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Original Article

Comparison of efficacy of 50% salicylic acid versus cryotherapy in the treatment of plantar warts

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Abstract

Introduction Human papilloma virus (HPV), which enters the body through skin breaks and wounds and develops as a lesion on the soles or toes, is the source of plantar warts.. There are many treatment options for plantar warts. Topical treatments are acceptable to the patients in general because of their pain free nature and less cost. Cryotherapy is a second line treatment for plantar warts. The aim of the study is to compare the efficacy of 50% salicylic acid vs. cryotherapy in the treatment of plantar warts.

Methods A total of 98 patients (49 in each group; Group A and Group B) were enrolled for this study. Group A was exposed to cryotherapy every two weekly with a minimum of 4 sessions and assessed at the end of 12th week of initiation of therapy. Group B was given 50% salicylic acid to be applied daily at home every night and removal of the dead tissues with abrasive stone in the morning for a total of 8 weeks. Final observation for efficacy was done at the end of 12th week. Efficacy was defined here as 50% reduction in the size of wart as measured at baseline. No change in size or less than 50% reduction in size was considered as non-efficacious and partially effective respectively.

Results Complete response was seen in 26.5% of patients in group A and 18.4% patients in group B. Almost similar number of patients did not respond to either of the two treatment modalities. The efficacy was found in 34.7% in group A while in group B, the efficacy was 30.6%.

Conclusion Our study reveals no significant difference between efficacy of 50% salicylic acid and cryotherapy in treatment of plantar warts.

Key words
Cryotherapy; Plantar warts; 50% Salicylic acid.

Introduction

Human papilloma virus (HPV) causes benign skin lesions, on soles of patients, that are called plantar wart/s. that have more than 100 known types. Majority of plantar warts are caused by type 1, 2 or 4 HPV.[1] Human papilloma virus is a double stranded DNA virus and it commonly causes infections on face, hands, feet and perineal areas.[2] Plantar warts are often self-limiting. They can be painful at times. Plantar warts are contagious as they happen to spread among family members sharing shoes, using swimming pools or people walking bare footed.[3] Treatment of plantar warts is often challenging. Various therapeutic modalities that have been used for treating plantar warts have not been successful every time.[4,5] These include topical acids, cryotherapy, electrodessication and immune therapy. Patients prefer topical treatments because they are pain free and pocket friendly. One of the most common topical treatments in usage of salicylic acid.[6]

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Cryotherapy is a second line treatment for plantar warts. It consists of liquid nitrogen at -196°C applied to the wart. It causes inflammation through cell mediated response and clears the HPV infected keratinocytes.[7] All treatments available for warts do not kill the virus but initiate an immune response against human papilloma virus that clears the virus infected cells in the skin.[3]

In an international study done in UK, two hundred and forty patients were randomized into two groups, A and B, comprising of 117 and 123 patients in cryotherapy and salicylic acid groups respectively. There was no evidence of a difference in clearance rates between the treatment groups at 12 weeks.[8] In a secondary analysis of a randomized control trial at Netherlands, concluded that salicylic acid has a cure rate of 25% while cryotherapy has a cure rate of 68%. The sample size of our study is also based on this study.[9,10] Two studies including a Cochrane review and Bruggink *et al.* concluded that cure rates for warts are 15%, 49% and 8% for salicylic acid, cryotherapy and no treatment at all respectively.[11]

In the past 7 years, no comparative study has been done for recording the difference between the efficacy of cryotherapy and salicylic acid in treatment of plantar warts on national level. The present study will help us understand the outcomes of the proposed two treatment modalities. Hence recommendations will be given to Dermatologists on the basis of response of warts to the two options.

Methods

We conducted this Randomized control trial in the Department of Dermatology, Hayatabad Medical Complex, Peshawar, over a period of six months from 28-11-2019 to 27-05-2020. The study comprised of two groups of 49 patients each. Sample size was calculated by, "Fleiss, statistical methods for rates-and proportions, formulas 3.18 and 3.19 using open epi sample size calculator". The data for calculation of sample size was taken from previously mentioned study in the introduction.[10] Sampling technique was consecutive non-probability sampling. Both genders aged 13 to 50 years having single or multiple wart/s on plantar aspect of feet were included. Patients having diabetes mellitus, peripheral neuropathies, HIV were excluded from this study.

Approval for this research was taken from hospital ethical committee. Those patients fulfilling the inclusion criteria were enrolled in the study. The purpose and benefit of the study were explained to them and were assured complete confidentiality. Demographic data like name, age, sex, address, phone number of all patients were noted.

Patients was randomly assigned into group A and B, using block randomization. Group A was exposed to cryotherapy every two weekly with a minimum of 4 sessions and assessed at the end of week 12 of initiation of therapy. Group B was given 50% salicylic acid to be applied daily at tissues with abrasive stone in the morning for a home every night and removal of the dead total

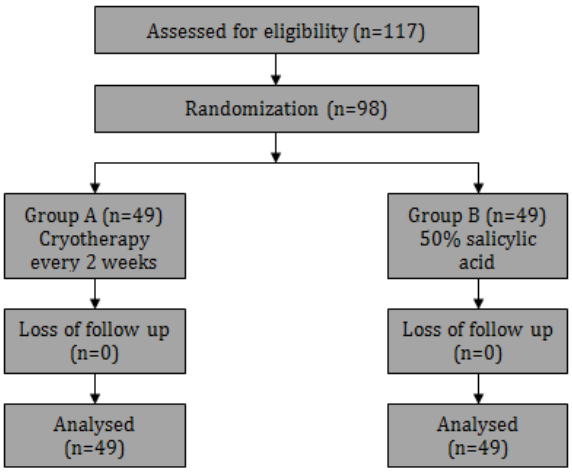

Figure 1

of 8 weeks. They were assessed at the end of week 12 of initiation of treatment. Assessment was done to determine efficacy in terms of clearance of the lesions from baseline. Information was recorded in special proforma. SPSS version 23 was used for analysis of data. Mean±SD was calculated for numerical variables. Frequencies and percentages were calculated for categorical variables like gender and efficacy. Chi-square test was used to compare efficacy of treatments in the two groups, p value ≤0.05 was considered as significant. Tables were used to present the results.

Results

A total of ninety eight enrolled patients were randomized into two groups of 49 patients each. Group A was exposed to cryotherapy while Group B was given 50% salicylic acid. The mean age was higher in group B (32.5 years±10) compared to group A (30.2 years±9.4) **(Table 1)**. In both groups a higher percentage of males were enrolled as compared to females **(Table 2)**. P value showed that the difference between enrolled genders was statistically not significant **(Table 3)**. Overall efficacy of the two treatments was almost similar with no statistically significant difference **(Table 4)**.

Table 1 Distribution of patients by age.

Age (Year)	*Group A (Cryotherapy) n (%)*	*Group B (Salicylic acid) n (%)*
14-19	6 (12.3%)	5 (10.2%)
20-35	26 (53.0%)	23 (47.0%)
36-50	17 (34.7%)	21 (42.8%)
Total	49 (100.0%)	49 (100.0%)
Mean ±SD	30.2 ±9.4	32.5 ±10.0

Table 2 Distribution of patients by gender.

Gender	*Group A (Cryotherapy) n (%)*	*Group B (Salicylic acid) n (%)*
Male	30 (61.2%)	30 (61.2%)
Female	19 (38.8%)	19 (38.8%)
Total	49 (100%)	49 (100%)

Table 3 Distribution of patients by response.

Response	*Group A (Cryotherapy) n (%)*	*Group B (Salicylic acid) n (%)*
Complete	13 (26.5%)	9 (18.4%)
Partial	4 (08.2%)	6 (12.2%)
No response	32 (65.3%)	34 (69.4%)
Total	49 (100.0%)	49 (100.0%)

P value: 0.399

Table 4 Comparison of efficacy.

Efficacy	*Group A (Cryotherapy) n (%)*	*Group B (Salicylic acid) n (%)*
Yes	17 (34.7%)	15 (30.6%)
No	32 (65.3%)	34 (69.4%)
Total	49 (100%)	49 (100%)

P value: 0.333

Discussion

Majority of people develop plantar wart/s at some point in their lives. Although plantar warts are mostly self resolving, that is they will go away on their own without treatment, many people still choose to get treatment for it, for a number of reasons, such as discomfort or the fact that it prevents them from participating in sports and other everyday activities.[13,14] Plantar warts can be treated in a variety of ways, such as using cryotherapy, topical medications, surgical curettage, and alternative and complementary therapies. There is still a never-ending hunt for a safe and economical therapy for plantar warts.[15]

Cryotherapy is a method for freezing and destroying aberrant skin cells that need to be removed using an extremely cold liquid spray or tool. Although the procedure has been known since long, dermatologists may now utilize it more often because of its wide availability. The method is additionally referred to as cryocautery or cryosurgery.[16] Salicylic acid is an organic acid, basically a monohydroxybenzoic acid. It is crystalline, devoid of color and works as a plant hormone. It originates from salicin's metabolism. It is a significant active metabolite of acetylsalicylic acid. However, its most well-

known application is certainly in the management of acne.[16]

Our study shows mean age of patients to be 30.3 years with an SD of ±9.4 and 32.5 years with a SD of ±10 in cryotherapy and salicylic acid groups respectively **(Table 1)**. This observation is almost similar to a study conducted by Bruggink *et al.* who reported the mean ages of enrolled patients to be 30.1 years and 30.2 years for cryotherapy and salicylic acid respectively.[17] The similarity between both studies can be explained on the basis of similar inclusion criteria. The other plausible reason could be that demographics of warts are independent of geographical variation hence world wide almost similar age groups are affected by plantar warts.[17]

In our study, a higher percentage of males were enrolled as compared to females in both group A and B **(Table 2)**. This finding is contradictory to study conducted by Bruggink *et al.* where a higher percentage of females were seen as compared males in each group.[17] This difference might be because in our part of the world more males are involved in jobs and earning livelihood for their families. Thus they have more chances of contracting the disease due to its contagious nature. Secondly due to male dominance in our province, males have more access to hospitals. Hence there are more chances of male being enrolled as compared to females although this difference might not exist in reality.

In our study, complete response was noted in 26.5% of patients in group A and 18.4% of patients in group B. In a study conducted by Bruggink *et al.*[17] complete clearance was noted in 34% of those patients who were treated with cryotherapy and 31% in those treated with salicylic acid groups. The results were almost similar with p value of 0.399 between the two groups due to similar strengths and duration of agents used in both studies. Another study done by M. Rademaker *et al.* showed a complete clearance response in 58%, 16% had partial clearance and 25% had no improvement at all with only cryotherapy.[20] The difference of the reported study from our study can be due to the fact that they went for aggressive cryotherapy under general anesthesia while we only brought into practice the conventional cryogun for delivery of the liquid nitrogen.[20] For salicylic acid, a study conducted by Daniel Lopez *et al*. showed complete eradication in 53.3% of patients after a single application and 46.7% patients showed complete eradication after 2 applications. The difference is because in addition to salicylic acid, two other anti wart chemicals, cantharidin and podophyllotoxin were also included in the solution while we only used salicylic acid.[21]

The efficacy in our study was almost same for both groups (34.7% vs. 30.6%) with a p-value of 0.333. The cure rates in a study conducted by Bruggink *et al.* also showed similar efficacy using cryotherapy and salicylic acid groups (14% vs. 14%).[17] The similarity might be because of similar time duration, strength of treatments in both studies and same inclusion and exclusion criteria.

Conclusion

From our study, we conclude that 50% salicylic acid and cryotherapy have comparable efficacy in the treatment of plantar warts. Therefore, either treatment modality can be employed as per patient and/ or physician preferences.

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