

Topical pyruvic acid (70%) versus topical salicylic acid (16.7%) compound in treatment of plantar warts: A randomized controlled trial

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Abstract

Background: Recurrence rate is considerable with current topical treatments of plantar warts. We compared the efficacy of topical pyruvic acid (70%) with salicylic acid (16.7%) compound in treating multiple plantar warts.

Materials and Methods: In this randomized controlled trial, 60 patients with multiple plantar warts were equally randomized to receive either pyruvic acid 70% or compound salicylic acid solution (salicylic acid 16.7%, lactic acid 16.7%, and collodion 100%) that was topically applied twice a day for 4 weeks. Patients were visited every 2 weeks for 1 month after starting treatment and then every 1 month for another 2 months. The number and size of warts, treatment complications (pain, burning, scar, pigmentation, and crust), and recurrence were evaluated.

Results: Warts' number was decreased by $-13.12 \pm 25.6\%$ with pyruvic acid and by $-23.0 \pm 28.0\%$ with compound salicylic acid ($P = 0.159$) after treatment. Warts' size was decreased by $-43.47 \pm 57.0\%$ with pyruvic acid and by $-37.40 \pm 32.76\%$ with compound salicylic acid ($P = 0.615$) after treatment. There was no difference between the two groups in cumulative incidence of treatment complications ($P > 0.05$). Also, there was no difference between the two groups in recurrence rate at 2 months (10 vs. 16.7%, $P = 0.500$) or at 3 months after treatment (3.3 vs. 6.7%, $P = 0.335$).

Conclusion: Topical pyruvic acid and compound salicylic acid had the same efficacy and complications in treating plantar warts. Decision for choosing the treatment can be made based on the costs and individual factors as well as patients preferences.

Key Words: Pyruvic acid, salicylic acid, verruca vulgaris, warts

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INTRODUCTION

Plantar warts are often self-limiting. But, in some cases, they can be bothersome and painful. In such situations, and also for decreasing disease duration, treatment is recommended. There are various treatment options for warts including topical and local invasion therapies (e.g., acids, cryotherapy, and electrodesiccation) and immune therapy.

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Choosing a treatment is dependent on the patient's characteristics, treatment complications, as well as the lesion locations.^[1] These treatments are, however, not completely successful.^[2-4] Invasive techniques are not completely proved to treat warts and as today, there is not a high quality study to evaluate these methods and their complications and threats. Almost in all therapies, recurrences are reported.^[5,6]

Topical treatments are more attractive because of their more simplicity and less costs. Salicylic acid solution is one of the most commonly applied and useful topical agents in the treatment of warts. However, recurrence (up to 30%) is also reported by this treatment.^[3,7] Other topical agents that can be applied in treatment of warts are alpha hydroxy acids (AHAs) considering their favorable keratolytic characteristics.^[8-10] Pyruvic acid is an enole isomer of AHAs, an alpha keto acid, and a strong keratolytic agent.^[11] Very few studies are, however, conducted on the efficacy of pyruvic acid or other AHAs in treatment of warts. In this study we aimed to evaluate and compare the efficacy and complications of pyruvic acid and compound salicylic acid solutions in treating multiple plantar warts.

MATERIALS AND METHODS

Patients and setting

This randomized controlled trial was done in three University Hospitals in Isfahan city, Iran between September 2013 and May 2014. Patients aged 12 years and above who were referred with multiple warts (at least 2) were consecutively included into the trial. Diagnosis of warts was based on physical examinations by an experienced dermatologist. Patients with mosaic warts, those who were already under any treatment for warts, and pregnant or lactating women were not included in the trial. Considering type I error of 0.05 and study power of 0.8, a total of 60 patients were needed for the study. The study was approved by the Ethical Committee of the Isfahan University of Medical Sciences and all patients assigned written consent form. The study is registered at the clinicaltrials.org (NCT02151630).

Intervention

Patients were equally randomized into two groups of pyruvic acid (PA) and salicylic acid (SA) using table of random numbers in three blocks (for the three study centers). The PA group received pyruvic acid solution 70% prepared by dissolving the pyruvic acid in a water/ethanol solution (Azmiran Co., Tehran, Iran). The SA group received a combination of salicylic acid 16.7%, lactic acid 16.7%, and

collodion 100% (Kimiagar Toos Co., Mashhad, Iran). Solutions were packed in 10cc alphabetical coded bottles and distributed among the study centers. A dermatologist educated patients to apply a drop of the solution on each wart lesion with a clean swap. Patients were advised to apply the solution twice daily for a period of 4 weeks and not to rinse off the medicine after treatment. Patients also applied the petrolatum to the surrounding normal skin to protect against the corrosive effect of the concentrated acid. Warning signs such as erythema/edema were noted to the patients and treatment used to be discontinued if such signs were observed. The attending dermatologist and patients were not aware about the assigned treatments.

Assessments

Patients were visited by a dermatologist for every 2 weeks for 1 month (during treatment) and then every 1 month for 2 months after the end of treatment (follow-ups). On each visit, warts were inspected to determine the size and number. For this aim, we limited the borders of each lesion by a special marker in such a way that the wart appeared to be delimited and thus we could measure the diameter of each lesion. Measurement of the lesions was done with a ruler regardless of hyperkeratosis or other features of the lesions. The size of the warts was calculated as the mean size of all the warts. We count the number of the warts regardless of the size of the lesions. Any wart totally non-detectable by inspection and touch was considered as healed. Hyperkeratotic or flat lesions were considered the same in this study and there was no difference in evaluation or measurement of these lesions.

Treatment complications such as pain, burning, scars, pigmentations, and crust were recorded on each visit. Complications were recorded per patient, regardless of number of lesions that had been complicated. Recurrence rate was evaluated 1 and 2 months after the end of the treatment. Recurrence rate was also recorded per patient.

Data analyses

Data are expressed as mean \pm standard deviation (SD) or number (%). Data were evaluated for normal distribution and parametric and non-parametric tests were applied. Comparison between the two groups was done by the independent sample *t*-test or the Mann-Whitney U test for quantitative variables and the Chi-square test for qualitative variables. Trend of changes in the number and size of warts in each group was evaluated by the Friedman test. Analyses were done using the SPSS software version 16.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 72 patients with multiple plantar warts were evaluated for our study eligibility. Twelve patients were not eligible to enter the study; six had mosaic warts, two were pregnant, and four were not willing to participate. Sixty patients were included in the study and completed the study and follow-ups (Figure 1, patients' flow diagram).

Patients included 22 (36.7%) males and 38 (63.3%) females with age range from 15 to 60 years (mean \pm SD of age = 30.2 ± 12.3). There was no difference between the two groups regarding age ($P = 0.877$) or gender ($P = 0.211$). The mean \pm SD of the number and size of warts in each group over the study period is reported in tables 1 and 2, respectively. There was no difference between the two groups in warts' number ($P = 0.935$) or size ($P = 0.165$) at baseline. The number of warts was decreased after the treatment in both groups (in both groups, $P < 0.001$) (Table 1, Figure 2). The percent of change in warts' number after treatment was not different between the PA and SA groups (-13.12 ± 25.6 vs. $-23.0 \pm 28.0\%$, $P = 0.159$).

Warts' size was decreased after treatment by $-43.47 \pm 57.0\%$ in the PA group ($P = 0.017$) and by $-37.40 \pm 32.76\%$ in the SA group ($P < 0.001$)

(Table 2, Figure 3). The percent of change in warts' size after treatment was not different between the PA and SA groups ($P = 0.615$).

Mean cumulative incidence of each treatment complication in the study groups are represented in Table 3. Pain, burning, scars, pigmentations, and

Table 1: Number of warts in each group during the study period

	Pyruvic acid N=30	Salicylic acid N=30	P [†]
Baseline	6.87 \pm 2.71	6.83 \pm 2.73	0.935
2 nd week	5.17 \pm 2.3	4.70 \pm 1.78	0.529
4 th week	3.83 \pm 2.13	3.30 \pm 1.78	0.388
2 nd month	2.27 \pm 1.44	2.33 \pm 1.42	0.988
3 rd month	1.33 \pm 1.44	1.90 \pm 1.60	0.178
P value [‡]	<0.001	<0.001	

Data are presented as mean \pm SD. [†]Mann-Whitney U test; [‡]Friedman test

Table 2: Size (cm) of warts in each group during the study period

	Pyruvic acid N=30	Salicylic acid N=30	P [†]
Baseline	1.8 \pm 1.21	2.07 \pm 1.02	0.165
2 nd week	1.58 \pm 0.91	1.65 \pm 0.74	0.455
4 th week	1.35 \pm 0.89	1.17 \pm 0.53	0.901
2 nd month	0.9 \pm 0.79	0.97 \pm 0.64	0.426
3 rd month	0.88 \pm 1.53	0.78 \pm 0.64	0.363
P value [‡]	<0.001	<0.001	

Data are presented as mean \pm SD. [†]Mann-Whitney U test; [‡]Friedman test

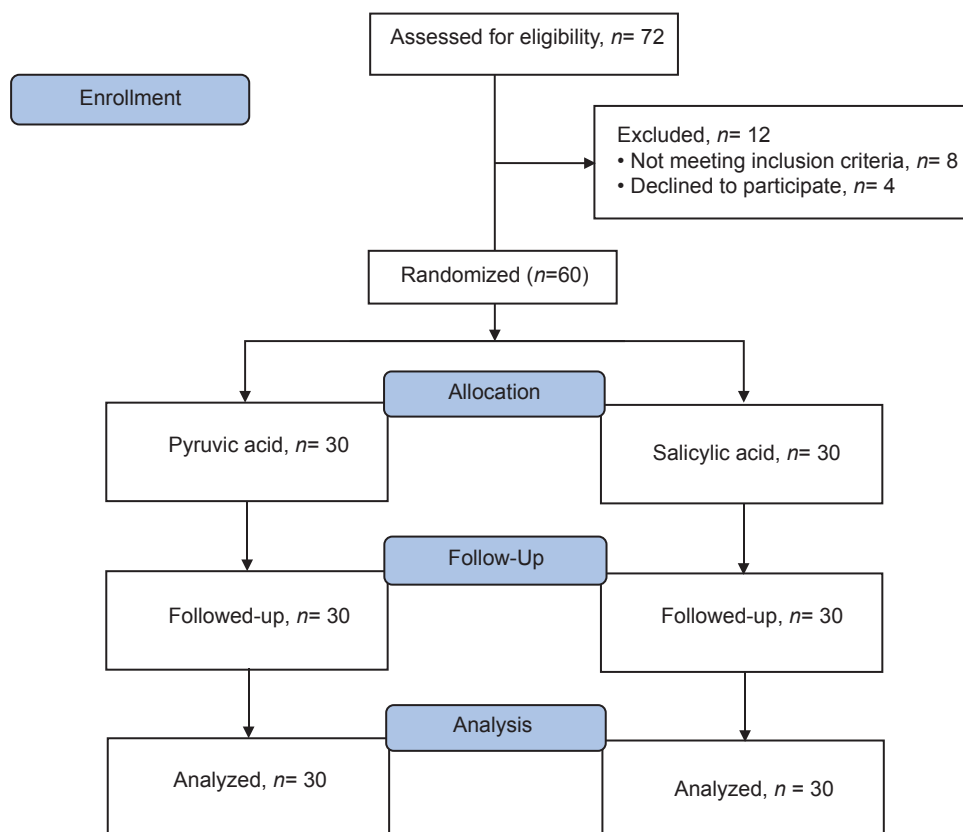


Figure 1: Patients' flow diagram

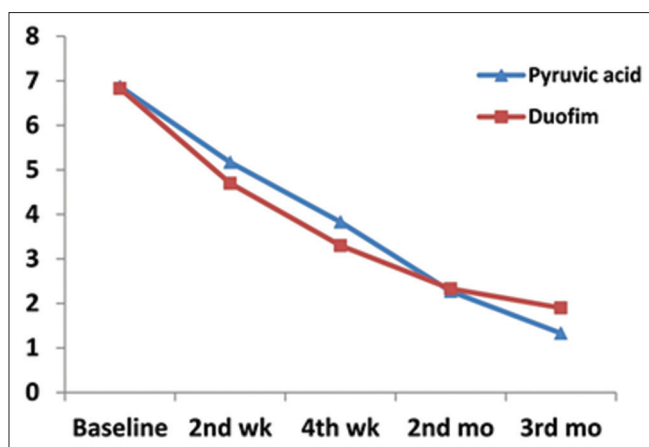


Figure 2: Trend of changes in the number of warts during the study period

Table 3: Mean cumulative incidence of treatment complications in each group

	Pyruvic acid N=30	Salicylic acid N=30	P ^a
Pain	1.33±1.02	1.20±0.99	0.611
Burning	2.13±0.86	1.83±1.14	0.430
Scar	0.53±1.27	0.60±1.19	0.611
Pigmentation	1.46±1.75	1.56±1.59	0.665
Crust	1.33±0.99	1.26±1.25	0.608

Data are presented as mean±SD. ^aMann-Whitney U test

crust were not significantly differing between the two groups. The recurrence rate of warts in the PA and SA groups was 10% and 16.7% at the second month ($P = 0.500$) versus 3.3% and 6.7% at the third month ($P = 0.335$), respectively.

DISCUSSION

The aim of the present study was to evaluate and compare the efficacy and safety of pyruvic acid and compound salicylic acid solutions in treating multiple plantar warts. Both treatments were effective and similar in decreasing the number and size of the warts, and also were similar regarding the recurrence rate. Accordingly, pyruvic acid and compound salicylic acid solutions are the same in terms of safety and efficacy in treating multiple plantar warts.

Many studies tried to find an ideal way to treat skin warts but it seemed impossible, because the complete removal of virus has not been possible since today. Khattar *et al.*, in a randomized controlled study, compared zinc oxide versus salicylic acid/lactic acid combination in the treatment of warts. According to their results, zinc oxide was more effective (50% complete cure) than salicylic acid (42% complete cure) in treating warts. It must be mentioned that in this study there was an imbalance

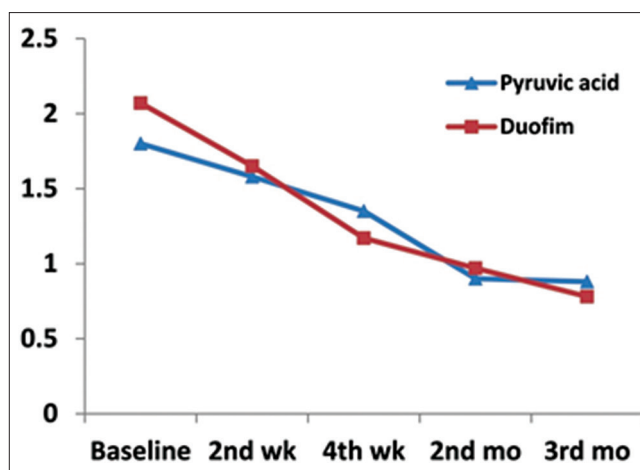


Figure 3: Trend of changes in the size of warts during the study period

in patient exclusion between the two groups which might affect their results; patients who were treated with salicylic acid were excluded more frequently than the other group.^[12] In another study, which was open label and conducted by Coskey *et al.*, 120 children who suffered from plantar warts were treated with salicylic acid 30% in combination of podophyllin 5% and cantharidin 1%. This study reported effectiveness of the treatment in 67.5% of the patients.^[13] It must be noted that the salicylic acid concentration in this study (30%) was higher than the solution that we applied in our study (16.7%) which can justify the relatively high treatment response by the Coskey *et al.* study compared with ours. According to the presence of different concentrations of salicylic acid, Kwok *et al.* conducted a systematic review and found no difference in effectiveness among different concentrations of salicylic acid. However, most of the reviewed trials had low qualities and limitations and a precise conclusion was not possible.^[6] Accordingly, it is necessary to conduct more head to head studies as well as dose-response trials to find the most effective yet safe dose of the salicylic acid as well as other topical medicines for treatment of warts.

Although several studies are conducted on salicylic acid, few trials investigated other possible topical treatment of warts. Hursthouse *et al.* reported that 5-fluorouracil 5% is better than placebo in treatment of viral warts.^[14] The study by Capertone *et al.* reported the effectiveness of the AHAs in treatment of acantholysis of epidermis (without any damage to dermis). In their study, different concentrations of AHAs were used for lesions with different thicknesses (AHA 40% for thin and AHA 70% for lesions with more than 2 mm depth). Adhesive dressings and petrolatum-based ointment have also been applied to prevent fluid accumulation and

crust.^[8] In our study, we did not use any dressing which might increase the complications. In another study, Ebrahimi *et al.* demonstrated that silver nitrate 10% have efficacy to treat common warts.^[15] In a meta-analysis done by Kwok *et al.*, salicylic acid therapy was demonstrated as the first-line therapy for warts though it did not completely cure the warts. Therefore, cryotherapy is recommended as the second-line therapy. Aggressive cryotherapy has more efficacy than gentle one, but it has more side effects as well. This meta-analysis has recommended 5-fluorouracil and bleomycin as third-line therapy.^[3] Bruggink *et al.* study revealed that cryotherapy is the most effective technique to treat common warts. They suggested all methods in treating plantar warts including cryotherapy, topical salicylic acid, and supportive management after 13 weeks had the same outcomes and benefits and no relevant differences were demonstrated.^[16] This controversy among studies can be explained largely by differences in patients' characteristics, e.g., types of warts. The topical treatment dosage is also important as the study by Cockayne *et al.* showed no differences between cryotherapy and topical salicylic acid 50% in treating plantar warts.^[17] These studies revealed that if we have to choose between cryotherapy and topical treatments, we should consider parameters such as availability, costs, side effects, etc., Cryotherapy is a more expensive procedure and patients prefer topical treatments like salicylic acid and this method is more attractive in clinical settings.^[16]

Some strengths of our study included its design, matching biological variables, and no drop-out during follow-up. We tried to differentiate efficacy and complications of the two topical treatments which were not done before. One of our limitations was the short duration of treatment and follow-up. Treatment and follow-up duration of 8 weeks and 6 months, respectively, are recommended.

CONCLUSIONS

Between using topical salicylic acid and pyruvic acid, there is no difference in efficacy and safety. Decision to choose between these two methods can be made based on costs and individual factors as well as patients' preferences.

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