±6.46	0.011*
Range	20.0-39.0	16.0-41.0	
Occupation			
Housewife	8 (26.7)	3 (10.0)	0.179
Employee	1 (3.3)	4 (13.3)	
Unskilled worker	7 (23.3)	5 (16.7)	
Student	14 (46.7)	18 (60.0)	
Residence			
Rural	21 (70.0)	17 (56.7)	0.284
Urban	9 (30.0)	13 (43.3)	

*Statistically significant. CO_2, carbon dioxide.

Table 2 Clinical data of the studied groups

	Group A (CO_2 laser) *N*=25	Group B (cryotherapy) *N*=27	*P*
Wart duration (months)			
Mean±SD	8.00±7.19	13.10±13.47	0.295
Median (range)	5.0 (1.0-30.0)	11.0 (1.0-48.0)	
Number of warts			
Mean±SD	1.73±1.41	2.13±1.72	0.272
Median (range)	1 (1-7)	1 (1-7)	
Size of warts (cm)			
Mean±SD	0.25±0.29	0.31±1.17	0.011*
Median (range)	0.12 (0.01-1.00)	0.09 (0.01-9.00)	

*Statistically significant. CO_2, carbon dioxide.

Table 3 Distribution of warts among the studied groups

Site of warts	Group A (CO_2 laser) *N*=25 [*n* (%)]	Group B (cryotherapy) *N*=27 [*n* (%)]	*P*
Hand	16 (53.3)	19 (63.3)	0.432
Face	4 (13.3)	2 (6.7)	0.671
Leg	2 (13.3)	4 (3.3)	0.353
Scalp	4 (6.7)	1 (13.3)	0.671
Foot	1 (3.3)	3 (10.0)	0.612
Arm	1 (3.3)	1 (3.3)	1.000
Elbow	1 (3.3)	0	1.000
Neck	1 (3.3)	0	1.000

CO_2, carbon dioxide.

Table 4 Comparison between the two studied groups as regards the number of warts before and after treatment

Number of warts	Group A (CO_2 laser) Mean±SD	Group B (cryotherapy) Mean±SD	*P*
First visit			
Mean±SD	1.73±1.41	2.13±1.72	0.272
Median (range)	1 (1-7)	1 (1-7)	
Second visit			
Mean±SD	1.41±1.65	1.93±1.62	0.091
Median (range)	1 (0-7)	1 (0-7)	
Third visit			
Mean±SD	0.68±1.31	1.56±1.76	0.007*
Median (range)	0 (0-5)	1 (0-6)	
Fourth visit			
Mean±SD	0.56±1.33	0.81±1.36	0.125
Median (range)	0 (0-5)	0 (0-5)	

*Statistically significant. CO_2, carbon dioxide. *P*: comparison between group A and group B.

Table 5 Percent of change in the number of warts among the two studied groups

Percent of change in the number of warts	Group A (CO_2 laser)	Group B (cryotherapy)	*P*
Mean±SD	83.33±35.36	65.34±44.26	0.074
Median (range)	100.0 (0.0-100.0)	100.0 (0.0-100.0)	

CO_2, carbon dioxide.

Table 6 Comparison between the two studied groups as regard the size of warts before and after treatment

Size of warts	Group A (CO_2 laser)	Group B (cryotherapy)	*P*
First visit			
Mean±SD	0.25±0.29	0.31±1.17	0.011*
Median (range)	0.12 (0.01-1.00)	0.09 (0.01-9.00)	
Second visit			
Mean±SD	0.15±0.23	0.21±1.16	0.125
Median (range)	0.06 (0.00-0.90)	0.04 (0.00-9.00)	
Third visit			
Mean±SD	0.05±0.11	0.13±0.77	0.458
Median (range)	0.00 (0.00-0.56)	0.02 (0.00-6.00)	
Fourth visit			
Mean±SD	0.04±0.10	0.11±0.77	0.605
Median (range)	0.00 (0.00-0.49)	0.00 (0.00-6.00)	

*Statistically significant. CO_2, carbon dioxide. *P*: CO_2 laser versus cryotherapy.

assessment of two different treatment protocols. Patients were recruited from the Outpatient clinics of Assuit College Hospitals and Luxor fashionable sanatorium, Egypt, from February 2018 to August 2019.

A total of 25 patients were treated with CO_2 laser and 27 patients were treated with cryotherapy. The quantity and length of treatment of warts was decided before and after the treatment by way of scientific and dermoscopic examination.

There are numerous studies on the efficacy of cryotherapy for the treatment of viral warts, with unfavorable consequences attributed to this method, although no data have compared this approach with CO_2 laser for the treatment of warts.

In our study, the age of patients ranged from 16 to 40 years (27 males and 25 females). The most common sites of treatment of warts were the palms, face, and legs, and the least affected sites were elbow and neck. Evaluation of the anatomic distribution between the two groups discovered no widespread distinction. Similar effects regarding the anatomic distribution of warts have been stated by Maryam and colleagues.

In the present study, we carried out the two-cycle freeze-and-thaw method with the use of a spray gun for treatment of warts with an interval of 3 weeks for every session up to a few sessions.

For choosing the best interval, Boroujeni and Handjani did not find any distinction between 1, 2, and 3-week periods. It seems that the number of sessions decides the efficacy of treatment of warts, not the time interval among each consultation. In some research studies, two cycles of freeze and thaw showed a better result than the best one cycle in plantar warts, whereas this was no longer the case for warts on different parts of the body, including the fingers [12].

To our knowledge, there is no study comparing CO_2 laser with cryotherapy in the treatment of common warts, although comparisons of other lasers have been undertaken.

In a study by Maryam and colleagues, pulsed dye laser did not show superiority in the remission rate when compared with cryotherapy in the treatment of not-unusual warts. However, patients who underwent pulsed dye laser treatment completed remission faster.

In the present study, after three sessions of treatment with CO_2 and cryotherapy, the percent reductions in both the number and size of warts were higher among patients treated with CO_2 laser than those treated with cryotherapy (83.33 ± 35.36 vs. 65.34 ± 44.26, $P = 0.074$, and 87.44 ± 25.33 vs. 84.75 ± 28.65, $P = 0.514$, respectively).

Among our patients, the whole treatment of common warts treated with three periods of cryotherapy had a treatment rate of 60%. A study by Ahmed and colleagues, mentioned a 44 and 47% cure rate with cryotherapy and the use of the spray gun and a cotton swab, respectively. This distinction between our effects and the aforementioned article can be due to the difference in sickness chronicity and compliance with follow-up.

Boroujeni and Handjani (2018) reported that the number of sessions to treat plantar warts was much

Table 7 Percent of size reduction of treated warts in the two studied groups

Percent of size reduction	Group A (CO_2)	Group B (cryotherapy)	*P*
Mean±SD	87.44±25.33	84.75±28.65	0.514
Median (range)	100.0 (0.0-100.0)	100.0 (0.0-100.0)	

CO_2, carbon dioxide.

Table 8 Dermoscopic evaluation of treated warts in the two studied groups

Improvement	Group A (CO_2 laser) [*n* (%)]	Group B (cryotherapy) [*n* (%)]	*P*
Complete improvement	20 (80.0)	16 (59.3)	0.105
Partial improvement	5 (20.0)	11 (40.7)	

CO_2, carbon dioxide.

less with the use of CO_2 laser than cryotherapy. They concluded that CO_2 laser is superior to cryotherapy in efficacy. Comparable effects were mentioned in our study, where CO_2 laser group patients confirmed better outcomes regarding the scale and number of warts than the cryotherapy group.

Our study is the first study to used dermoscopy, which is a completely effective device in the assessment of the effects of cryotherapy and CO_2 laser in the treatment of common warts. With the application of dermoscopy, the scientific analysis of warts showed increased sensitivity and specificity. Moreover, we were able to decide more correctly whether or not further sessions were needed with its use before each treatment session. Some lesions appeared healed to the naked eye, but dermoscopy found minimal papilliform surfaces, which necessitated additional treatment sessions for the entire plan. This is in agreement with Abdel-Azim *et al*. [13].

In line with Li *et al*. [10], the dermoscopic functions of not-unusual warts were mosaic, exophytic keratotic projection, knob, daisy flower, and nonparticular styles, and the vascular systems had been inside the form of a dotted, linear, hairpin, and coiled vessels. According to Aqil *et al*. [14], the dermoscopic aspects observed in common warts have been the presence of multiple dense papillae, centered by red loops surrounded by whitish halos and irregularly distributed blackheads giving a so-called frogspawn look; linear and irregular hairpin vessels surrounded by a whitish halo and punctate hemorrhages were also objectified.

This is in agreement with our present study. These dermoscopic features of warts decreased after treatment with CO_2 laser and cryotherapy, and this is concomitant with the clinical cure of warts.

Conclusion

Viral warts are common pores and skin sicknesses that are commonly managed using many treatment modalities. We compared cryotherapy and CO_2 laser as primary treatment options for warts and used dermoscopy to assess the results. We observed that each strategy was effective in the treatment of warts, with minimum headaches, and that CO_2 laser is superior to cryotherapy in the treatment of commonplace warts. The most common dermoscopic feature of not-unusual warts is frogspawn, a mosaic sample with hemorrhagic blood vessels that may be pink or black thrombosed dotted vessels. Dermoscopy advanced our diagnostic and assessment accuracy of studied cases of commonplace warts. It helped us in determination of the time of cure in warts, in which session we got no dermoscopic criteria of warts, this means cure of wart.

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Conflicts of interest
There are no conflicts of interest.

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