Received: 15 December 2020 | Revised: 9 July 2021 | Accepted: 26 July 2021

DOI: 10.1111/dth.15073

DERMATOLOGIC THERAPY WILEY

ORIGINAL ARTICLE

Therapeutic efficacy and safety of three different modalities in pediatric patients with plantar warts

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Abstract

Human papillomavirus infection is relatively common in communities. Thus, determining an effective and painless treatment method, especially in pediatric patients is of utmost importance. This study aimed to compare the outcomes of three different methods of treating plantar warts in pediatric patients. Children with verruca plantaris treated with a salicylic acid–lactic acid combination once daily (SA/LA 1), a salicylic acid–lactic acid combination applied in three to seven layers under occlusion every 3 days (SA/LA 2), or a combination of 5-fluorouracil (0.5%) and salicylic acid (10%) (SA/5-FU) were evaluated retrospectively. Treatment responses and recurrence rates were also evaluated after a minimum of 4 months. Among the 98 children with verruca plantaris, 19 were treated with SA/LA 1, 53 were treated with SA/LA 2, and 18 were treated with SA/5-FU; the eight patients who received cryotherapy were excluded. The mean treatment duration was significantly shorter in the SA/LA 2 group than in the SA/LA 1 group and the SA/5-FU group. ($p = 0.000$ for both) Application of a salicylic acid–lactic acid combination in multiple layers under occlusion is a safe, painless, and effective treatment method for plantar warts in children.

KEYWORDS
pediatric, treatment, verruca plantaris

1 | INTRODUCTION

Warts are very common in the pediatric population. However, treatment of warts in children is a problematic as they can have difficulty tolerating painful treatment methods. Therefore, painless treatment methods are required. The most frequent and current treatment methods include application of salicylic acid, combinations of salicylic acid and lactic acid, combinations of salicylic acid and 5-fluorouracil (5-FU), and cryotherapy. Other treatment options include application of cidofovir, formaldehyde solution or gel, glutaraldehyde 10% solution, silver nitrate, laser treatment, systemic retinoids, and topical immunotherapy (Squaricaciddibutylester).[1,2] Cost effectiveness and adverse effects (such as pain) are the determining factors when choosing a treatment option in the pediatric age group. Thus, this study aimed to compare the clinical efficacy of three different methods used to treat plantar warts in children.

2 | MATERIALS AND METHODS

Ninety-eight children with verruca plantaris who were treated at our clinic between October 2016 and August 2020 were evaluated retrospectively. Demographic and clinical characteristics of the children, including age, gender, previous treatments, duration of warts, and number of lesions, were obtained from the hospital database. Treatment response and recurrence rates were evaluated after at least 4 months after treatment.

2.1 | Application of treatments

2.1.1 | SA/LA 1 group

A commercially available topical ointment containing 167 mg salicylic acid and 167 mg lactic acid was applied to the warts once daily after removing the remaining white layer from the previous application.

2.1.2 | SA/LA 2 group

A commercially available topical ointment containing 167 mg salicylic acid and 167 mg lactic acid was applied to the warts in seven layers, with each layer been dried with a hair dryer before applying the next layer. The treatment area was covered with a bandage (Figure 1). The patients were followed up and the treatment was reapplied every 3 days. The remaining ointment was removed before repeating the procedure (Figures 2 and 3). Patients who showed clinical improvement received one more application of the ointment in three layers.

2.1.3 | SA/5FU group

A commercially available topical ointment containing 0.5% 5-FU and 10% salicylic acid was applied three times daily after removing the remaining white layer from the previous application.

All treatments were administered until all warts disappeared. If patients were non-responsive, treatments were halted after 4 months.

2.2 | Statistical analysis

IBM SPSS Statistics 23 (SPSS Inc., Chicago, IL) was used for overall analyses. Results, reported as mean ± SD, were compared across the three groups using the one-way analysis of variance, followed by the post hoc Tukey test when the p-value was <0.05.

3 | RESULTS

A total of 98 patients between the ages 6 and 16 were included. Nineteen patients were treated with the salicylic acid–lactic acid combination once daily (SA/LA 1 group), 53 were treated with the salicylic acid–lactic acid combination applied in three to seven layers every 3 days (SA/LA 2 group), and 18 were treated with the 5-FU–salicylic acid combination three times daily (SA/5FU group). The remaining eight patients who were treated with cryotherapy were excluded from our study. The mean age ($p = 0.578$), mean number of lesions ($p = 0.169$), and mean duration of lesions before treatment ($p = 0.976$) did not differ significantly among the three groups (Table 1).

The treatment duration differed significantly among the three groups ($p = 0.000$). The mean treatment duration was shortest in the SA/LA 2 group, followed by the SA/5FU group and the SA/LA 1 group.

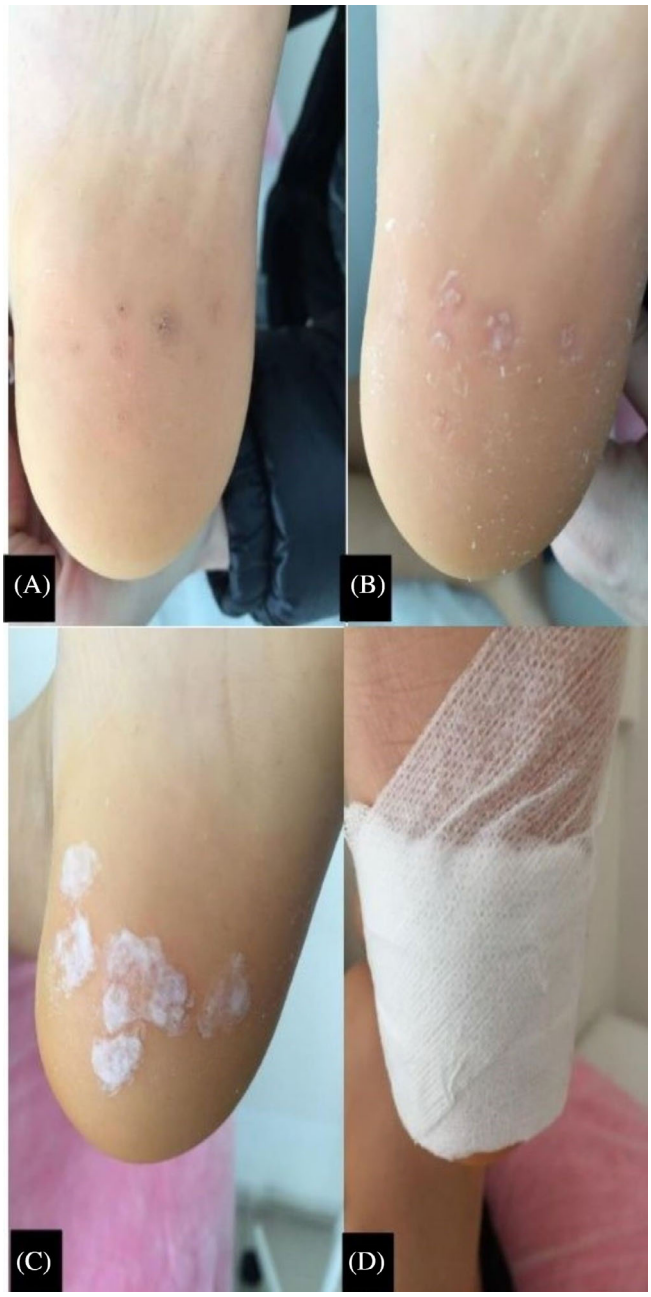

FIGURE 1 First day of application of salicylic acid–lactic acid combination as seven layers to a 11-year-old female patient (A) Plantar warts before treatment (B) After removal of the overlying hyperkeratosis with scalpel (C) After application of the salicylic acid–lactic acid combination in seven layers with each layer dried before applying the next layer, (D) After closure of the area with gauze bandage

The treatment duration was significantly shorter in the SA/LA 2 group than in the SA/LA 1 group and the SA/5FU group ($p = 0.000$ for both). Furthermore, it was shorter in the SA/5FU group than in the SA/LA 1 group, although the difference was not statistically significant (Table 2). All patients in the SA/LA 2 group experienced complete disappearance of warts and did not have any recurrence. Five patients in the SA/LA 1 group discontinued treatment and one-third patients were unresponsive to treatment, whereas four patients in the SA/5FU

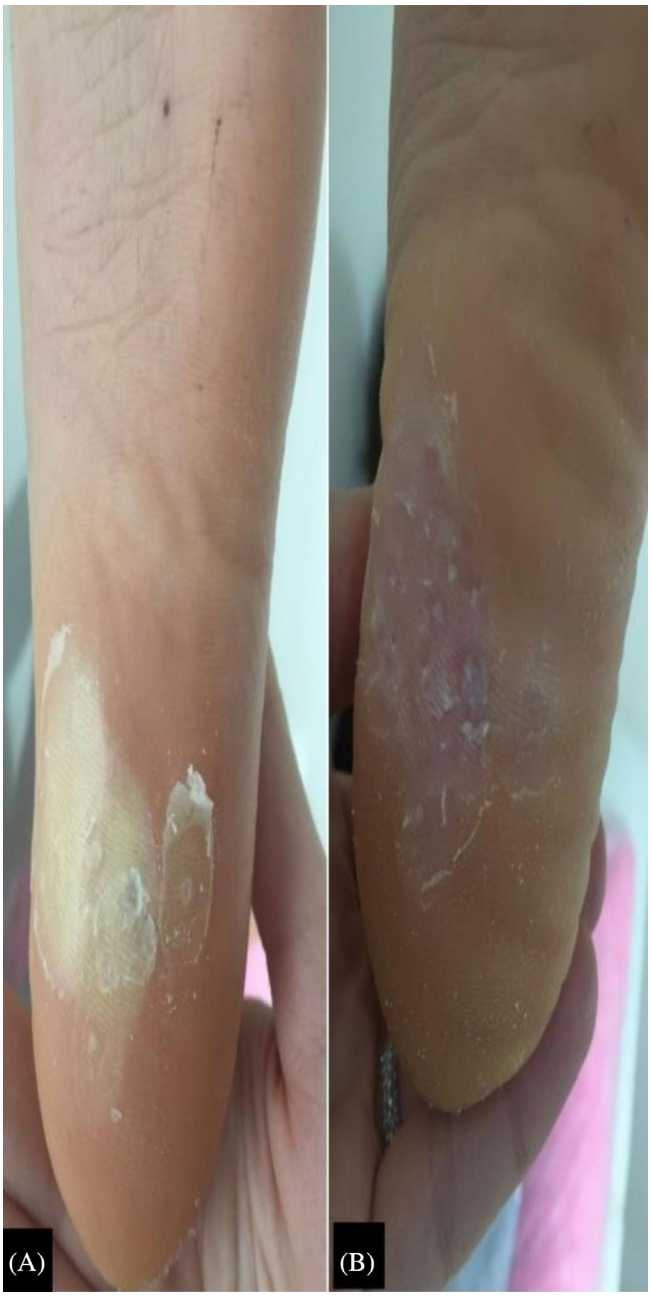

FIGURE 2 (A) On the third day of treatment (B) After removing the remaining ointment and redundant skin

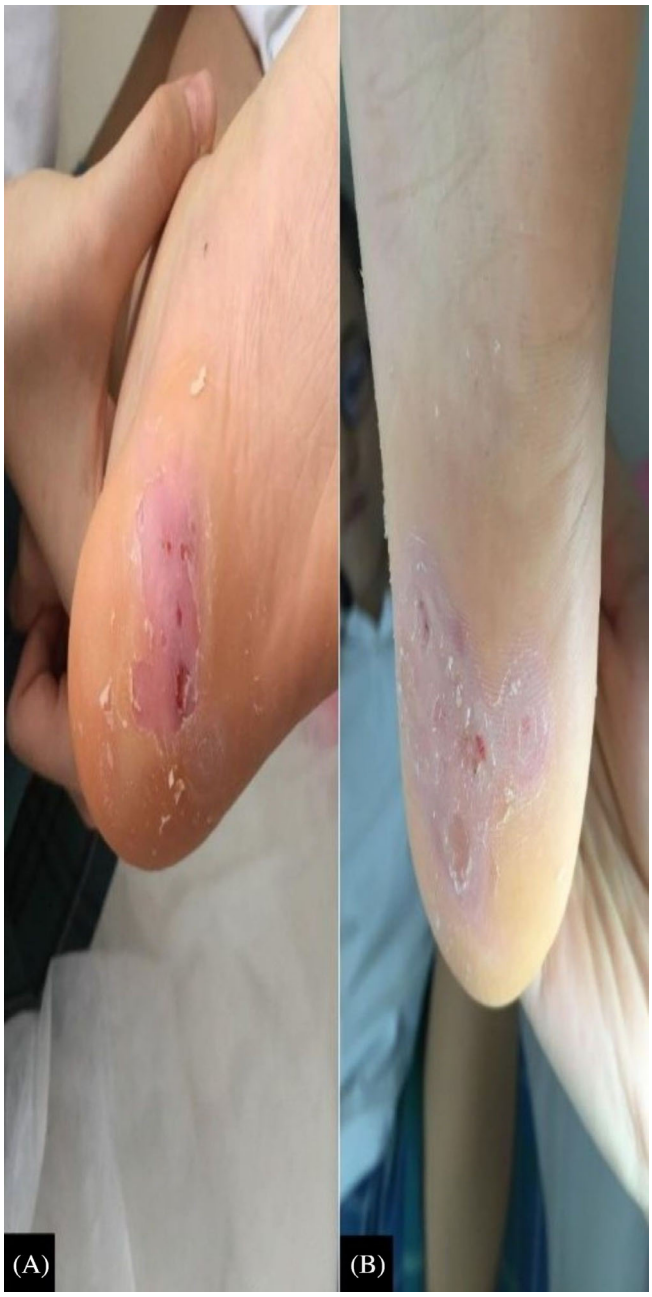

FIGURE 3 (A) On the 6th day of treatment (B) On the 12th day of treatment

group discontinued treatment and one patient was unresponsive to treatment.

All treatments were generally well-tolerated by the patients. Mild pain, skin irritation, burning and stinging sensation were observed in some of the patients. These adverse effects were mostly experienced towards the end of the treatments.

4 | DISCUSSION

Human papillomavirus (HPV) infection is one of the most common skin diseases worldwide. Although HPV infection can occur in all age groups, it is more common in pediatric populations. Prospective cohort studies with small sample sizes have reported that 5%–30% children and young adults are affected by HPV.[3–5] Palmoplantar warts are generally caused by HPV types 1, 2, 4, 27, and 57.[6]

Topical ointments containing salicylic acid are widely used in the treatment of these warts. High concentrations of salicylic acid are thought to increase epidermal cell exfoliation through irritation. It may also stimulate the patient's immune system against warts.[1] However, it irritates the skin surrounding the warts, leading to low treatment compliance and expectation of treatment benefits.[7] Topical 5-FU, which inhibits the proliferation of epidermal basal cells by blocking

TABLE 1 Age, number of lesions, duration of warts, and treatment durations

					95% confidence interval for the mean values			
		N	Mean ± SD	SE	Lower limit	Upper limit	Lowest value	Highest value
Age (years)	SA/LA 2	53	10.67±1.969	0.569	9.42	11.92	7	13
	SA/LA 1	19	11.25±2.121	0.750	9.48	13.02	7	14
	SA/5FU	18	10.50±1.581	0.500	9.37	11.63	8	13
	Total	90	10.77±1.851	0.338	10.08	11.46	7	14
Number of lesions	SA/LA 2	53	6.17±4.970	1.435	3.01	9.32	1	14
	SA/LA 1	19	8.50±4.751	1.680	4.53	12.47	2	15
	SA/5FU	18	4.90±3.957	1.251	2.07	7.73	1	14
	Total	90	6.37±4.657	0.850	4.63	8.11	1	15
The duration of warts before treatment (months)	SA/LA 2	53	4.667±2.6054	0.7521	3.011	6.322	1.0	10.0
	SA/LA 1	19	4.625±3.1139	1.1009	2.022	7.228	1.0	9.0
	SA/5FU	18	4.200±2.0976	0.6633	2.699	5.701	1.0	8.0
	Total	90	4.500±2.5155	0.4593	3.561	5.439	1.0	10.0
Treatment duration (days)	SA/LA 2	53	10.47±3.65	0.502	7.74	10.76	6	27
	SA/LA 1	19	21.74±11.87	11.874	9.46	37.54	8	60
	SA/5FU	18	18.94±7.86	1.853	12.42	24.58	8	35
	Total	90	14.54 ± 8.54	0.900	11.89	20.38	6	60

TABLE 2 Comparison of the mean treatment durations between treatment groups

Multiple comparisons								
		(I) groups	(J) groups	Mean difference (I-J)	SE	*p*	95% confidence interval for mean values	
							Lower bound	Upper bound
Treatment duration	Tukey HSD	SA/LA 2	SA/LA 1	−11.265[a]	1.876	0.000	−15.74	−6.79
			SA/5FU	−8473[a]	1.914	0.000	−13.04	3.91
		SA/LA 1	SA/LA 2	11.265[a]	1.876	0.000	6.79	15.74
			SA/5FU	2.792	2.308	0.451	−2.71	8.30
		SA/5FU	SA/LA 2	8.473[a]	1.914	0.000	3.91	13.04
			SA/LA 1	−2.792	2.308	0.451	−8.30	2.71

[a]$p < 0.05$ was considered statistically significant.

DNA synthesis, has also been shown to be effective in the treatment of palmoplantar warts.[1] Topical or intralesional 5-FU can lead to inflammation and occasionally erosion of the skin. Long-term adverse effects include hyperpigmentation and, more rarely, hypopigmentation.[1] A meta-analysis found that combinations of 10% salicylic acid and 0.5%–5% 5-FU were more effective than salicylic acid alone in treating palmoplantar warts, with treatment response rates of 63.4% and 11%, respectively.[8]

The present study found that the response to this combination therapy was more rapid than that to the once daily salicylic acid–lactic acid combination therapy, but slower than that to salicylic acid–lactic-acid combination therapy applied under occlusion. Similarly, a previous study reported that 17% salicylic acid applied as a single layer under occlusion everyday was more effective than a topical combination of salicylic acid–lactic acid applied twice daily, with the mean treatment durations until disappearance of warts of 96 and 87 days, respectively.[9] In the present study, the solution was applied in three to seven layers at 3-day intervals under occlusion in the SA/LA 2 group. The mean treatment duration in this group was significantly shorter than that of the SA/LA 1 group. These findings suggest that the application of multiple salicylic acid–lactic acid layers under occlusion at longer time intervals is more effective than the application of a single layer under occlusion every other day. The difference in treatment duration between studies may also be attributed to differences in the ages of the study populations. Our study evaluated only pediatric patients, who can show a more rapid response than older patients.

Both salicylic acid–lactic acid combination therapies were well tolerated by patients in the present study, with the highest treatment compliance in the SA/LA 2 group.

Previous studies have reported variable responses to these treatment modalities, with differences in patient age, compliance to treatment, immune status, location and duration of the lesions, the clinical form of the warts, the method of applying treatment, and the ability of the person performing the procedure.[10] In the present study, the treatment duration was shorter in the SA/LA2 group than in the other groups. None of the patients in the SA/LA2 group were unresponsive to treatment or discontinued treatment as they were examined by physicians every 3 days.

Although this study had a retrospective design, there were no significant differences in the mean age and lesion duration before treatment among the three groups. Furthermore, the site of lesion clinical manifestations and performance of the explorer were similar in the three groups, thereby enabling comparison of treatment responses.

The limitations of this study include its retrospective design and small sample size. Prospective studies with larger sample sizes are required to confirm the study findings.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTION

Emine Müge Acar was involved in interpretation of data and revising it critically for important intellectual content. Belkız Uyar was involved in conception and design, acquisition and interpretation of data, analysis and interpretation of data. Ömer Faruk Elmas was involved in drafting the manuscript and revising it critically for important intellectual content. Kemal Özyurt was involved in drafting the manuscript and revising it critically for important intellectual content. Mustafa Atasoy was involved in revising critically for important intellectual content. Ümit Türsen was involved in revising critically for important intellectual content. Torello Lotti was involved in revising critically for important intellectual content. The manuscript has been read and approved by all authors. Each author has participated sufficiently in the work and met the requirements for authorship.

ETHICS STATEMENT

All procedures were performed according to the Declaration of Helsinki, and the study was approved by the concerned Institutional Review Board. Written informed consent was obtained from all participants.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request. The datasets generated during and/or analyzed during the current study are available from corresponding author on reasonable request.

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How to cite this article: Acar EM, Uyar B, Elmas ÖF, et al. Therapeutic efficacy and safety of three different modalities in pediatric patients with plantar warts. *Dermatologic Therapy*. 2021;34(5):e15073. https://doi.org/10.1111/dth.15073