

Treatment of Plantar Verrucae Using 2% Sodium Salicylate Iontophoresis

Background and Purpose. Iontophoretic sodium salicylate treatment of plantar warts was studied. **Subjects.** Twenty patients with 104 plantar verrucae were studied. **Methods.** Two percent sodium salicylate solution was administered iontophoretically (22.5 mA-minute/electrode, 3 treatments at 6- to 9-day intervals). **Results.** Nineteen subjects were followed. Verrucae area declined in 15 subjects (78.9%) and increased in 2 subjects (10.5%). One subject (5.3%) no longer had verrucae, and 1 subject (5.3%) exhibited no change. Overall, the number of verrucae and total area decreased. Four of 6 subjects (66.6%) with initial complaints of load-bearing pain reported diminished pain following treatment. Two subjects whose verrucae's size increased reported an increase in pain at the end of the study. **Discussion and Conclusion.** Sodium salicylate iontophoresis appeared to compare favorably with other office-based interventions in diminishing the size of plantar warts and their associated pain. Application of iontophoresis to weight-bearing surfaces in some subjects appeared to decrease the pain and scarring associated with freezing and electrocautery and the fixation problems associated with medicated patches. [Soroko YT, Repking MC, Clemment JA, et al. Treatment of plantar verrucae using 2% sodium salicylate iontophoresis. *Phys Ther.* 2002;82:1184–1191.]

Key Words: *Iontophoresis, Plantar verrucae, Sodium salicylate, Warts.*

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Plantar verrucae (plantar warts) are viral infections of the skin resulting in small benign tumors on the sole of the foot.¹ The infecting agent is the double-stranded DNA-containing human papilloma virus (HPV), with deep plantar warts being associated with HPV-1 and most other common warts elsewhere on the body being associated with HPV-4.^{2,3} The HPV enters through the skin surface after direct contact with an infected person or with recently shed viruses that have remained alive in a warm, moist environment, such as a locker room floor.¹ The incubation period ranges from 1 to 8 months.¹ Verrucae can be painful as well as communicable.⁴

Children and young adults, especially young athletes, are particularly prone to plantar warts, but elderly people without diabetes are rarely afflicted with them.^{1,5,6} Although no data exist on the infection rate of plantar warts,⁷ it is estimated that 7% to 10% of children and young adults may be affected.^{1,4,8} Plantar warts appear to be more common in women than in men.

The lesions are flesh-colored growths characterized by circumscribed hypertrophy of the papillae of the skin with thickening of the granular and keratin layers of the epidermis.⁹ Unlike warts elsewhere on the body, plantar verrucae are flattened by pressure, are surrounded by a smooth collar of thickened horn or cornified epithelium, and are extended deep into the epidermis (rete pegs). This type of wart generally forms beneath pressure points of the metatarsal heads or heel. The warts, however, may occur anywhere on the sole.¹⁰

Plantar warts may be difficult to diagnose. They can be very painful, and they must be differentiated from calluses, keratomas, lichen planus, and foreign bodies.^{6,11} Plantar verrucae can be distinguished from corns or calluses because verrucae are tender to touch or pinching, there are no continuous skin lines of affected tissue, there is a sharply defined rounded lesion with a rough keratotic surface surrounded by a smooth collar of thickened horn, and there are multiple small black points (dilated capillary loops) with a tendency for

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Figure 1.
Typical appearance of plantar verrucae.

pinpoint bleeding once the horn layer is pared away (Fig. 1).^{7,10} The size and number of the plantar warts can vary. Often they are found in clusters called “mosaic warts.” By contrast, debridement of a corn reveals a single “eye” (called a “hen’s eye”).¹

The duration of plantar warts is variable, and some warts can regress spontaneously, whereas in some adults, older children, and immunocompromised people, they can persist for years.^{7,10} Spontaneous regression occurs sooner in children than in adults unless hyperhidrosis or orthopedic pathology exists.¹² In children, the average duration is probably less than 1 year, and 30% to 50% of the warts disappear spontaneously over a 6-month period.⁷ Although some warts can regress spontaneously, they can be a source of physical discomfort and communicable disease. Therefore, many patients seek medical treatment.

Numerous strategies have been used by dermatologists and primary care physicians to treat plantar warts. Treatments can be categorized as either “destructive” or “immunologic.”¹ Destructive therapies include cryotherapy (eg, liquid nitrogen, spray guns), surgery (eg, electrocautery, laser ablation, excision), and chemotherapy via liquids and patches (eg, salicylic acid patch, lactic acid, trichloroacetic acid, cantharidin, podophyllin, formalin, fluorouracil). Immunotherapies include treatment with dinitrochlorobenzene (DNCB, an immunologic sensitizer), interferon, poison ivy extract, and so on.¹³ The most common office treatments include freezing with liquid nitrogen and electrocautery. Although the application of liquid nitrogen via cryoguns has recently been reported to result in a 92.5% healing rate after 3 treatments,¹⁴ cryosurgery can be painful. Electrocautery may leave an atrophic scar.

Acid formulations come in both liquid and transdermal variations. The transdermal delivery system may be preferred by patients because of the simplicity of replacing the patch every 48 hours, whereas the drops must be applied every night. The acid penetrates to a depth of 3 to 4 mm in passive patch applications.¹⁵ We believe the biggest disadvantage of both liquid and patch applications is the treatment time and the requirement for stringent patient adherence. In addition, in our experience, patches can slip if placed on weight-bearing surfaces.

In 1969, Gordon and Weinstein¹⁶ described a treatment in which plantar warts were treated with a 2% sodium salicylic solution delivered by iontophoresis. Their treatment was based on the use of direct current (DC) pushing the negatively charged salicylate ions into the tissue. They studied 5 patients using a current intensity of 1 mA for 10 minutes 1 time per week until the warts disappeared. In all 5 patients, the warts disappeared within 2 to 3 treatments, but this was a descriptive study without controls.

We contend that there are several benefits of iontophoresis treatment versus other traditional treatments for plantar verrucae. Treatment appears to be less painful with iontophoresis. A low-grade DC current is applied with the patient experiencing a mild prickly sensation that is felt only during the treatment time. In contrast, liquid nitrogen usually produces a painful burning sensation during the treatment and lasting up to 72 hours posttreatment.¹ In our experience, patients are able to place full weight on their foot posttreatment, which often is not the case with other treatments of plantar verrucae. Iontophoresis leaves no scars on the treated tissue, and the treatment is less labor intensive and fewer treatments are required than with other treatment strategies.

Based on an article by Gordon and Weinstein,¹⁶ we have been using 2% sodium salicylic iontophoresis treatment of plantar verrucae since the 1970s. We viewed this treatment as an effective alternative to other treatments of plantar verrucae. However, there have been no follow-up studies examining the efficacy of 2% sodium salicylate iontophoresis treatment of plantar verrucae. The purpose of this descriptive study is to report the use of 2% sodium salicylate iontophoresis treatment of plantar verrucae on 20 consecutive referrals to the physical therapy clinic. We, however, like Gordon and Weinstein, did not conduct a clinical trial with random assignment to group and a control.

Table 1.
Initial Characteristics of the Participants

Sex	Age (y)					Duration of Verrucae (mo)			
	\bar{X}	SD	Range	Median	n (%)	\bar{X}	SD	Range	Median
Male	18.8	17.2	3.5–41.8	41.8	6 (31.6%)	37.3	45.2	6–120	15
Female	20.2	13.7	6.2–55.0	16.2	13 (68.4%)	21.5	30.8	6–120	12

Method

Subjects

The study population consisted of patients referred to the Marshfield Clinic-Wausau Center Physical Therapy Department for plantar wart treatment. Patients were screened for inclusion by use of the following criteria: they had plantar verrucae for 6 months or greater, they had no prior iontophoresis treatment for the wart(s), and they received no treatment for the wart(s) within 1 month of participation in the study. In addition, the participants had to have no history of immunocompromise, diabetes, or circulatory or sensory disorders, and they gave consent to participate in the study. In the case of minors, a parent or responsible guardian gave consent. Twenty patients (13 female, 7 male) satisfied the inclusion criteria and elected to participate. Fifteen of the 20 patients were under 20 years of age. All 20 patients completed the treatment protocol, but 1 patient refused to return for the follow-up assessment, leaving 19 patients for the analysis in this report (Tab. 1).

Seven subjects (37%) reported one or more unsuccessful prior treatments to remove their warts, including use of over-the-counter medications (4 subjects), liquid nitrogen (4 subjects), salicylic acid adhesive plasters, and electrosurgical dissection (1 subject each). One subject reported 5 prior treatments, including injection, cantharidin in acetone, and laser. Two subjects reported unspecified other treatments.

Treatment Protocol

The patients were placed on a plinth in a semi-reclined position with the lower leg exposed. The location and size (diameter in millimeters) of the plantar verrucae were recorded and photographed. The patients were asked to rate their load-bearing pain as a result of their plantar verrucae using a 0 to 10 ascending visual analog scale (0=no pain, 10=excruciating pain). Each verruca was cleaned with alcohol, and the wart horn was pared with a scalpel to decrease the skin impedance. Deeply fissured tissue was filled with petroleum jelly to impede the flow of current while leaving the intact skin surrounding the wart jelly-free to allow for salicylic acid penetration.

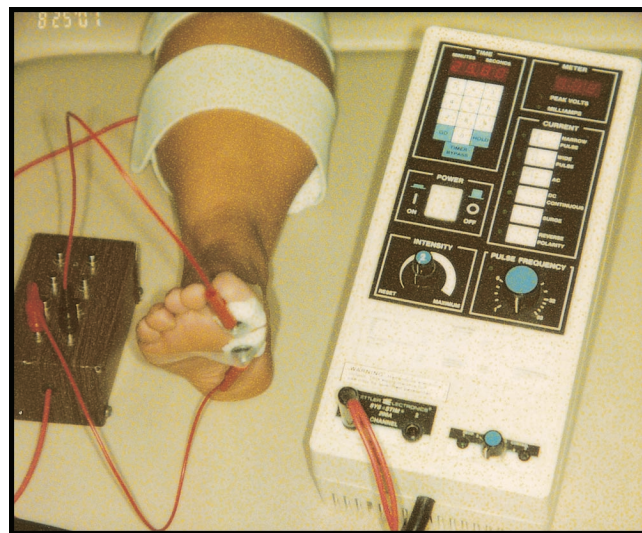


Figure 2.
Setup of iontophoresis treatment using Mettler electrical stimulation machine in direct current mode.

A 7.62- × 15.24-cm (3- × 6-in) dispersive pad was wetted with tap water and secured on the mid-belly of the ipsilateral gastrocnemius muscle using elastic straps. The active electrode was created by dampening two 12-ply 5.08- × 5.08-cm (2- × 2-in) gauze pads with a 2% sodium salicylate solution. The gauze pads were then folded twice to create a 2.54- × 2.54-cm (1- × 1-in), 8-layer electrode. The folded electrode was saturated with the 2% sodium salicylate solution and wiped over the verruca(e) to ensure wetness and to decrease impedance. The electrode was then placed over the surface of the wart or cluster of warts. The metal lead and gauze pad were affixed with tape (Fig. 2). The patients were informed that they might feel an itchy or prickly sensation during the treatment under the active or dispersive electrode. Any burning sensation indicated potential for skin burning secondary to the DC effects, and the current was decreased.

A Mettler electrical stimulation machine (Sys-Stim Model 206A*) was used. The output current lead was modified by running it through a current splitter to increase the active output channels from 1 to 8 potential

* Mettler Electronics Corp, 1333 S Claudina St, Anaheim, CA 92805.

Sample calculations for the adjustment of electrical current variables to equal 22.5 mA-min/electrode (not to exceed 0.23 mA/cm² or 1.5 mA per square inch of active electrode)

- If treating with one 2.54- × 2.54-cm (1- × 1-in) active electrode at 1.5 mA, the treatment time is 15 min.

$$1.5 \text{ mA/electrode} \times 15 \text{ min} = 22.5 \text{ mA-min/electrode.}$$

$$1.5 \text{ mA}/6.452 \text{ cm}^2 = 0.23 \text{ mA/cm}^2.$$

- If less current is tolerated per active electrode, increase the treatment time to reach 22.5 mA-min/active electrode.
- For example, if using one 2.54- × 2.54-cm (1- × 1-in) active electrode and only 0.9 mA current is tolerated, what should be the treatment time?

$$22.5 \text{ mA-min/electrode} \times 1 \text{ electrode}/0.9 \text{ mA} = 25 \text{ min.}$$

$$0.9 \text{ mA}/6.452 \text{ cm}^2 = 0.14 \text{ mA/cm}^2 \text{ current being delivered per active electrode.}$$

- If using two 2.54- × 2.54-cm (1- × 1-in) electrodes, the maximum current is 3.0 mA for 15 min to achieve 22.5 mA-min/electrode.

$$3.0 \text{ mA}/2 \text{ electrodes} = 22.5 \text{ mA-min/electrode.}$$

$$3 \text{ mA}/(2 \times 6.452 \text{ cm}^2) = 0.23 \text{ mA/cm}^2 \text{ current being delivered per active electrode.}$$

- If using more than 1 active electrode, divide the tolerated current by the number of electrodes to find the current intensity per electrode.
- For example, if using three 2.54- × 2.54-cm (1- × 1-in) pads, we may find that 4.0 mA is the tolerated current. What should be the treatment time?

$$4.0 \text{ mA}/3 \text{ electrodes} = 1.3 \text{ mA per active electrode. Treatment dose is } 22.5 \text{ mA-min/electrode. Therefore, } 22.5 \text{ mA-min/electrode divided by } 1.3 \text{ mA} = 17 \text{ min.}$$

$$4.0 \text{ mA}/(3 \times 6.452 \text{ cm}^2) = 0.21 \text{ mA/cm}^2.$$

Figure 3.
Sample calculations.

channels (Fig. 2). This allowed for more than one plantar wart area to be treated simultaneously. The stimulator was initially set with the following variables: continuous DC, 25 minutes' duration. The current was increased slowly in order to accommodate for DC sen-

sation. Once the maximum current that was tolerable to the patient was reached, the total treatment time was calculated and the treatment timer was set. Variables were subsequently adjusted so that the total treatment amounted to 22.5 mA-minute per electrode, with the maximum current never exceeding 0.23 mA/cm² (1.5 mA/in²) for the active electrode (Fig. 3).

At the end of treatment, skin areas were checked for skin color and clarity. We expected to find light pinkness of the skin. Any bright pinkness or blistering would have indicated DC burning, and appropriate burn treatment would have been initiated. No incidents, however, of blistering or burning occurred. The patients were asked to rate their load-bearing pain posttreatment.

Treatments were repeated once per week for a total of 3 sessions, with 6 to 9 days between treatment sessions. After the final session, no other treatment was allowed for a 3-month period. The 3-month period was chosen because epidermal turnover time in normal skin is 52 to 75 days.⁷ The patient was informed that the verrucae may turn black or dark brown within the 3 months following treatment as a result of verruca necrosis. Fourteen to 26 weeks (\bar{X} =16.7, SD=2.8, median=15.7) after the initial visit, the patient was rechecked for wart status. The treated wart area was photographed, and the wart size was measured if a wart was still present. Patients were again asked to rate their load-bearing pain on a 0 to 10 ascending scale.

Data Analysis

Data analysis consisted of descriptive summaries of verrucae dimensions and examination findings. Changes over time were assessed in terms of the numbers and total area of verrucae and were tested for statistical significance using the Wilcoxon signed rank test on paired differences (P =.05).

Results

The average number of verrucae per patient was initially 5.5 (SD=4.9, range=1-17), with a total of 104 verrucae

Table 2.
Numbers and Size of Verrucae (Sample Size=19)

	Initial Visit			3 Months Posttreatment			P ^a
	\bar{X}	SD	Range	\bar{X}	SD	Range	
No. of verrucae	5.5	4.9	1-17	3.7	3.8	0-15	.016
Total affected area (mm ²)	95.1	74.7	14-256	62.6	77.7	0-308	.007

^aWilcoxon signed-rank test on paired differences ($P=.05$).

treated. The patients had these warts anywhere from 6 to 120 months ($\bar{X}=26.5$, $SD=35.5$, median=12) (Tab. 1).

The mean total area of verrucae before treatment was 95.1 mm² (range=14-256 mm²) (Tab. 2). During the follow-up assessment, only one subject demonstrated 100% reduction (from 75 to 0.00 mm²). Three subjects exhibited large reductions: 99.9% (from 150.45 to 0.79 mm²), 97.7% (from 69.41 to 1.57 mm²), and 89.2% (from 43.24 to 4.67 mm²). Twelve other subjects also experienced measurable reductions in verrucae area (Fig. 4). One patient who initially had one wart exhibited no change. Two patients' verrucae increased in size (Fig. 5). Only 1 of 19 patients had no warts following treatment, but 15 of 19 patients (78.9%) exhibited reductions in verrucae area. The median change in area as a percentage of the initial measurement per patient was a decrease of 30% ($\bar{X}=27.4\%$, $SD=72.8\%$, range = -100% to +228%). There were decreases over time in both the number of verrucae and the area of the warts. There were no adverse events associated with the treatment.

Thirteen of 19 patients reported no initial pretreatment load-bearing pain and no pain at follow-up. Four patients reported a reduction of pain at the time of follow-up: from 9.0 to 5.0, from 3.0 to 2.5, from 2.5 to 0.0, and from 1.0 to 0.0. Two patients reported increased pain, and these were the patients who had increased verrucae size posttreatment (from 0.0 to 5.0, from 6.0 to 9.0). There were no cases of burning.

Discussion

Since the report of Gordon and Weinstein,¹⁶ no other reports describing the use of iontophoresis to deliver salicylic acid to plantar warts have appeared. Although our experience did not provide the healing rate initially reported by Gordon and Weinstein,¹⁶ we found that our outcomes compared favorably with those for other office-based treatments.¹⁷ Of the 15 patients with verrucae covering the largest areas, 2 patients' verrucae increased in area, 1 patient exhibited no apparent change, and 12 patients exhibited substantial reductions in area (Fig. 5).

One 4-year-old patient who had 3 plantar verrucae (Fig. 6A) had notable reduction in verruca area with one wart abolished (Fig. 6B) at the time of follow-up (initial mean area=23.14 mm², minimum=14.54, maximum=35.26; follow-up mean area=0.52 mm², minimum=0.00, maximum=0.79). Due to this patient's improvement, an additional follow-up was conducted 1 month following what

would have been the final assessment. The patient when seen 5 weeks later had complete abolishment of all verrucae.

Two patients had expanded plantar verrucae area at the time of follow-up. No intervention has ever been shown to be 100% effective for treatment of viral warts; therefore, our results were not surprising. Warts may even recur in 20% to 40% of cases using surgical excision or electrocautery.¹⁰ Human papilloma virus (viral protein and infectious particles) can exist in a subclinical state in tissues surrounding a lesion, leading to changes in the skin that cannot be seen with the naked eye. Were this the case, the 2.54- × 2.54-cm (1- × 1-in) electrode may not have covered an ample surface area of nonvisible affected tissue. Therefore, in some cases, treating only abnormal-appearing skin does not necessarily treat the field of viral particles around each lesion.⁴ Recurrence of this sort is known as the "Koebner phenomenon," also called the "isomorphic response," and refers to the appearance of new lesions along a site of injury.¹⁴

We believe the use of salicylic acid remains one of the safest wart treatments. It promotes keratolysis of virally infected tissue.¹³ Often used in combination with other acids, such as lactic acid, salicylic acid has recently been shown to most likely be the active ingredient. Fourier transform Raman spectroscopy has been used to show that salicylic acid (and not lactic acid or flexible collo-dion) bonds with HPV-containing verruca tissue.¹⁸

Because plantar warts are usually located on weight-bearing surfaces of the feet, treatment choices become limited. We argue that iontophoresis has the advantage of being painless, and most patients are able to bear weight on the area with no pain immediately following treatment. In addition, the treatment leaves no scars. In one of our patients, a 4-year-old, the verrucae were located on the heel, causing the patient to toe walk. After the third session, this patient had a completely normal gait. This contrasts dramatically with the pain that can follow the use of liquid nitrogen treatment.

Aggressive destructive treatment modalities (eg, cryosurgery, electrocautery), in our view, are undesirable due to

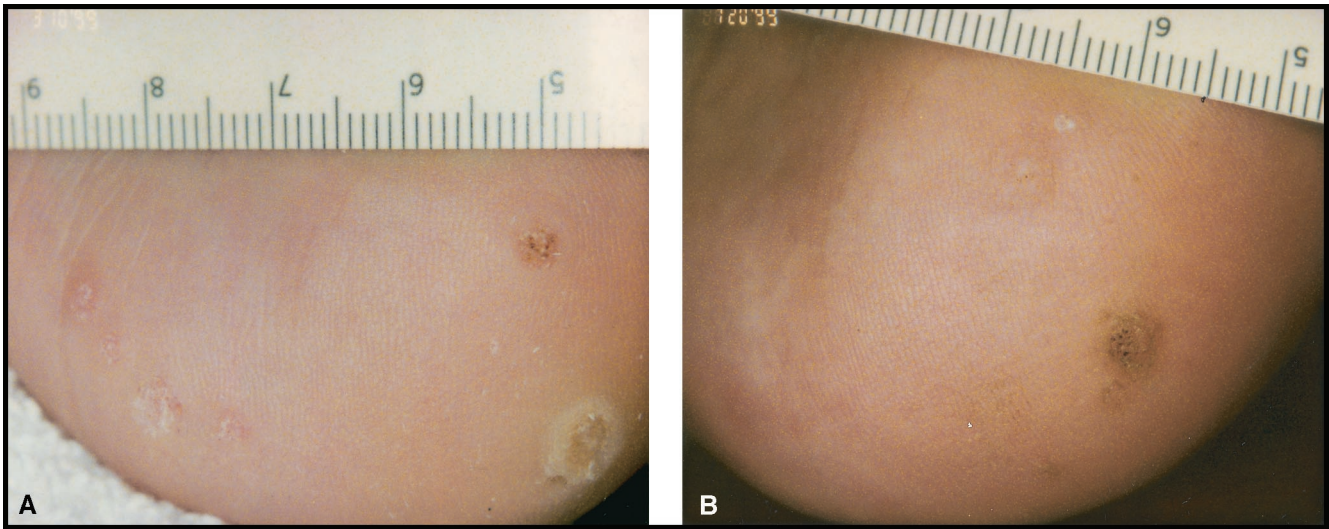


Figure 4. Verrucae demonstration of reduction in size and appearance with iontophoresis treatment: (A) before treatment, (B) after treatment and 3-month waiting period.

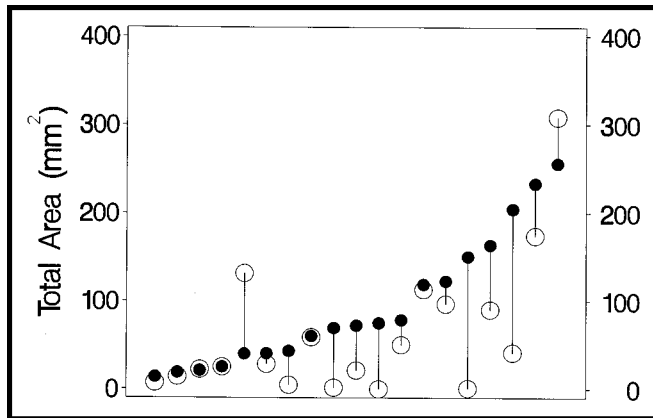


Figure 5. Total verrucae area, by patient, at the initial and follow-up assessments. Each filled circle (●) shows one patient's initial area and is connected to an open circle (○) showing the area at follow-up for the same patient.

resultant discomfort and interference with the patient's routine activities. Less aggressive chemical treatments, we believe, often do not yield desired results due to lack of patient adherence or ability to maintain contact of treatment agent with the wart.

Iontophoresis can be used to deliver the acid into the tissue in 20- to 30-minute sessions over only a few treatments. The acid is believed to penetrate to a depth of 10 mm when applied iontophoretically.¹⁹ Thus, favorable effects on deeply concentrated verrucae may occur. In addition, no patient adherence, other than appearing for the scheduled appointments, is needed. Iontophoresis as a clinical option has been used by physical therapists and dermatologists for over 50 years without documented severe adverse reactions.¹⁹⁻²² Our research demonstrates that iontophoretic application of salicylic

acid to plantar warts represents a viable option for treatment.

Limitations

We did not include a control group or a comparison group, so the response to treatment can only be assessed indirectly and may be influenced by confounding factors. A randomized controlled clinical trial is needed. It is often difficult to differentiate between a healed wart scar and a recurrent wart.¹ Furthermore, warts that do not resolve frequently proliferate.¹ Both of these phenomena would skew the results toward a lower frequency of healing than would be the case for responsive lesions only.

Suggestions for Further Research

The number of treatment sessions and the frequency of treatment we used were based on the article by Gordon and Weinstein,¹⁶ not on the half-life of the medication or the physiological response to DC. Manipulation of both the number and frequency of treatments may lead to better clinical outcomes. Because HPV can exist in a subclinical state, we suggest that the size of the active electrode should be increased to more thoroughly cover and treat the field of viral particles around each lesion. Comparison of DC with non-DC delivery of salicylic acid seems warranted. Recent literature on iontophoresis suggests that application of continuous DC may be limiting. Using reversed or pulsed DC has been reported to decrease skin irritation and thus allow higher medication dosages.²³

Conclusions

Based on our series of 19 patients, we feel that iontophoresis of salicylic acid provides a preferred treatment

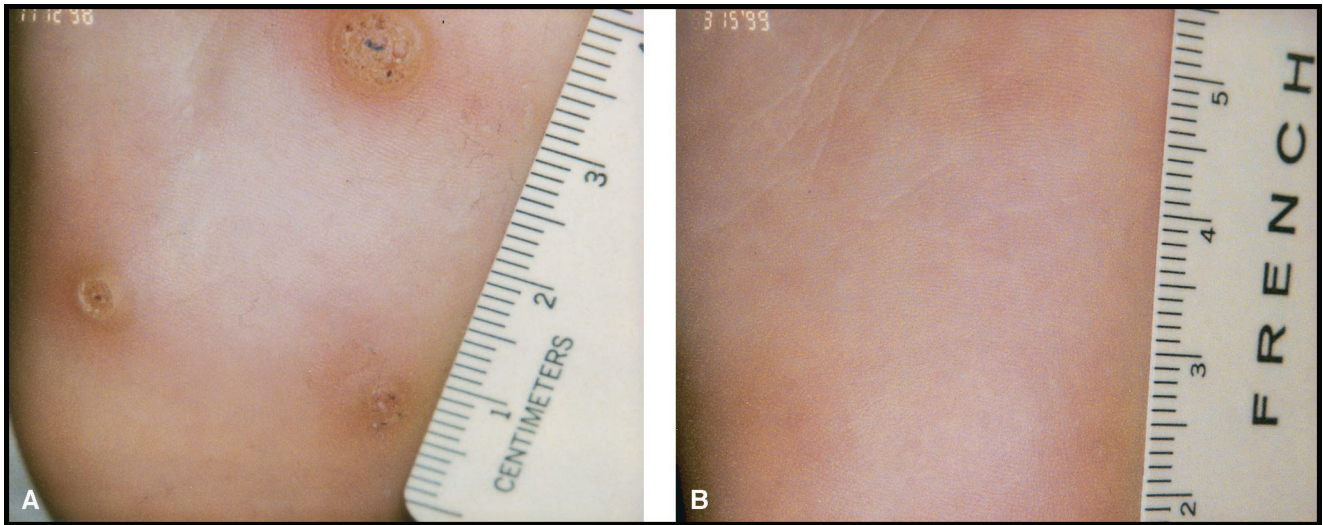


Figure 6. Plantar verrucae of 4-year-old patient (A) at the time of initial evaluation and (B) after treatment and 3-month waiting period.

option that offers results comparable to those of other more invasive, painful, time-consuming, and expensive interventions such as freezing, electrocautery, and medicated patches. Treating plantar warts with salicylic acid requires minimum patient adherence, is safe, and appears to have a minimum of deleterious side effects.

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