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Original Article

Comparison of efficacy of ablative CO_2 laser vs. liquid nitrogen cryotherapy in the treatment of palmoplantar warts

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Abstract

Background Viral warts are benign epidermal proliferations caused by Human Papilloma Viruses (HPVs). Various treatment modalities have been described for viral warts, all of these are associated with advantages and disadvantages. The appropriate treatment modality depends on the number, size, and location of the lesions in addition to patient's immunologic status.

Methods A total of 120 patients (60 patients in each group), fulfilling the inclusion and exclusion criteria, were enrolled in the study. Group A was treated with ablative CO_2 Laser continuous wave (CW) mode (4-6 watts) per lesion per week until clearing or treatment upto 8 weeks. In Group B patients were treated with liquid nitrogen cryotherapy (-196 ^oC) using cryospray method. Two freeze – thaw cycle method was applied once a week until clearing of all lesions or till maximum of 8 weeks. The data was recorded in terms of reduction of number, size or complete disappearance of warts and considered cleared if not visible to naked eye.

Results Mean age of patients in group A was 32.0±10.99 and in group B was 31.63±10.64 years. Efficacy was seen in 53 (86.33 %) patients in group A and 36 (60 %) patients in group B. Statistically significant difference in efficacy was found in ablative CO_2 Laser group as compared with liquid nitrogen cryotherapy (p=0.0004).

Conclusion The results of this study reveal that ablative CO_2 Laser is more efficacious than liquid nitrogen cryotherapy in treating palmoplantar warts in terms of complete clearance.

Key words
Palmoplantar warts, ablative CO_2 laser, liquid nitrogen cryotherapy.

Introduction

Viral warts are benign epidermal proliferations caused by a DNA-containing human papilloma virus (HPV) clinically characterized by hypertrophic growths that may be found on any area of the body.[1] Warts are classified mainly into verruca vulgaris or common warts, verruca plana, verruca plantaris & condylomata accuminata.[2]

Warts are common throughout the world. They can occur at any age but are unusual in infancy and early childhood. Various studies estimated that 2–30% of school-age children and young

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adults have warts. A study from the Netherlands showed that plantar warts were the most common, present in 70% of the primary school-age children who had warts, whilst common warts were present in 42% of the affected children.[1]

More than 100 HPV genotypes have been isolated and sequenced; the actual number of HPV genotypes is even higher.[3] Common warts are due mainly to HPV-2, but can also be due to types 1, 4, 27 and 57. Plantar warts are caused by HPV-1, 2, 4, 27 or 57. The deep 'myrmecia' form is due to HPV-1. Smaller lesions may contain HPV 2, 4, 27 or 57, while mosaic warts are commonly caused by HPV-2. Plane warts are due mainly to HPV-3 and 10.[1]

There is much debate regarding appropriate treatment option for warts. No specific antiviral therapy against warts is available. Salicylic acid, Glutaraldehyde, Formalin, Topical 5-fluorouracil, Caustics, Retinoic acid, Vitamin D analogues are first line options for treatment. Second line treatment options include Cryotherapy, Laser, Hyperthermia, Surgery, and Photodynamic therapy. Podophyllin and podophyllotoxin, Imiquimod, Topical immunotherapy, Intralesional immunotherapy, Interferon, H2 receptor antagonists, Zinc, Oral retinoids, Intralesional bleomycin, Cidofovir, Psychological methods are listed as third line options for the treatment of warts.[1,4] Amongst these options, destructive/ ablative therapy is treatment of choice at most of the centers. Cryotherapy with salicylic acid found no difference in effectiveness, with overall cure rates of 50-70% after three or four treatments in cases of non-genital cutaneous warts.[5]

The liquid nitrogen leads to wart necrosis, and multiple treatments result in remission rates of 78% to 88%.[6] But the CO_2 laser shows a significantly lower incidence of inflammation with less morbidity during healing of lesion. In a study comprising 71 recalcitrant warts in 22 patients, 90% were successfully retreated giving a success rate of 95.5% illustrating the efficacy of technique in favorable outcome.[7] Also, in comparison, efficacy of CO_2 laser treatment of external genital warts was approximately two-fold greater than liquid nitrogen cryotherapy, and it was associated with lower recurrence rate.[8] 95% were successfully treated in terms of complete clearance of warts by CO_2 Laser and 46.2% by cryotherapy.[8]

Limited local data is available to compare the efficacy of ablative CO_2 laser and cryotherapy in the treatment of palmoplantar warts. Warts are quite commonly seen in our population and leads to pain, discomfort, and cosmetic concerns in patients resulting in poor quality of life. Therefore, there is a need to find an effective treatment option of this condition with minimum side effects. Cryotherapy needs specialized administration and is associated with adverse effects especially pain and pigmentary changes. Ablative CO_2 Laser is associated with less morbidity and lower side effects. The aim of our study was to compare the efficacy of ablative CO_2 Laser vs liquid nitrogen cryotherapy in the treatment of palmoplantar warts. The rationale of this study is to provide an effective and safe treatment modality for palmoplantar warts that will improve patients' quality of life.

Methods

This randomized controlled trial was conducted in Department of Dermatology, Services Institute of Medical Sciences (SIMS)/ Services Hospital Lahore, during the period from July 2018 to December 2018 after taking permission from the ethical committee of SIMS. A total 120 clinically diagnosed patients of palmoplantar warts of either gender, age ranging from 18 to 60 years, with any number or duration of warts

were enrolled in the study, after taking written informed consent. Patients taking any topical treatment in recent 4 weeks and Laser treatment in recent 8 weeks for warts were excluded from the study. Other exclusion criteria included warts with evidence of any superadded infection (clinically found or on culture if and when required), patients with immune deficiency disorders or on immunosuppressant drugs, pregnant and lactating females. A detailed history and clinical examination were carried out to determine the number of lesions, site of involvement and the type of warts. Participants were randomly allocated to two groups, by using balloting method.

In group A, 60 patients were treated with ablative CO_2 Laser CW mode (4-6 watts) per lesion per week (with 1 to 2mm surrounding area) until clearing of lesion or up to maximum of 8 weeks with simultaneous counting of number and size of lesion at week 4, week 6 and week 8 of treatment.

In group B, 60 patients were treated with cryotherapy with liquid nitrogen (-196 ^{0}C). Cryospray method was used for all applications. Two freeze – thaw cycle method[9] was applied once a week until clearing of all lesions or till a maximum of 8 weeks. To assess the clearance of warts, counting of lesions was done at the end of week 4, week 6, and week 8 of the treatment period. The patients were followed up for a period of a further 8 weeks. The data was recorded in terms of reduction of number, size or complete disappearance and considered cleared if not visible to the naked eye. Photographs were taken at baseline and then at each follow up visit. Efficacy of the treatment was measured in terms of complete clearance of the warts i.e. no longer visible to the naked eye with restoration of normal skin, assessed clinically at 8 weeks after completion of treatment.

SPSS version 21 was used to analyze data. Quantitative variables like age were presented as mean and standard deviation while qualitative variables like sex of patients & efficacy was presented in the form of frequency and percentages. Comparison of efficacy between both groups (ablative CO_2 Laser and cryotherapy) was made by using chi square test, p value of ≤ 0.05 was considered significant.

Data was stratified for the effect modifiers i.e. type and site of warts, number of lesions, age, and gender. Post stratification chi square test was used taking p value of ≤ 0.05 as significant.

Results

A total of 120 patients, 60 cases in each group, were studied. All patients completed the study period and there were no drop outs. Mean age was 32.0±10.99 years and 31.63±10.64 years in group-A and B, respectively. Age distribution of the patients was done, it showed that 32 (53.33%) patients in group-A and 33 (55%) patients in group-B were between 18-30 years of age whereas 28 (46.67%) patients in group-A and 27 (45%) patients in group-B were between 31-60 years of age. Gender distribution of patients revealed that 38 (63.33%) patients in group-A and 40 (66.67%) patients in group-B were male whereas 22 (36.67%) patients in group-A and 20 (33.33%) patients in group-B were females.

Our results showed that 35 (58.33%) cases in group A and 31 (51.66%) in group B had plantar warts whereas 25 (41.66%) cases in group A and 29 (48.33%) in group B had palmar warts. Distribution of results according to type of warts showed that 45 (75%) in both groups A & B had common warts while patients in groups A & B having mosaic warts were 15 (25%).

The results of our study showed that according

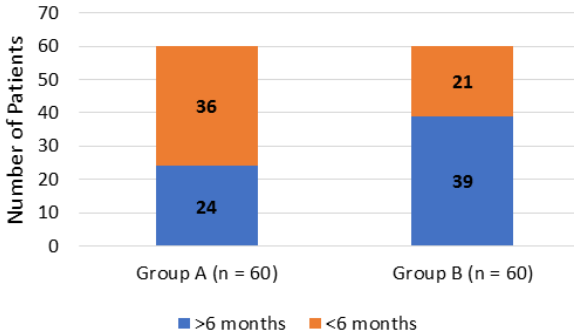

Figure 1 Distribution of patients by duration of disease.

Table 1 Efficacy of Ablative CO_2 laser & cryotherapy.

Group	*Efficacy*		*Total*	*P value*
	Yes n (%)	*No n (%)*		
Group-A (Ablative CO_2 Laser)	53 (88.33)	7 (11.67)	60	0.0004
Group-B (Cryotherapy)	36 (60.0)	24 (40.0)	60	

Table 2 Stratification by age.

Age (Year)	*Group*	*Efficacy*		*Total*	*P value*
		Yes	*No*		
18-30	Group-A	29	3	32	0.01
	Group-B	11	22	33	
31-60	Group-A	24	04	28	0.000
	Group-B	25	02	27	

Table 3 Stratification by gender.

Gender	*Group*	*Efficacy*		*Total*	*P value*
		Yes	*No*		
Male	Group-A	32	06	38	0.01
	Group-B	24	16	40	
Female	Group-A	21	01	22	0.005
	Group-B	12	08	20	

to the duration of disease 36 (60%) patients in group A and 21 (35%) in group B had warts for less than 6 months whereas 24 (40%) in group A and 39 (65%) in group B had warts for more than 6 months **(Figure 1)**.

Moreover, 44 (73.33%) patients in group A & 50 (83.33%) in group B had less than 3 warts per person and 16 (26.67%) patients in group A & 10 (16.67%) in group B had more than 3 warts.

Comparison of efficacy of ablative CO_2 Laser versus liquid nitrogen cryotherapy in the treatment of warts in our study showed that in 53 (88.33%) patients in group-A and 36 (60%) in group-B the treatment was efficacious whereas 7 (11.67%) patients in group-A and 24 (40%) in group-B did not achieve efficacy, p value was 0.0004 **(Table 1)**.

The data was stratified for age, gender, duration of disease, site of warts, type of warts & number of lesions (individual patient) and the results are shown below **(Table 2-7)**.

Discussion

Viral warts are benign epidermal proliferations caused by human papilloma virus (HPV) affecting mainly school aged children and young adults.[1,3] Warts may be found on any area of the body although hands and feet are most commonly involved. The papillomaviruses (PVs) cause benign and malignant proliferative lesions of mucosal and cutaneous epithelia.[10]

Patients seek treatment of their palmoplantar warts because of cosmetic appearance or pain.[11] Multiple treatment modalities have been described for warts which include topical therapies (Salicylic acid, Glutaraldehyde, Formalin, Occlusion, Topical 5-fluorouracil, Caustics, Retinoic acid, Vitamin D analogues), ablative therapies (Cryotherapy, Laser, Hyperthermia, Surgery, Photodynamic therapy), Oral therapies (Zinc, retinoids), intralesional therapies (Bleomycin, 5-fluorouracil), and psychological methods.[1]

All these treatment options are associated with advantages and disadvantages. The appropriate treatment modality depends on the number, size, and location of the lesions in addition to patient's immunological status. The ideal treatment is the one that could clear the lesions completely with

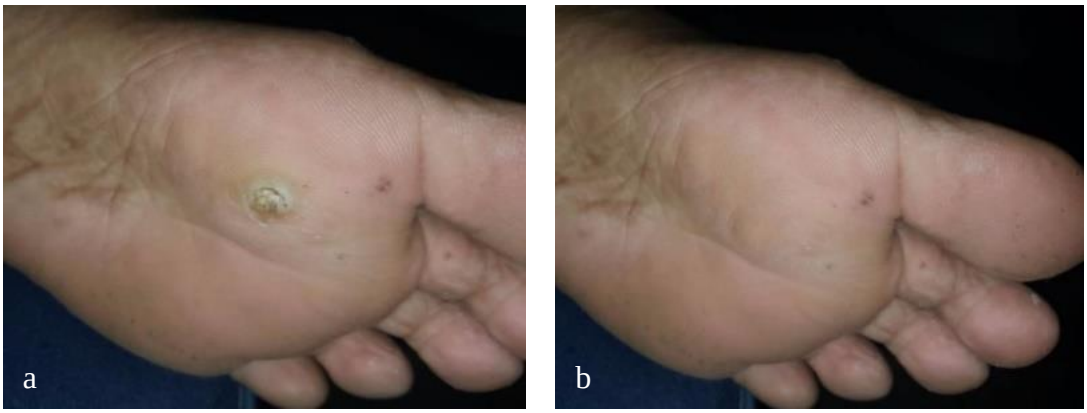

Figure 2 Plantar wart cryotherapy a) Pre-Procedure b) Post-Procedure

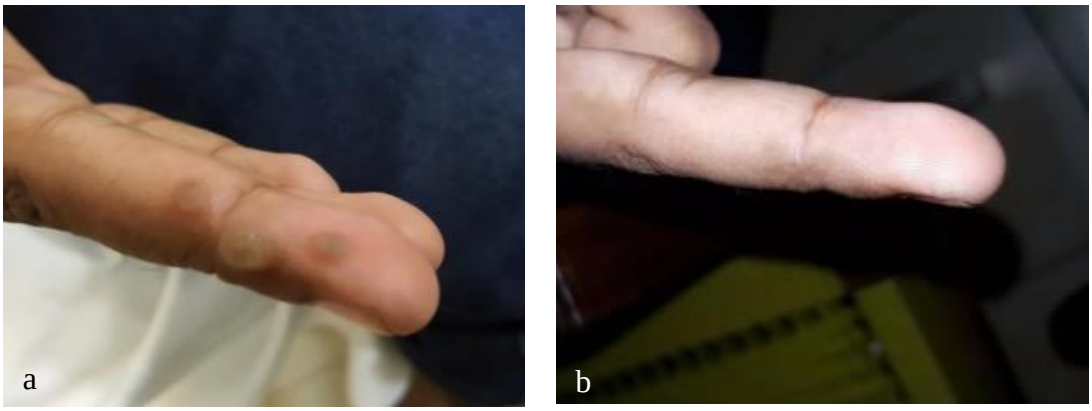

Figure 3 Palmar wart ablative CO_2 Laser a) Pre-Procedure b) Post-Procedure

Table 4 Stratification by duration of disease.

Duration	*Group*	*Efficacy*		*Total*	*P value*
		Yes	*No*		
<6 months	Group-A	35	01	36	0.01
	Group-B	16	05	21	
>6 months	Group-A	18	06	24	0.06
	Group-B	20	19	39	

Table 5 Stratification by site of warts.

Site of warts	*Group*	*Efficacy*		*Total*	*P value*
		Yes	*No*		
Plantar Warts	Group-A	30	05	35	0.08
	Group-B	21	10	31	
Palmer Warts	Group-A	23	02	25	0.21
	Group-B	15	14	29	

Table 6 Stratification by site of warts.

Type of warts	*Group*	*Efficacy*		*Total*	*P value*
		Yes	*No*		
Common Warts	Group-A	38	07	45	0.02
	Group-B	25	20	45	
Mosaic Warts	Group-A	15	00	15	0.03
	Group-B	11	04	15	

Table 7 Stratification by number of lesions per person.

Number of lesion	*Group*	*Efficacy*		*Total*	*P value*
		Yes	*No*		
1-3 lesions	Group-A	41	03	44	0.000
	Group-B	30	20	50	2
> 3 lesions	Group-A	12	04	16	0.42
	Group-B	06	04	10	

minimal side effects, (e.g. pain, hypo or hyperpigmentation, scars, local and systemic adverse effects).

The statistics of our study revealed that out of 120 cases (60 in each group), 53.33% (n=32) in group-A and 55% (n=33) in group-B were between 18-30 years of age whereas 46.67% (n=28) in group-A and 45% (n=27) in group-B were between 31-60 years of age, showing concordance with a previous studies depicting increase incidence of warts in early adolescence

and adults.[1] These results are indicating involvement of young individuals in agricultural activities and contact sports (football, hockey, swimming etc.) leading to inoculation of HPV into the skin and appearance of warts.

Regarding gender, 63.33% (n=38) in group-A and 66.67% (n=40) in group-B were males whereas 36.67% (n=22) in group-A and 33.33% (n=20) in group-B were females. This finding is attributed to the fact that less females are involved in outdoor sports & activities. They may prefer local remedies at home.

As far the site of wart is concerned, 58.33% (n=35) patients in group A and 51.66% (n=31) in group B had plantar warts whereas 41.66% (n=25) in group A and 48.33% (n=29) in group B had palmar warts. A study in Netherland showed plantar warts to be present in 70% of patients and 42% children having common warts.[3] These findings are in contrast to our study where 75% of patients were having common warts. This contrast may be due to difference in age group presented and included in our study. There is a need of future research to confirm this finding.

Comparison of efficacy of ablative CO_2 Laser versus liquid nitrogen cryotherapy in the treatment of warts in our settings showed efficacy in 88.33% (n=53) patients in group-A and 60% (n=36) in group-B. Statistically significant difference was found in the efficacy of both groups (p value 0.0004). We compared our results with a previous study, where 95% were successfully treated in terms of complete clearance of warts by CO_2 Laser and 46.2% by cryotherapy.[8] These findings are in agreement with our study.

A study by Oni G *et al.*[7] reviewed the results of patients with recalcitrant warts treated using CO_2 Laser. They recorded seventy-one recalcitrant warts treated in 22 patients, all as day case procedures. A total of 54.5% of patients had complete remission after one treatment and the average length of follow-up was 71.5 months. Recurrence occurred on average 5.29 months following treatment. Of those patients, 90% were successfully retreated, giving an overall rate of 95.5%.[7]

According to a recent study by Petrov *et al.*[12] CO_2 Laser is effective in healing and regeneration of skin because of its efficiency and safety.[12]

The major benefit of using the CO_2 Laser over conventional approaches is the minimized scarring and faster healing increasing patient`s satisfaction with treatment. Care is necessary with regard to recurrence as virus may persist in the surrounding tissue.

In current study, efficacy of ablative CO_2 Laser was found to be better than cryotherapy in the treatment of palmoplantar warts with the p value of 0.0004 which is considered as statistically significant.

The limitation of our study is that we did not analyze and compare the side effects of both treatment modalities.

Conclusion

In the light of current study and its results, it is concluded that ablative CO_2 Laser is more efficacious then liquid nitrogen cryotherapy in treating palmoplantar warts in terms of complete clearance and hence ablative CO_2 Laser should frequently be used as preferred treatment option for palmoplantar warts.

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