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ORIGINAL ARTICLE

Comparison of long-pulsed Nd: YAG laser with cryotherapy in treatment of acral warts

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Abstract

Acral warts are considered as prevalent reasons for dermatologic consultations and remain an important continuing challenge until now because there is no consensus about optimal therapeutic modality. This study investigated the efficacy of long-pulsed Nd: YAG laser therapy and cryotherapy in treatment of acral warts. Patients who underwent treatment with cryotherapy or long-pulsed Nd: YAG laser therapy for symmetrical and bilateral warts on the extremities (hand and foot) that is confirmed by an expert dermatologist from May 2016 until March 2018 were assessed for enrollment in our study. Laser and cryotherapy sessions were applied every 2 weeks for a maximum of six sessions. Patients followed up and evaluated 3 months after the last treatment. Data were analyzed by SPSS (v.21. IBM Inc. IL). The P value less than 0.05 was considered significant. From 60 enrolled patients, 134 lesions were treated using cryotherapy and 114 other lesions treated with laser beam. Thirty-four males (average age 26.85 ± 7.528 years) and 26 females (average age 26.73 ± 5.640 years) participated. Finally, it was a significant reduction in both lesion width ($P = 0.000$) and length ($P = 0.000$) after the sessions of cryotherapy. The width and length of lesions is reduced significantly after each session of laser therapy similarly ($P = 0.000$). Cryotherapy and long-pulsed Nd: YAG laser are effective on the reduction of both width and length of lesions. Clinically, the methods are not different in their ultimate effects.

Keywords Acral wart · Long pulsed Nd: YAG laser · Cryotherapy

Introduction

Viral warts are among the most prevalent benign cutaneous lesions that are caused by more than 100 serotypes of human papillomavirus (HPV). They can stimulate proliferation of squamous epithelial cells [1]. Warts can appear in different places on the body including limbs, genital area, oral mucosa, and larynx [1].

Although the warts have been seen at any age and both genders, there is a high prevalence of these skin lesions at the age of 12 to 20 years [2]. Warts have different types, of which about 70% of cases are the typical type and verruca plantaris [2, 3]. The incubation period for clinical warts is between a few weeks to more than 1 year [2, 3]. Transmission pathways of viruses related to warts are direct and indirect [2, 3]. Defects of immune system, direct contacts of hand and foot to infected areas such as walking barefoot in public locker rooms and common bathing areas can be identified as the common risk factors of acral warts [4]. Warts can lead to cosmetic and psychological problems and also pain, discomfort, and inflammation, if in under pressure areas [2–4].

Diagnosis of the symptomatic warts is based on a clinical examination and in suspicious cases; it is possible to identify the components of the viruses by electron microscope, polymerase chain reaction, and DNA hybridization [3–5]. Due to the non-presence of specific antiviral treatments for HPV, the current main therapeutic options for warts include the destruction of visible lesions by physical or chemical methods and immunomodulator therapies [6–8]. Ablative therapies using cryotherapy, electro-cutter, and lasers are able to cure lesions with a small amount of local and systemic complications and minimal pain during a short time [6–8]. Some studies reported that long pulsed neodymium-doped yttrium aluminum garnet (Nd: YAG) laser therapy can treat acral warts and improve clinical outcomes clearly [9, 10]. There are little evidences about the comparison of long-pulsed Nd: YAG laser therapy and cryotherapy in the wart clearance. This study was

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Table 1 The distribution of limbs in cryotherapy and laser therapy groups were proper and insignificant, statistically

Limb		Type		*P* value
		Cryotherapy	Laser therapy	
Hand	Right	28 (51.9%)	26 (48.1%)	0.727
	Left	41 (48.8%)	43 (51.2%)	
Foot	Right	39 (65.0%)	21 (35.0%)	
	Left	26 (52.0%)	24 (48.0%)	
Total	Right	67 (58.8%)	47 (41.2%)	
	Left	67 (50.0%)	67 (50.0%)	

designed to compare long-pulsed Nd: YAG laser therapy and cryotherapy in terms of clearance rate, and recurrence of warts and complications in cases with acral warts.

Materials and methods

Patients selection

This clinical trial was approved at Review Board of *Shahid Beheshti University of Medical Sciences (SBUM)*, Tehran, Iran. Cases with symmetrical and bilateral warts on the extremities (hand and foot) that were confirmed by an expert dermatologist from May 2016 until March 2018 were assessed for enrollment in our study.

After taking the informed consent from participants, they underwent treatment with cryotherapy or long-pulsed Nd: YAG laser therapy.

Exclusion criteria

Patients with incomplete medical records were removed. Moreover, patients with any history of immunosuppressive conditions such as congenital immunodeficiency diseases, malignancies, diabetes mellitus, alcohol consumption, the use of immunosuppressive agents and drugs during the past 4 weeks, the use of topical antiviral drugs in the past 2 weeks, and also current pregnancy and lactation were delisted.

The study protocol and statistical analysis

Patients with symmetrical and bilateral acral warts enrolled in this clinical trial. (Fig. 1a). Pretreatment information including the demographic data of the patients and the initial characteristics of the warts such as the location, size and the duration of lesions existence, and the post-treatment data such as the response rate to each therapeutic intervention were evaluated and recorded in the questionnaire for each patient during the study period. At first, lesions on each side of the patient body were assessed and recorded. Then one side selected for laser therapy and another side for cryotherapy, randomly.

After disinfection and application of topical anesthetic upon warts, we utilized a 1064-nm long-pulsed Nd: YAG laser system (model: Hyperion, rating 230 V, 50 Hz, 3600 VA). Also we applied air cooling system (Dosis M&M, model: KOOLIO, power AC22 0 V, 50 Hz, 1300VA) coupled with hand piece of the laser. Before each pulse, we allowed the skin for 10–15 s to become some degree cooler to reduce the pain and tissue damage. After that the laser was fired.

Specific laser parameters we chose were as follows: spot size 5 mm; pulse duration 20 msec; and fluence 200 J/cm2.

Table 2 Comparison of mean ± SD of lesion's length and width between hand and foot treated with laser modality; these data belong to 69 lesions on hand and 45 lesions on foot

	Intervention phase	Limb	Mean ± SD	*P* value*
Length of lesion	Before laser therapy	Hand	6.72 ± 6.27	0.000
		Foot	13.57 ± 8.38	
	After first laser therapy	Hand	3.73 ± 5.61	0.000
		Foot	8.81 ± 6.56	
	After second laser therapy	Hand	1.34 ± 3.31	0.407
		Foot	1.51 ± 3.13	
	After third laser therapy	Hand	0.95 ± 2.68	0.552
		Foot	1.26 ± 2.93	
Width of lesion	Before laser therapy	Hand	6.59 ± 6.28	0.000
		Foot	13.62 ± 8.34	
	After first laser therapy	Hand	3.73 ± 5.62	0.000
		Foot	8.83 ± 6.55	
	After second laser therapy	Hand	1.34 ± 3.31	0.407
		Foot	1.51 ± 3.13	
	After third laser therapy	Hand	0.97 ± 2.70	0.549
		Foot	1.28 ± 2.95	

**P* values calculated using Mann–Whitney test in the case of abnormal distribution

Table 3 Comparison of mean ± SD of lesion's length and width of hand and foot after cryotherapy method; these data belong to 69 lesions on hand and 65 lesions on foot

	Intervention phase	Limb	Mean ± SD	*P* value*
Length of lesion	Before cryotherapy	Hand Foot	6.53 ± 4.83 14.56 ± 11.28	0.000
	After first cryotherapy	Hand Foot	3.07 ± 3.69 9.92 ± 9.45	0.000
	After second cryotherapy	Hand Foot	0.98 ± 2.64 3.20 ± 7.30	0.003
	After third cryotherapy	Hand Foot	0.40 ± 2.00 1.52 ± 3.91	0.008
Width of lesion	Before cryotherapy	Hand Foot	6.57 ± 4.82 14.58 ± 11.26	0.000
	After first cryotherapy	Hand Foot	3.13 ± 3.69 9.83 ± 9.46	0.000
	After second cryotherapy	Hand Foot	0.98 ± 2.64 3.16 ± 7.30	0.004
	After third cryotherapy	Hand Foot	0.40 ± 2.00 1.52 ± 3.91	0.008

**P* values calculated using Mann–Whitney test in the case of abnormal distribution

Three stacked pulses were applied to each wart until the lesion burnt out, as the end point (Fig. 1c). If the lesion was larger than 5 mm, then stacked pulses repeated to cover the entire lesion surface. There were no immediate side effects except a tolerable pain, and a mild temporary erythema resolving after some hours.

In cryotherapy side, warts were placed under cryopreservation with liquid nitrogen at a temperature of − 196 °C in open spray mode until freezing of lesion totally with a 2-mm margin of surrounding tissue. The freeze time was about 20–40 s depending on the lesion size and subsequent freeze-thaw cycle was done for the larger ones. The end point for this method was forming the halo 2–3-mm margin. (Fig. 1b).

In this method patients felt mild discomfort and pain similarly.

Patients had assessed with their doctor by a phone call to report any possible side effects.

Fig. 1 Bilateral palmar warts in a 20-year-old woman before treatment (**a**), also end point of each session for cryotherapy (**b**) and laser therapy (**c**) were shown

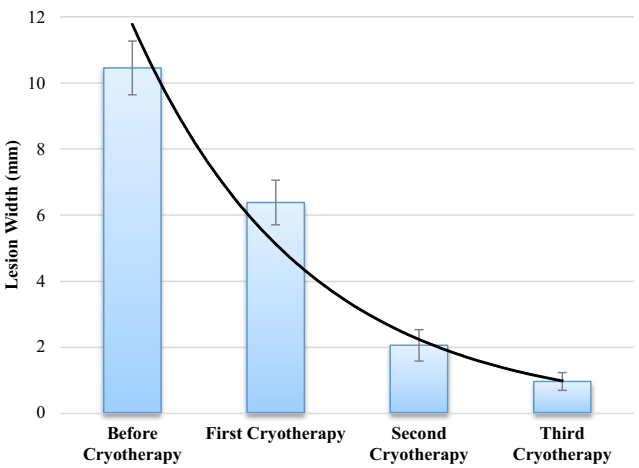

Fig. 2 Comparison of mean ± SD of lesion's width changes by the sessions of cryotherapy; the width of lesion is reduced significantly after each session of cryotherapy ($P = 0.000$)

Healing time for both methods were about 7–10 days.

Laser and cryotherapy sessions were applied every 2 weeks until clearance of the lesions or for maximum of three sessions. Patients were followed up and evaluated in each session and 3 months after the last treatment.

Statistical analysis

The analysis of the parametric data was expressed based on the mean and standard deviation. Qualitative and classified data were presented based on the number and percentage and the univariate analysis on quantitative and qualitative data using Student's *t* test and chi-square test. Data were analyzed by SPSS (v.21. IBM Inc. IL). The *P* value less than 0.05 was considered significant.

Results

In total, 60 patients with 248 lesions on hands and foots were evaluated for in this clinical trial. Patients included 34 males and 26 females with the average age of 26.85 ± 7.528 for men and 26.73 ± 5.640 for women, respectively (*P* value 0.945). The youngest patient was 14 years old and the oldest one was 44 years old. In total, 134 lesions were treated using cryotherapy and 114 other lesions treated with laser beam. There were 21 males and 17 females on cryotherapy; further 13 males and 9 females also treated with laser. The distribution of samples for each limb was not significantly different from others (Table 1).

Lesion's length and width were reduced meaningfully during therapeutic sessions with both modalities

In most cases, the lesions on the feet were significantly larger than the lesions on the hands in a way that at the initial treatment sessions, there was a significant difference among the size of lesions (*P* value 0.000). Notably, the size of lesions was reduced significantly after the first laser therapy session, and after the second and third sessions there were no significant difference between lesions sizes on the hand or foot (*P* value > 0.05). (Table 2).

Similar to laser therapy, the lesions on cryotherapy side were larger at feet initially. But, the lesion's size differences between hand and foot were significant even at the last therapeutic sessions (*P* value 0.008) (Table 3).

The net effect of laser therapy and cryotherapy on the lesion's length and width

In total, there was a significant reduction in both lesion width (Fig. 2; $P = 0.000$) and length (Fig. 3; $P = 0.000$) by the means of cryotherapy compared to pre-treatment lesions. Same results were obtained by laser therapy (Figs. 4 and 5).

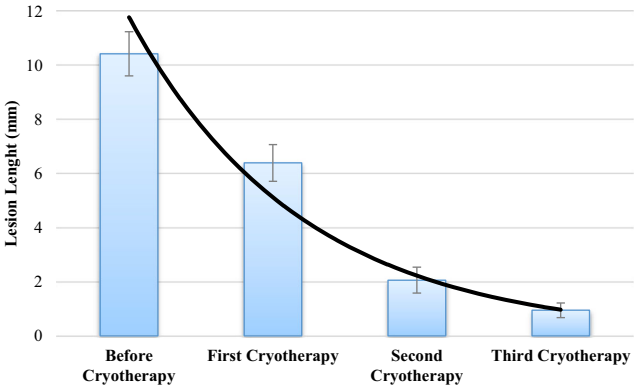

Fig. 3 Comparison of mean ± SD of lesion's length changes by the sessions of cryotherapy; the length of lesion is reduced significantly after each session of cryotherapy ($P = 0.000$)

There was a significant difference between first session of laser therapy and cryotherapy in both lesion's width and length (Fig. 8). But after second and third sessions of both treatments, no significant difference was observed.

The response to the therapy is sex-independent

The sex of patients was not a determinative effector on the patient's response to the therapy. Both sexes had similar lesion larger width and length before starting therapy and changes after each sessions were similar (Figs. 6 and 7; $P = 0.986$ for width changes and $P = 0.991$ for length changes).

There were no significant side effects (necrosis, infection, hematoma, etc.) with any modality in follow-ups. Only there were mild temporary erythema and pain after both modalities. Of note, patients reported slightly more pain by laser which was not significant. Cryotherapy was

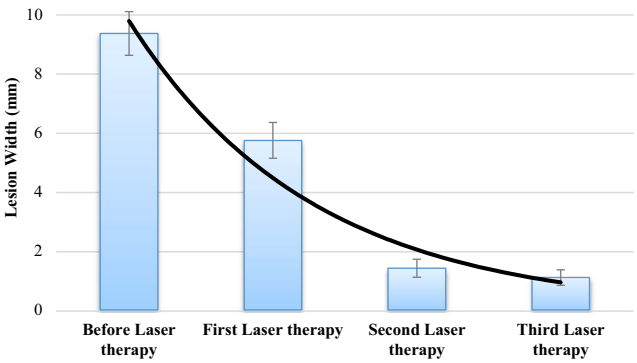

Fig. 4 Comparison of mean ± SD of lesion's width changes by the sessions of laser therapy; the width of lesion is reduced significantly after each session of laser therapy ($P = 0.000$)

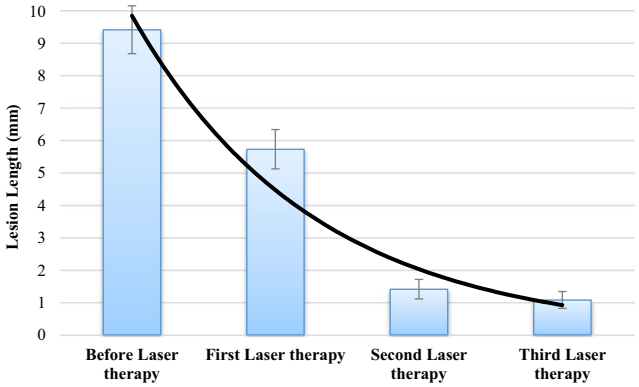

Fig. 5 Comparison of mean ± SD of lesion's length changes by the sessions of laser therapy; the length of lesion is reduced significantly after each session of laser therapy ($P = 0.000$)

associated with bulla formation in some larger lesions but this was not observed after laser therapy (Figs. 8)

Discussion

Acral warts can be considered as prevalent reasons for dermatologic consultations and remain an important continuing challenge until now because there is no consensus about optimal therapeutic modality [11]. The majority of acral warts will disappear without certain treatment spontaneously. Infectivity, discomfort, cosmetic impairment, and avoidance from doing sports and physical activity in daily life on account of these warts are the most prevalent reasons for beginning of treatment [12]. There are several therapeutic options for treatment of warts such as topical salicylic acid, bleomycin, cantharidin, dinitrochlorobenzene, 5-flurouracil, laser therapy, and cryotherapy. It is obvious that multiple factors including costs of treatment, complications of therapy especially pain, rate of success, easy to use, clinical benefits and adverse effects, and compliance play valuable roles for selecting the most appropriate treatment [13, 14].

The present trial investigated the efficacy of long-pulsed Nd: YAG laser therapy and cryotherapy in cases, who suffered from acral warts.

According to our findings, long-pulsed Nd: YAG laser therapy can reduce width and length of lesions compared to prior of treatment. In a study conducted by El-Mohamady Ael-S and colleagues, it was reported that long-pulsed Nd: YAG and pulsed dye laser therapies can be considered as effective therapeutic choices for plantar warts [15]. Their findings were same as our results and approved that long-pulsed Nd: YAG laser therapy have appropriate ability in the treatment of acral warts [15]. Although they expressed that long-pulsed Nd: YAG laser has more pain and clinical complications compared to pulsed dye laser [15].

Regarding the findings, cryotherapy can decrease width and length of lesions strongly compared to pretreatment. Cockayne and colleagues reported that cryotherapy and salicylic acid were equally effective for clearance of acral warts [16]. On the other hand, El-Tonsy et al. expressed that there is human papillomavirus deoxyribonucleic acid in all 100% and also 96% of untreated and cryotreated warts respectively [17]. They explained that human papillomavirus can be more vulnerable to laser therapy comparing to cryotherapy and suggested that laser therapy may be superior to cryotherapy [17]. However, our study showed that the net effect of both therapeutic methods is reducing the lesion's size and also these treatments at the end of the treatment do not have significant difference in terms of clinical improvement of the warts.

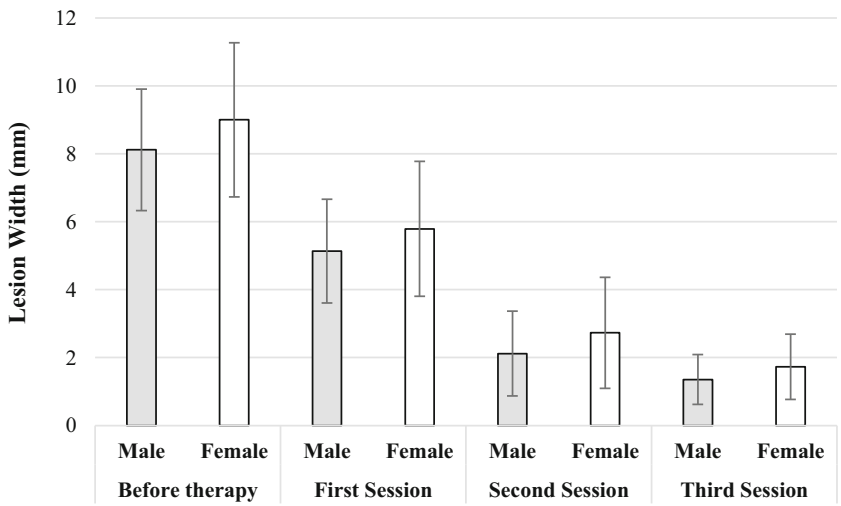

Fig. 6 Comparison of mean ± SD lesion's width changes between male and female patients; there was no significant difference between male and female category and the sex was not determinative variable ($P = 0.986$)

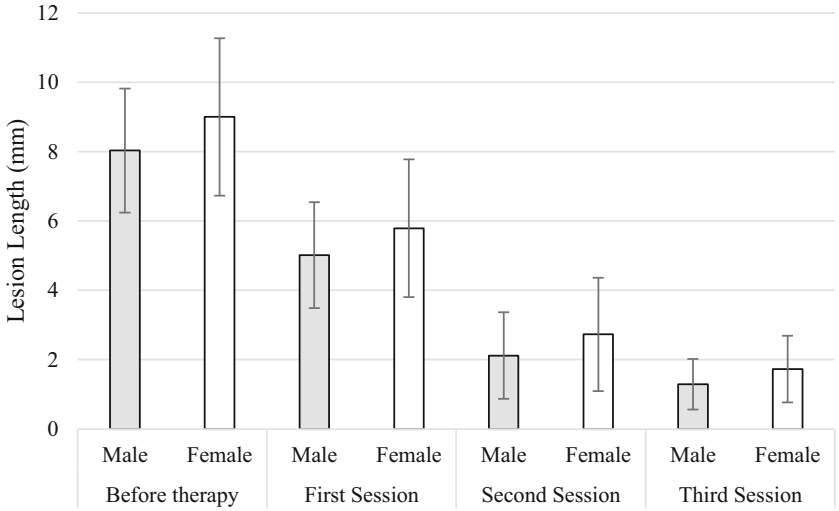

Fig. 7 Comparison of mean ± SD lesion's length changes between male and female patients; there was no significant difference between male and female category and the sex was not determinative variable ($P = 0.991$)

Of note, the mean size of lesions on the foot was more than warts on the hands. However, laser therapy could reduce lesion sizes in a way that at the last treatment session, there was no significant difference between the size of lesions on the hand and foot. On the other hand, the difference between hand and foot lesions was significant until the last session of cryotherapy.

Both sexes had similar lesion width and length before starting therapy and similar changes after therapy at first, second, or third sessions. The El-Mohamady Ael-S et al. study also reported that there was no considerable correlation between size of the warts and any of clinical data (e.g., age, sex, and sites of lesions) [15].

Based on findings, we can conclude that the response to the therapeutic methods was not dependent on the sex, limb side, and the type of limb.

Both methods were effective on the reduction of both width and length of lesions and there was insignificant result between them; however, clinically, the methods are not different in their ultimate effects.

Conclusion

As noted above, both long-pulsed Nd: Yag laser therapy and cryotherapy are effective modalities for treatment of acral warts. The ultimate effect of both modalities was similar but patients experience slightly more pain by laser therapy. Finally of note, this study emphasizes therapeutic effects of both, with no superiority. Although more study need to clarify the therapeutic approaches.

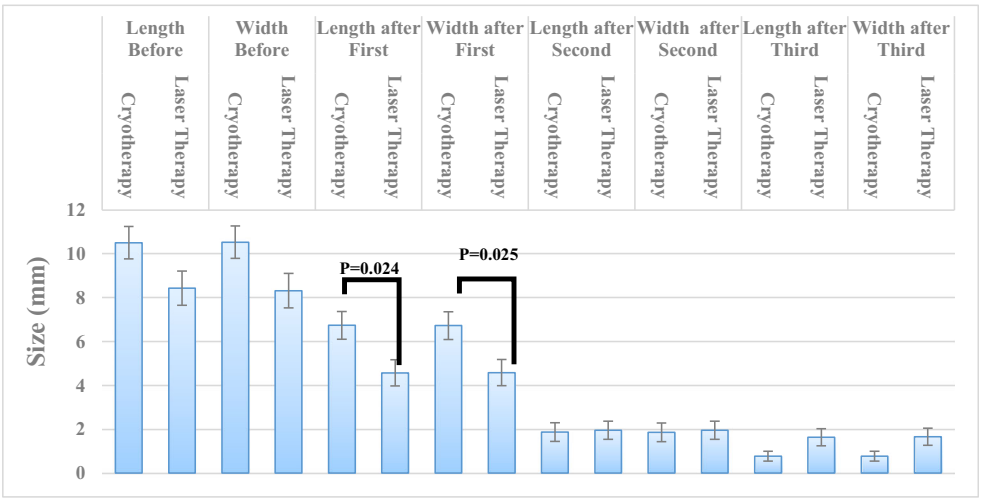

Fig. 8 Comparison of lesion's size (length and width) in each step and using of each therapeutic approach. Only, there was a significant difference between first session of laser therapy and cryotherapy in both lesion's width and length (*P* values are shown on the columns). Data are mean ± SD

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

IRIB approval status Reviewed and approved by Shahid Beheshti University of Medical Sciences IRIB; approval #IRCT 2016050127707 N1.

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