Journal of Pakistan Association of Dermatologists. 2019; **29(1)**: 35-39.

Original Article

Comparison of efficacy between intralesional bleomycin and cryotherapy in plantar warts

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Abstract

Objective To compare the efficacy of intralesional bleomycin and cryotherapy in treating plantar warts.

Material and Methods A total of 160 patients (80 in each group) were enrolled, who were randomly divided into 2 groups. Group A was treated with 0.1% intralesional bleomycin and group B was treated with liquid nitrogen with a cotton swab. Follow-up was carried out at 02, 04 and 06 weeks and the final efficacy was calculated at the end of 06 weeks.

Results Out of 160 patients, 32 (40.0%) male and 48 (60.0%) female were enrolled in intralesional bleomycin group; 30(36.5%) male and 50 (62.5%) females were included in cryotherapy group. Mean±SD of age in intralesional bleomycin and cryotherapy was 28.24±4.2 with C.I (27.30-29.17) and 27.56±3.8 with C.I (26.71-28.40) years, respectively. In comparison of both groups 90% efficacy was found in intralesional bleomycin group whereas 72.5% in cryotherapy group and p value was found to be highly significant i.e. (P=0.005).

Conclusion Intralesional bleomycin is more effective than cryotherapy in the treatment plantar warts.

Key words
Intralesional, bleomycin, plantar warts, cryotherapy.

Introduction

Warts are scaly, rough, spiny papules or nodules that can be found on any cutaneous surface.[1] They are the cutaneous manifestations of human papilloma virus (HPV) infection.[2] Over 100 HPV types are recognized, with affinity for different sites of the body. The clinical appearance of warts is variable and depends to some extent on the type of HPV involved and the site of infection.[3-5]

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Diagnosis of warts is usually based on clinical examination.[6] Warts are treated by different physical modalities like electrocautery, cryosurgery, topical salicylic acid, lactic acid, topical imiquimod, different lasers and intralesional drugs with variable results.

Cure rates for cryotherapy vary widely, depending on the treatment regimen. It is easy to apply but has the disadvantage of being painful with post procedure blister formation and hyperpigmentation. A novel method to treat warts is by intralesional bleomycin at low concentration. It has an antitumor, antibacterial and antiviral activity.

Material and Methods

It was a randomized control trial carried out in the Outpatient Department of Dermatology, PNS Shifa Hospital, Karachi. The study was carried out from November 2016 to May 2017. One hundred and sixty patients with warts (80 patients in each group) were enrolled. Patients were divided randomly in 02 groups (A and B) using random number tables. Sample size was calculated using expected frequency of efficacy of bleomycin and cryotherapy. Patients from 20-50 years of age of both gender diagnosed as plantar warts of up to 03 months of duration were enrolled after taking written informed consent. Exclusion criteria included patients who were previously treated for warts by any methodology, patients with history of vascular diseases, chill blain, immunocompromised or taking immune suppressive drugs. All selected patients were registered; their demographic data, history and clinical features were recorded. Group A received intralesional bleomycin 0.1% therapy until the lesion blanched. It was prepared manually by diluting 15 mg powder in 5 ml distilled water and then each ml was further diluted by adding 2ml of 2% lignocaine, double the amount taken from the vial, so that concentration became 1mg/1ml (0.1%). Group B patients were treated with liquid nitrogen with the help of a cotton swab wrapped on a wooden stick and applied firmly with 01 mm extra healthy skin margin until the lesion blanched. Patient was discharged without any home treatment and called for follow-up visits at 2nd week, 4th week and finally at 6th week of procedure for assessment of efficacy. Efficacy was determined by the principle investigator under supervision of a senior dermatologist. The treatment was considered effective; if it completely cleared the wart, at the final evaluation i.e. 6th week.

Study data was entered and analyzed in SPSS version 21. Continuous variables like age, duration of disease & size of wart were expressed in mean & standard deviation (Mean±SD). Categorical variables like gender, residence, site of wart & the outcome variable (efficacy) were expressed in frequencies and percentages. Effect modifiers like age, gender, residence, site of wart, duration of disease & size of the wart were stratified by the application of chi-square considering a *p*-value of <0.05 as statistically significant.

Results

In this study mean ±SD of age in Group-A and Group-B was 28.24±4.2 with C.I (27.30-29.17) and 27.56±3.8 with C.I (26.71-28.40) years respectively**.** Mean ±SD of duration of disease in Group-A and Group-B was 1.25±0.89 with C.I (1.05-1.44) and 0.98±0.56 with C.I (0.85-1.10) months respectively**.** Gender distribution was as; 32 (40.0%) males and 48 (60.0%) females were enrolled in Group-A and 30 (36.5%) males and 50 (62.5%) females were included in Group-B**.**

In comparison of both groups, efficacy was found in 72 patients (90%). Group A (intralesional bleomycin group) whereas in 58 patients (72.5%) treatment was efficacious in Group-B (cryotherapy group). *p*-value was found to be highly significant i.e. (P=0.005) as shown in **Table 2**.

Table 1 Demographic data of both groups

Age(years)		*n*	*Minimum*	*Maximum*	*Mean*	*±SD*	*95% C.I*
Group	Group A	80	20	50	28.24	4.2	27.30-29.17
	Group B	80	20	50	27.56	3.8	26.71--28.40
Gender (m/f)		*Male*			*Females*		
Group	Group A	32 (40%)			48 (60%)		
	Group B	30 (36.5%)			50 (62.5%)		
Duration (months)		*N*	*Minimum*	*Maximum*	*Mean*	*±SD*	*95% C.I*
Group	Group A	80	1	3	1.25	0.89	1.05-1.44
	Group B	80	1	3	0.98	0.56	0.85-1.10

Table 2 Comparison of efficacy in both groups

Group	*Efficacy*		*P-value*
	Yes	*No*	
Group A	72 (90.0%)	8 (10.0%)	0.005
Group B	58 (72.5%)	22 (27.5%)	

Discussion

Various studies have been done on the use of intralesional bleomycin for the treatment of recalcitrant warts with clearance rates ranging from 14 to 100 percent.[7] Most of the data suggest that bleomycin is effective in over two thirds of cases with minimal adverse effects.[7] However, in a review by Gibbs *et al*. no evidence was found for the consistent efficacy of intralesional bleomycin.[8]

Aguis *et al*. used intralesional bleomycin therapy in 47 patients with 138 plantar warts that were resistant to freezing with cryotherapy and showed an efficacy rate was 89.9%.[9] Bunney *et al*. did a study on 59 matched pairs of hand warts in 24 patients with intralesional bleomycin, with a normal saline placebo injected into the warts in the same patient as control, witnessed a cure rate of 76%.[10] In another study be Munn *et al*. bleomycin was dropped on to the wart and then pricked into the wart showed a clearance rate of 92%.[11]Multiple puncture technique was used to introduce bleomycin in warts in a study, also mentioned a success rate of 92%.[12]Hayes and O'Keefe used diluted concentrations (0.05%) of bleomycin injected in 62 warts of 26 patients where efficacy rate was 76%.[13]

A study by Bourke *et al*. showed the clearance rate of 66% in the group treated weekly, 47% in the group treated every 2 weeks, and 30% in those treated every 3 weeks.[14] However, the clearance percentage is related to the number of treatments received, and independent of the interval between treatments. It was noted that, most of the trials of cryotherapy studied different regimens rather than comparing cryotherapy with other treatments or placebo. Although, there is more controversy about its efficacy, most studies showed lower cure rates for cryotherapy when compared with other studies done on bleomycin. An Iranian study compared the efficacy of bleomycin with cryotherapy on the same patients' group.[15] They used 0.05% bleomycin solution and a single freeze cryotherapy cycle on the alternate limbs of the same patient presenting with almost symmetrical and bilateral presentation of warts. In this study, they found that the clearance rate for intralesional bleomycin was 87.6% for warts, and 86.4% of patients treated with bleomycin were cleared. They found cryotherapy to have a wart clearance rate of 72.3%, and in 68.2% of patients treated with cryotherapy were cleared. They estimated that bleomycin was 1.23 times more efficacious than cryotherapy. In our study, the success rate in both groups was found relatively higher. Ninety-seven percent wart clearance rates and 94.9% patient clearance rate

for bleomycin compared to 90% wart clearance rate and 72.5% patient clearance rate for cryotherapy. The relative risk found in the study was 7.67, which indicates that bleomycin was 7 times more efficacious than cryotherapy in clearing warts. Here, 0.1% bleomycin solution and double-freeze thaw cycle technique was used. The patients selected here had limited number (maximum 5 warts) of warts. All these factors might have contributed to the higher rate of success. In bleomycin-treated patients, there was a significant positive correlation found between the surface area of wart and the amount of bleomycin needed to treat the wart.

Present study showed highly significant difference in efficacy of warts treated with intralesional bleomycin and cryotherapy and P value found to be (P=0.005). Pain was the major troublesome factor both in intralesional bleomycin and cryotherapy. Pain duration was shorter in bleomycin group compared with discomfort in cryotherapy group, which might continue for 6-12 hours after cryotherapy. Probably 02% lignocaine that was mixed to dilute bleomycin solution helps to avoid pain during intralesional injection, which is usually experienced by patients when the solution is not mixed with local anesthetic solution. In few patients of bleomycin group severe pain, hemorrhagic eschar formation and localized sclerosis was noted especially when the warts were at finger tips and toes. These side effects healed completely in two weeks. They can be prevented by decreasing the quantity of injected solution and avoiding over blanching of the lesions at digits. Dyspigmentation was seen during follow up in both groups in significant number of cases. Due to higher post-inflammatory reaction pattern, dyspigmentation was more severe in cryotherapy treated patients. Although dyspigmentation was gradually clearing out but how long it takes to resolve could not be ascertained due to limited time period of the study. Other side effects were not recorded. Difference in the recurrence of warts was not significant in both groups.

Conclusion

Intralesional bleomycin injection is significantly more effective than cryotherapy and is a safe alternative for the treatment of cutaneous warts.

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