

# Comparing Pulsed-dye Laser with Cryotherapy in the Treatment of Common Warts

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**Introduction:** No modality has been identified as the treatment of choice for treating common warts. Cryotherapy and pulsed-dye laser (PDL) are among common modalities for treating these lesions. The aim of this study was to compare pulsed dye laser with cryotherapy in terms of efficacy and complications.

**Material & Methods:** Of a total of 46 patients enrolled in this study, 7 patients withdrew the study, 20 patients underwent cryotherapy and 19 patients underwent PDL. Patients underwent a maximum of 4 therapeutic sessions at 3-week intervals in both groups. They were assessed for the remission rate (complete and partial), side effects and recurrence rate in each session and 1 month after termination of the treatments.

**Results:** At the end of the study complete remission was achieved in 37.8% of patients in cryotherapy group and in 52.3% of patients in PDL group. This difference wasn't statistically significant ( $P=0.229$ ), though after first and second sessions of treatment complete and excellent partial remission occurred more in PDL group with significant difference ( $P=0.007$  and  $P=0.021$ ). Pain and bulla formation occurred statistically higher in cryotherapy group ( $P=0.002$  and  $P=0.001$ ). Other complications were rare in both groups.

**Conclusion:** In terms of efficacy, we couldn't demonstrate the superiority of pulsed-dye laser therapy to cryotherapy in treating common warts. Both methods were safe for long-term complications but PDL was much safer for short-term complications.

**Keywords:** wart, pulsed-dye laser, cryotherapy, efficacy, side effects

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## INTRODUCTION

Viral warts are benign neoplasms of skin and mucosa, involve nearly 7-10% of population and cause a large burden of time and cost on dermatologic centers<sup>(1)</sup>. Despite their silent course and healing spontaneously, long time persistency and cosmetic problems owing to warts are not acceptable by patients<sup>(1,2)</sup>. Several approaches have been provided

for the treatment of warts including cryotherapy, topically applied acids, electrosurgery, CO<sub>2</sub> and Pulsed-dye laser, cytotoxic agents, allergic contact agents and recently introduced imiquimod<sup>(3-11)</sup>. Cryotherapy with liquid nitrogen, as a conventional therapy, is used currently among dermatologists with an efficacy reported between 45%-75% and occasional complications including pain, blistering and hypopigmentation.<sup>(3,9,12-14)</sup> Pulsed-dye laser in

a wavelength of 585nm or 595nm acts selectively on dilated vessels of derm (in the basis of the wart) and coagulate them according to "selective photothermolysis theory" and causes damage of main feeding vessels of the wart and subsequently eradicates it<sup>(15)</sup>. Other possible mechanism of PDL may be induction of immune system response<sup>(16)</sup>. PDL results in less pain and scar comparing to CO<sub>2</sub> laser and cryotherapy and seems a method worth to be evaluated more<sup>(9,17,18)</sup>. In this study we aimed to compare these two methods in terms of efficacy and complications in a prospective randomized clinical trial.

## MATERIAL & METHODS

A randomized controlled clinical trial was performed on a population of patients with a diagnosis of common warts in Department of Dermatology of Razi hospital in Tehran, between February 2007 and February 2008. Patients above 60 years old, with immunodeficiency, with a history of haemostatic disturbances or a history of previous interventions within last month were excluded. Genital, plantar, filliform or plane warts were also excluded. After explaining the disorder, its therapeutic approaches and details of treatments, inform consents were obtained from patients. Patients' information including age, gender, history of previous treatments of the warts, initial size, anatomic location and duration of the lesions were noted. Patients were divided randomly into two groups, to undergo either cryotherapy or PDL therapy.

liquid Nitrogen cryotherapy was administered by a cotton-tipped applicator on the surface of the warts for two 15-second freeze-thaw cycles in a way that caused a white annular halo, 1-2 mm around every wart.

We employed Candela flash lamp pumped PDL (CPDL) with a wavelength of 585 nm, constant

pulse duration of 1.5 ms, spot size of 7 mm and energy influence of 15 j/cm<sup>2</sup> (DCD was off). Two pulses were received in each location with 1-2 mm overlap and covering 1-2 mm of normal skin just around the wart. Interval duration between sessions was 3 weeks in the both groups. Patients were visited 3 weeks after each session: the size of warts (if not disappeared) was measured through its lengths and the surface. The complications were also recorded. For the residue of the lesions (if existed) the treatment was repeated again. Each patient received at most 4 sessions. Each patient was visited by the same dermatologist (who was blinded to the treatment) 1 month after disappearance of the lesion or a month after 4 sessions of treatment. Patients who lost two sessions of treatment were excluded.

Response to treatment was defined as bellow:

"Complete remission" as the complete clearance of the lesion and return of dermatoglyphic lines, "Excellent partial remission" as a decrease up to 75-99% of the wart size. "Good remission" as a decrease up to 50-75% of the wart size and "Weak remission" as a decrease under 50% in the wart size.

The data was analyzed by chi-square via Excell 2007.

## RESULTS

A total number of 39 patients enrolled in the study (21 male and 18 female). Of these, 20 patients underwent cryotherapy and the 19 else underwent laser therapy. In the cryotherapy group 9 patients were male and 11 others were female. The patients' age was between 20 to 60 years with a mean of  $26.2 \pm 14.45$  years and the mean duration of their lesions was 17.7 (3-120) months. In the PDL group 12 patients were male and 7 patients were female. Patients aged between 10 to 46 years with a mean of  $24.42 \pm 11.53$  years and the mean duration of their disease was  $12.9 \pm 10.49$  months. The mean

**Table 1.** Age of patients and lesion duration in PDL and Cryotherapy groups.

Group	min	max	mean	Std. deviation
Cryotherapy				
Age (year)	9.0	60	26.2000	14.50445
Lesion duration (month)	3.0	120	17.7000	25.85811
PDL				
Age	10.0	46	24.4211	11.53408
Lesion duration (month)	2.0	36	12.9474	10.49060

## Comparing PDL with Cryotherapy

age of both groups didn't differ significantly ( $P=0.305$ ). The mean duration of disease didn't differ significantly between two groups (table1).

The total number of treated warts was 82, 37 in cryotherapy group and 45 in PDL group.

The anatomic distribution of warts in each group is reported in table 2.

Except for dorsal aspect of the hands and fingers, comparison of the distribution between 2 groups revealed no significant difference. In cryotherapy group the mean size of warts before treatment was  $19.73 \pm 14.4 \text{ mm}^2$  and in PDL group was  $12.98 \pm 7.89 \text{ mm}^2$ . The mean sizes of warts were significantly different between two groups ( $P=0.0043$ ). The mean size of the lesions and the mean decrease in lesions' size after each session are mentioned in table 3.

During the study (up to 1 month after last therapeutic session), recurrence occurred in 2 lesions (5.4%) in the cryotherapy group and in 3 lesions (6.6%) in PDL group that wasn't significantly different between two groups ( $P=1.000$ ).

*Complications:* Percentage of complications is mentioned in table 4.

## DISCUSSION

Up to date physical treatments of wart, offered in practice, include cryotherapy,  $\text{CO}_2$  laser, PDL laser and surgery. There is a high trend among dermatologists to administer cryotherapy and several investigators have reported a clearance rate ranging 45-75% for this method<sup>(3,9,12-14)</sup>. It acts through induction of death in epidermal cells where

**Table 2.** Mean size of lesions and Mean decrease of size after each session of treatment in PDL and Cryotherapy group

Grop	Cryo therapy		PDL 585nm	
	mean	Std. deviation	Mean	Std.deviation
Diff 2,1 (mm <sup>2</sup> )	5.98	5.93	5.58	4.77
Diff 3,1 (mm <sup>2</sup> )	11.62	9.55	9.11	6.68
Diff 4,1 (mm <sup>2</sup> )	14.70	12.25	10.91	8.07
Diff 5,1 (mm <sup>2</sup> )	15.62	11.10	11.60	8.29
First measure (mm <sup>2</sup> )	19.73	14.41	12.98	7.89
Second measure	13.84	10.99	7.40	6.03
Third measure	8.11	7.28	3.87	3.58
Forth measure	5.03	5.05	2.07	2.57
Fifth measure	4.11	5.56	1.38	2.37

**Table 3.** Complete and partial remission by cryotherapy and PDL after each session of treatment.

	Efficacy				
	Complete remission	Excellent remission	Good remission	Week remission	total
After 1st session of therapy					
CRYO	0 (0%)	0 (0%)	7 (18.9%)	30 (81.1%)	37 (100%)
PDL	3 (6.7%)	4 (8.9%)	12 (26.7%)	26 (57.8%)	45 (100%)
After 2nd session of therapy					
CRYO	3 (8.1%)	4 (10.8%)	20 (54.1%)	10 (27%)	37 (100%)
PDL	11 (24.4%)	9 (20%)	17 (37.8%)	8 (17.8%)	45 (100%)
After 3rd session of therapy					
CRYO	8 (21.6%)	11 (29.7%)	12 (32.4%)	6 (16.2%)	37 (100%)
PDL	18 (40%)	16 (35.6%)	6 (13.3%)	5 (11.1%)	45 (100%)
After 4th session of therapy					
CRYO	14 (37.8%)	10 (27%)	10 (27%)	3 (8.1%)	37 (100%)
PDL	23 (51.1%)	15 (34.1%)	3 (6.8%)	3 (6.8%)	45 (100%)

**Table 4.** Complications of treatment in PDL and Cryotherapy group.

Group	Pain		Bulla		Scar		Hyperpig		Hypopig		Infection		Total
	yes	no	yes	no	yes	no	yes	no	yes	no	yes	no	
Cryotherapy %	70.3%	29.7%	51.4%	48.6%	0%	100%	13.5%	86.5%	2.7%	97.3%	2.7%	97.3%	100%
PDL %	35.6%	64.4%	8.9%	91.1%	0%	100%	4.4%	95.6%	6.7%	93.3%	0%	100%	100%

viral particles have resided. Its clearance rate has been shown to be influenced by aggressivity of the procedure, double versus single freeze and longer freeze-thaw cycles<sup>(1)</sup>. The number of therapeutic sessions is beneficial for better response but not beyond 3 months of therapy<sup>(13,19)</sup>. Different therapeutic intervals at 1, 2 or 3 weeks haven't been shown important<sup>(20)</sup>. K Andrews recommended cryotherapy as excellent especially for hairless regions in patients with fair skin<sup>(21)</sup>. Cryotherapy can be used easily and rapidly with a low risk of infection. Its adverse effects include pain, blistering, hypopigmentation and hair loss of affected region and rarely scar formation<sup>(12)</sup>. In recent decade PDL has become of special concerns in the treatment of warts. According to photothermolysis theory, light in special-wavelengths can selectively be absorbed by hemoglobin. PDL Radiation appears likely to act on dilated vessels of papillary dermis in the basis of the wart employing this theory. Since PDL ablates only vessels of warts and doesn't cause destruction of other skin tissues, complications such as scar, atrophy, bulla formation, infection, post procedure hemorrhage and pain are thought to be rare. Despite minor pain or discomfort, erythema and occasional blistering, other side effects have rarely been reported<sup>(9,17,18,22,23)</sup>. Earlier studies had reported significant efficacy of PDL in the treatment of recalcitrant warts though recent studies didn't agree and considered PDL with moderate efficacy (an efficacy ranging 21-95% among earlier and recent studies)<sup>(9,10,17,18,22-26)</sup>. Though PDL still remains more effective among recalcitrant lesions rather than nonrecalcitrant lesions<sup>(10)</sup>. It is perceived that some factors may take role in creating such discrepancy among prior studies. In a study by Dr Mirshams and Dr Mehrian, comparing two different wavelengths of PDL, 585nm vs 595nm in a controlled trial, no difference was demonstrated in either wavelength, neither in each session of treatment nor at the end of the treatment<sup>(27)</sup>. Complete remission constituted 75% of cases receiving PDL 585nm and 69% of cases receiving PDL 595nm. In that study, distribution of lesions according to initial sizes and anatomic locations was similar between two groups. In Bunny's study the response rate was higher among patients who received treatment at 3-week intervals (75%) rather than patients who received treatment at 4-week intervals (40%)<sup>(3)</sup>. Jacobson et al reached

a complete remission of 68% in recalcitrant warts and a complete remission of 41.7% in new warts (without a history of previous procedures)<sup>(22)</sup>. Robson found a complete response of 76% by PDL among 80 recalcitrant warts and of 51% among 35 nonrecalcitrant warts<sup>(9)</sup>. Passeron et al tried PDL 595 on 19 patients with warts in 3 sessions and found a clearance rate of 64%<sup>(28)</sup>. A review offered by Robson containing prior studies, suggests that number of PDL pulses per location may take a major role in the outcome discrepancies<sup>(9)</sup>.

The only study that had done a comparison between PDL and cryotherapy is provided by Robson et al<sup>(9)</sup>. He administered PDL with a wavelength of 585nm, energy of 9-9.5/cm<sup>2</sup> and spot size of 5mm. In that study complete remission occurred in 70% of patients who underwent conventional therapy and in 66% of patients who underwent PDL 858nm and such dissimilarity wasn't statistically significant. He also found no difference between these methods in the treatment of recalcitrant warts. Our methods of treatment were similar to Robson's method. In our study complete remission was achieved in 51.1% of patients in PDL group and in 37.8% in cryotherapy group. We found no significant difference between PDL 585 and cryotherapy in the achievement of complete remission and excellent partial remission after 4 sessions (at the end of the study) though after receiving only 1 or 2 sessions of therapy lesions showed better response in PDL group rather than cryotherapy with statistical significance. In regard to our open randomized trial, this better response in PDL group may be biased by our open selection of patients that permitted a greater mean size of lesions and a greater number of lesions located on dorsal aspect of hands and fingers in the cryotherapy group. Bigger lesions or those located on the dorsal aspect of hands and fingers may need more sessions of treatment to become predominantly clear. But still this better response after 1<sup>st</sup> and 2<sup>nd</sup> sessions in PDL group and not after 3<sup>rd</sup> and 4<sup>th</sup> sessions of therapy may contribute to much more dependence of remission rate by cryotherapy on the number of therapeutic sessions rather than PDL. On the other hand, it may reflect the need for less therapy sessions by PDL until whole lesion disappears. Similar to Robinson, There was a tendency to better response in PDL group among recalcitrant warts. Though

not statistically significant, but it was suggesting PDL in preference to cryotherapy. Recurrence rate was 5.4% in the cryotherapy group and 6.6% in PDL group that was totally lower than what was reported by Robson. In regard to our last visit, 3 or 4 weeks after last therapeutic session, it was a short follow-up period to enable us to judge about the recurrence.

Among our patients, as shown in table 4, pain during procedure and bulla formation occurred more in cryotherapy group with significant difference ( $P=0.002$  &  $P=0.001$ ). Bulla occurred only in 4 patients of PDL group. No atrophic or hypertrophic scar was seen in either group. There were rare cases of hypo and hyperpigmentation among both groups. One case of infection with severe pain, exudative discharge and a positive smear for gram positive cocci occurred only in cryotherapy group. Epidermal damage and bulla formation in either method can lead to subsequent infections. Hence we recommend that all patients apply antiseptic solutions after each session of treatment with the use of prophylactic antibiotics.

## CONCLUSION

Although some trials have been shown that PDL is more efficient than cryotherapy in treating common warts, based on our study we can only show that PDL is just safer than cryotherapy.

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