Journal of Pakistan Association of Dermatologists. 2019; **29(4)**: 412-417.

Original Article

Comparison between the efficacy and safety of podophyllin resin versus cryotherapy in treatment of anogenital warts

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Abstract

Objective To compare the efficacy and safety of podophyllin resin VS cryotherapy in treatment of anogenital warts.

Methods A total of 104 patients were enrolled, 52 in each group A & B. Group A was treated with cryotherapy and Group B was treated with podophyllin resin. Findings were noted in already devised proforma. Patients were evaluated at last follow up visit to assess results.

Results 88% of patients in group a showed excellent results at the end of treatment whereas this figure was 8% in group B.

Conclusion Cryotherapy was found to be more effective and safe than podophyllin resin in treatment of anogenital warts.

Key words
Genital warts, human papillomavirus, cryotherapy, topical podophyllin resin, condylomata acuminata.

Introduction

Condylomata acuminata is one of the most common sexually transmitted infections all over the world, with an incidence of 0.6%–1.2% in males and females and this condition is mainly seen between 20–25 years of age. Mostly they constitute subclinical infection with human papillomavirus (HPV) 6 or (HPV) 11. Different treatment modalities are available, but failure of treatment and recurrence after visible clearance of warts are seen with almost all methods. In United States of America there are estimated to be five hundred thousand to ten hundred thousand new cases per year.[1]

The aim of treatment is to clear warts as treatment reduces infectivity. Treatment options depend upon the size, location, number and morphology of lesions, as well as cost, convenience, side effects and patient preference. Self-administered modalities like podophyllin or imiquimod are increasingly recommended. Podophyllin resin, cryotherapy, surgical excision and imiquimod are the most safe, effective and convenient options.[2,3]

Podophyllin resin contains a mixture of antimitotic compounds among which podophyllotoxin is the main ingredient which impedes mitotic activity in rapidly dividing cells by preventing the arrangement of chromosomes

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on spindle during metaphase of mitosis, thus inhibiting proliferation of virus (HPV) containing keratinocytes.[4]

Cryotherapy done by liquid nitrogen (-196F) causes immediate freezing and coagulative necrosis of target cells and simultaneous release of inflammatory mediators in vicinity, causing rapid death of target cells.[5]

Methods

One hundred and four patients were enrolled in this clinical trial. Patients with clinically visible anogenital warts between age of 16-60 years of either gender were considered for the study and were enrolled after informed written consent. Pregnant and immunocompromised patients were excluded from the study. Photographs were taken before and after treatment **(Figure 1 & 2)** and record was maintained in devised proforma. Patients were randomly divided into two groups (A and B) containing equal number of patients, 52 in each group. The patients in group A were treated with liquid nitrogen cryotherapy. Cryotherapy was done for 10 sec at weekly interval for 4 weeks. Those in group B were treated with podophyllin resin. Twenty five percent podophyllin resin was applied topically with cotton bud twice weekly for four weeks, under supervision, to the appropriate area. Surrounding skin was protected by applying petroleum jelly. Patients were instructed to wash off the resin after 4 hours. In both groups, follow up for resolution/ recurrence of warts was done at week 04 and week 08 of initiation of treatment. The therapy was considered efficacious when reduction in number of warts was observed at follow up visits. The treatment which resulted in more clearance of warts, based on clinical observation, was considered more efficacious. Response to treatment was graded as 'excellent'>90% clearance, 'good' 60 to 89% clearance, 'satisfactory' 30-59% clearance and 'poor' <30% clearance.

Results

Out of total hundred and four patients, 52 were assigned group A and 52 were in group B. There were 22 (42%) female patients in group A and 25 (48%) in group B. Thirty (58%) patients were male in group A and 27 (52%) were male in group B **(Figure 3)**. Male to female ratio was found to be 1.36:1 in group A and 1.08:1 in group B. The age range was 16 to 60 years. Most of the patients belonged to age range of 21 years to 30 years (36% in group A and 42% in group B).

Figure 1 **a.** Before treatment **b.** After treatment - Cryotherapy

Figure 2 **a.** Before treatment **b.** After treatment – Cryotherapy

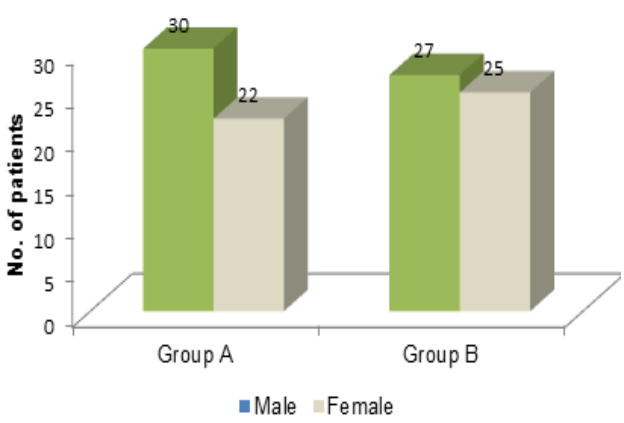

Figure 3 Sex Distribution of Patients

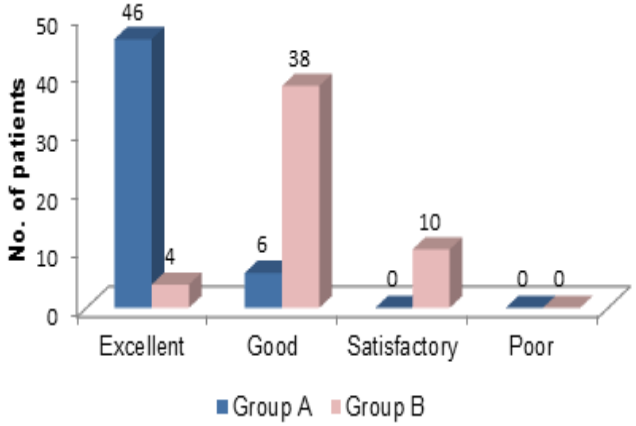

Figure 4 Comparison of response to treatment on two months follow up

After 08 weeks follow up, 'excellent' response was seen in 88% of patients in group A and in only 8% of patients in group B (p-value = <0.001). 'Good response' was seen in 11.5% of patients in group A while it was seen in 73% of patients in group B which is statistically significant (p-value = <0.001). 'Satisfactory' response was not seen in any patient in group A but it was seen in 19% of patients in group B, and no patient showed poor response in both groups after two months follow up **(Figure 4)**. Pain was the most common side effect experienced by patients in group A (43%), whereas patients in group B experienced itch as the common side effect (93%).

Discussion

Anogenital warts is one of the most frequently occuring sexually transmitted diseases. Management of anogenital warts is variable, effective and well established now. Cryotherapy and podophyllin resin are in practice for treatment of anogenital warts with significant success.[1,2] Clinical trials comparing different treatment options have reported variable success in the treatment of anogenital warts.[3,5]

In the present study, male to female ratio was 1.36:1 in group A and 1.08:1 in group B. In a study reported by Stephen et al.[6] male to female ratio was 1.46:1 which is close to the figures in our study. This is probably due to the fact that warts are easily visible in male patients, as compared to female patients in whom anogenital warts are not always visible on external genitalia. Tsu et al.[7] found this ratio to be 1:1.4 in their study which could be due to the reason

that in the Western society females are not as hesitant as females in our society to seek medical help in problems associated with genitals.

In this study, the age range of patients was 16-60 years. In another study carried out by Steben[8] et al. the age range of patients was 14-60 years. In some other studies, similar age range has been reported.[9,10] Most of the patients enrolled in our study belonged to the age group of 21-30 years (78%). This is comparable with the study done by Scheinfeld et al;[11] in which 80% of patients were in the age between 17-33 years. In another study reported by Tsu et al.[7] the highest incidence of condyloma acuminata was seen among adults having age between 15-25 years. The age of acquiring HPV infection mainly depends upon the norms and moral values of the society and sexual practices of individuals and in this age of life most people are sexually active.

Patients included in our study were treated by 10 seconds freeze cycle of cryotherapy and showed excellent results in 88.5% patients at eight weeks follow-up. Conolly et al;[12] conducted a trial comparing ten seconds freeze cryotherapy versus traditional short freeze cycle and found that 64% of patients were cleared by ten seconds freeze cycle as compared to 39% who were treated by traditional short freeze cycle. He concluded that ten seconds freeze was more effective than traditional short freeze duration method. Bourke et al.[13] who compared the efficacy of cryotherapy at weekly, two weekly and three weekly intervals, found that warts were cleared in 66% of patients who were treated at weekly interval as compared to 30% in the group who were treated at three weekly intervals and showed that weekly cryotherapy was more effective than three weekly. The percentage of patients cured by cryotherapy treatment was less in above mentioned trials than what we found in our study, which was 88% ($p < 0.001$). The difference in results could be due to the difference in duration or the anatomic site of the warts in their study, as heavily keratinized warts of longstanding duration and warts of different anatomic sites respond differently to the treatment options. Exclusion of immunocompromised patients is another reason that our results are better.

Two treatment modalities were compared in our study and it was observed that cryotherapy was more effective than podophyllin. In a study conducted by Stone et al.[14] different treatment options were tried to see their effect on anogenital warts and it was observed that cryotherapy was more effective than podophyllin, which concurs with our study. Pouran et al.[15] also compared podophyllin resin and cryotherapy in the treatment of anogenital warts and found podophyllin to be more efficacious. This difference could be due to the difference in number of treatment sessions and interval between sessions. The efficacy of podophyllin is also influenced by its shelf-life, stability, technique of application and duration of warts because warts of lesser duration respond better to podophyllin. When Bashi SA[16] compared the above mentioned treatment options, he reported that number of treatment sessions required to cure anogenital warts was less for cryotherapy than for podophyllin, thus concluding that cryotherapy was more effective than podophyllin. Follow up for resolution/ recurrence was done for 08 weeks in our study, it is same as in the study of Pouran et al.[15] When Edwards et al.[17] conducted a trial on treatment of anogenital warts, they followed up the patients for three months and reported that significant improvement was seen within six weeks of initiation of therapy, and re-attendance was unsatisfactory at three months follow up. Though long follow up time helps to determine the recurrence of warts and long term outcome of treatment option can be commented, but at the

same time long follow up is directly proportional to number of defaulters of trials and re-infection by the pathogen causing difficulty in concluding about the efficacy of that specific therapy.

In this study comparison of side effects of both treatment modalities, was also carried out. Side effects such as pain, itching and mild local inflammatory reactions were observed in both groups but more in patients treated with podophyllin, except for pain which was reported in more patients treated by cryotherapy. Such effects have also been reported in other international studies.[9,12,15,18,19]

Cryotherapy seems to be particularly suitable for those patients having widely scattered warts and most departments of dermatology have access to cryotherapy procedure for outdoor patients. Podophyllin resin is a reasonable alternative treatment option, which mostly gives good results in the treatment of warts.[18]

Conclusion

We found cryotherapy more effective and safe than podophyllin resin in treatment of anogenital warts.

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