

ORIGINAL ARTICLE

The treatment of plantar warts using microwave—A review of 85 consecutive cases in the United States

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Abstract

Background: Plantar warts (verrucae plantaris) are a common source of pain for patients and are often refractory to treatment. Previous work has shown a high clearance rate of verrucae using a surface-based microwave device (Swift®).

Aims: To assess the efficacy, defined as the complete visible clearance of warts, in patients with verrucae plantaris receiving microwave treatment.

Patients: We undertook a retrospective review and identified records of 85 patients who underwent a course of microwave treatment at a single US-based podiatry centre. Efficacy was analyzed on the basis on intention-to-treat.

Results: In patients who received ≥ 1 session there was a complete clearance rate of 60.0% (51/85) (intention-to-treat; 59 patients completed treatment, 26 lost to follow-up) and 86.4% (51/59) per treatment completion; no significant differences in clearance rates of children and adults were observed (61.0% [25/41] vs. 59.1% [26/44]). There were 31 patients who received three sessions of microwave therapy with a clearance rate of 71.0% (22/31) as per intention-to-treat (27 patients completed treatment, 4 lost to follow-up). An average of 2.3 sessions (SD: 1.1; range: 1–6) was required for the complete clearance of plantar warts. Complete clearance was also observed in some patients with recalcitrant warts following additional treatment sessions (42.9% [3/7]). A significant reduction in wart related pain was reported for all patients undergoing treatment. Some patients continued to report a reduced amount of pain post-therapy compared with pretherapy.

Conclusions: Microwave treatment of verrucae plantaris appears to be a safe and effective procedure.

KEYWORDS

foot, HPV, microwave, verruca, wart

1 | INTRODUCTION

Warts are a common dermatological diagnosis caused by the human papillomavirus (HPV). Lesions arising on the skin can present a therapeutic challenge, particularly those arising on the plantar surface of the foot (verrucae plantaris). Clinical experience and guidelines suggest that plantar lesions are more resistant to traditional treatments like cryotherapy and salicylic acid compared with lesions elsewhere on the skin leading to chronicity, particularly in adults.¹ Moreover, lesions can be a cause of embarrassment and limit sporting and other activities.² In 2000, Dyall-Smith remarked how little verruca treatments had changed since the 1950's and this still holds true today.^{3,4}

Traditionally, freezing of warts or cryotherapy has been the mainstay of treatment. However, research in the last decade or so has studied the positive effects of heating the skin in the treatment of tumors and skin cancers.⁵ Heating the skin to just above normal body temperature (hyperthermia) using various methodologies has been shown to have a range of positive benefits on modifying the immune response.⁶ The Swift® microwave unit (Emblation Limited, UK) is a medical device licensed in the USA and Canada for the treatment of surface lesions by utilizing microwave energy to heat skin through the application of a probe.^{7,8} The device was FDA cleared in 2018 for the coagulation of soft tissue during noninvasive procedures.⁷ It was Health Canada approved in 2017 for microwave treatments in the fields of dermatology and podiatry.⁸ To date, there has been no efficacy data reported from the United States for the treatment of plantar warts. The present study reviews the outcomes of microwave treatment for plantar warts from an early adopting podiatry clinic in New York.

2 | METHODS

We performed a retrospective review of all patients who had undergone a course of microwave treatment for their verrucae plantaris at one podiatry practice location. All patients provided consent. Exclusion criteria were diabetics, those with peripheral vascular disease as evidenced by lack of palpable pedal pulses, and women who were pregnant. Pain symptoms associated with warts were assessed using a 10-point pain scale (ranging from 0—no pain to 10—worst pain imaginable) prior to the first treatment and at the final assessment appointment.

A course of treatment was defined as at least one session of microwave treatment with a follow-up appointment at least 4 weeks after the last session. Treatment response was defined as complete visible clearance of the wart, with return of the normal dermatoglyphics across the skin previously occupied by the wart. In each treatment session, local hyperthermia was induced through repeated microwave applications lasting 2 s each, which supplied energy at a frequency of 8 GHz and an average power of 8.0 W (SD: 0.3; range 6–8). Pretreatment paring or debridement were not routinely performed unless the wart surface did not provide a flat surface for the microwave applicator tip. Each wart received an average of five

microwave applications per session (SD: 0.1; range 5–6). After the primary session of treatment, additional treatment sessions could be provided at a follow-up if treatment response was not achieved. If treatment discomfort occurred, administration of a local or topical anesthetic was considered.⁹ All verrucae were treated and reviewed at each visit by the same clinician (RMC).

Of note, patient treatment was ongoing during the period of the US SARS-CoV2 (COVID-19) pandemic. Review of data records in this period resulted in an undesirable proportion of subjects (40%) not pursuing full courses of treatment and follow-up as a result of ongoing pandemic restrictions of travel and lifestyle. To account for the missing data in as conservative a method as possible, an intention-to-treat (ITT) analysis was primarily used where subjects considered lost to follow-up were counted as treatment failures. This provides for a “worst-case” scenario of treatment efficacy, and the resulting ITT data here is likely an underestimate of actual microwave efficacy for plantar warts, had the patients pursued full courses of treatment and follow-up. Despite the challenging clinic period, the overall number of patients completing full courses of treatment remained suitably high (>50 patients) to allow for reliable statistical analysis; hence efficacy analysis per treatment completion were conducted as well.

Data were tabulated using the Excel® software package and analyzed using one-way ANOVA, paired t-test, and the chi-square test; $p < 0.05$ is considered statistically significant.

3 | RESULTS

3.1 | Patient characteristics

Upon review of the data, a total cohort of 85 patient records (38 females and 47 males), totaling 254 verrucae plantaris were available for inclusion in the review representing a complete, consecutive cohort of cases from March 2019 to December 2020 (Figure 1). The age of the study cohort ranged from 5 to 78 years (mean: 28.6 [SD: 20.7]), with an average of 3.17 verrucae diagnosed per patient (SD: 6.74; range: 1–50), and a mean baseline patient-reported pain score of 3.4 out of 10 (SD: 1.1; range: 2–8). Evidence of treatment recalcitrance, defined as verrucae either persisting for ≥ 24 months or with inadequate response after ≥ 2 treatments, was seen in 25.9% (22/85) and 34.1% (29/85) of patients, respectively.¹⁰ Patients, on average, had two or three previous unsuccessful treatments with other modalities prior to receiving microwave. For patients whose treatment response to microwaves was inadequate after the first session, additional sessions were administered with an average intertreatment interval of 1.4 months (SD: 1.1; range 1–7). Post-treatment assessments were conducted at an average of 2.0 months (SD: 2.0; range 1–12) after the last session.

Baseline and disease severity parameters stratified by the number of completed treatment sessions are summarized in Table 1. We observed a higher proportion of recalcitrant verrucae plantaris associated with patients requiring ≥ 3 treatment sessions; specifically, the proportion of patients with persisting verrucae for ≥ 24 months increased from 16.7% (5/30) and 11.8% (2/17) to 32.3% (10/31) and

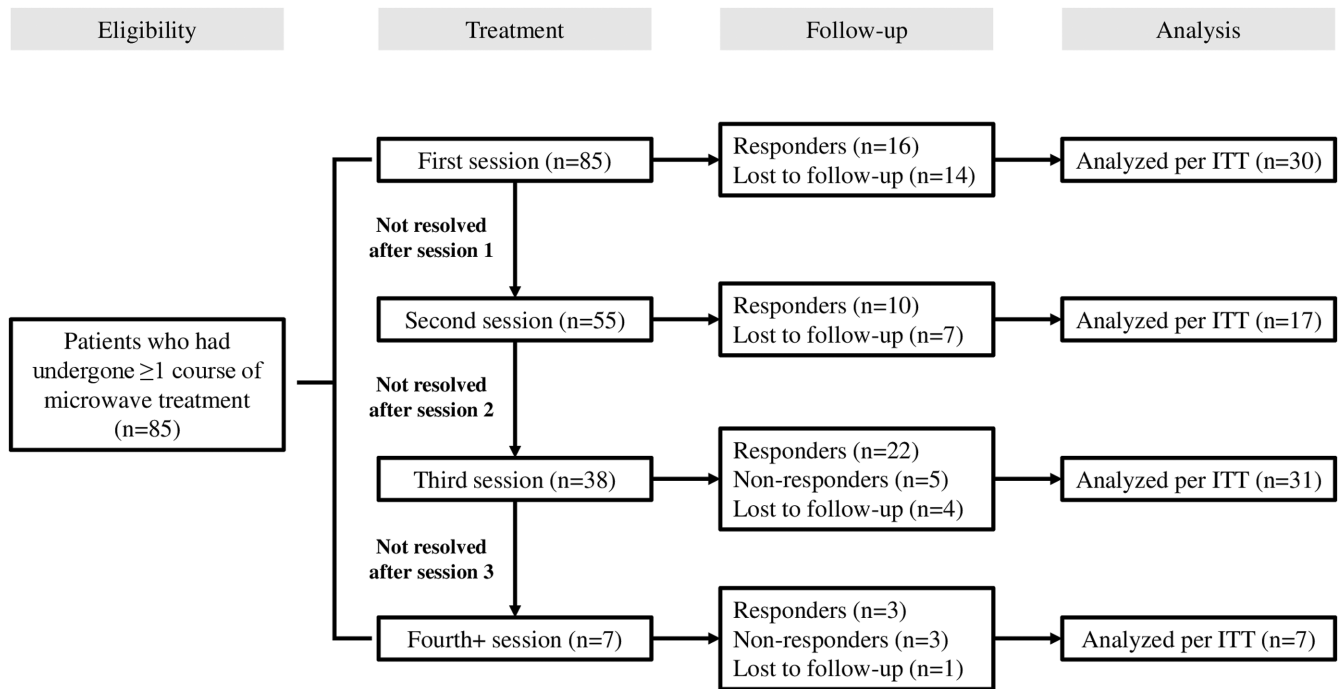


FIGURE 1 Study design. From March 2019 to December 2020, medical records of 85 patients with verrucae plantaris who had undergone one or more sessions of microwave treatment were reviewed. Clinical data were assessed based on the number of microwave therapy sessions administered. Missing data due to lost to follow-up were imputed as nonresponders. ITT, intention-to-treat.

TABLE 1 Baseline characteristics of 85 patients with verrucae plantaris who had undergone one course of microwave treatment ranging from completing one session to four or more sessions.

Parameters	Microwave Treatment			
	1 Session (n = 30)	2 Sessions (n = 17)	3 Sessions (n = 31)	4+ Sessions (n = 7)
Female % (n)	43.3 (13/30)	41.2 (7/17)	48.4 (15/31)	42.9 (3/7)
Male % (n)	56.7 (17/30)	58.8 (10/17)	51.6 (16/31)	57.1 (4/7)
Age, year				
Mean (SD)	23.4 (17.2)	19.5 (16.9)	34.2 (23.4)	47.7 (11.1)
Median (range)	16.5 (6–63)	13 (7–67)	36 (5–78)	53 (24–56)
No. of warts				
Mean (SD)	3.7 (5.6)	2.1 (3.4)	3.4 (8.8)	1.9 (1.1)
Median (range)	2 (1–30)	1 (1–15)	1 (1–50)	2 (1–4)
Duration of lesions % (n)				
< 24 months	83.3 (25/30)	88.2 (15/17)	67.7 (21/31)	28.6 (2/7)
≥ 24 months	16.7 (5/30)	11.8 (2/17)	32.3 (10/31)	71.4 (5/7)
No. of prior failed treatments % (n)				
< 2 treatments	80 (24/30)	64.7 (11/17)	61.3 (19/31)	28.6 (2/7)
≥ 2 treatments	20 (6/30)	35.3 (6/17)	38.7 (12/31)	71.4 (5/7)
Baseline pain score				
Mean (SD)	3.3 (1.2)	3.8 (1.5)	3.3 (0.9)	3.3 (0.8)
Median (range)	3 (2–7)	3 (2–8)	3 (2–5)	3 (3–5)

71.4% (5/7) for patients requiring one session, two sessions, three sessions or ≥4 sessions, respectively (Table 1). Similar increases were also observed in proportion of patients with histories of two or more prior failed treatments.

3.2 | Efficacy of microwave treatment

Of the 85 patients who received ≥1 microwave session, a total of 59 patients completed their treatment and 26 were lost to follow-up

(30.6% [26/85]). There were 51 patients who achieved the treatment endpoint during follow-up (60.0% [51/85] clearance rate as per intention-to-treat; clearance rate as per treatment completion was 86.4% [51/59]; Table 2). Representative cases of complete and partial resolution are shown in Figures 2 and 3, respectively. Patients required an average of 2.3 sessions (SD: 1.1; range: 1–6) to achieve the treatment end point. Most patients included in this study required up to three treatment sessions over approximately 12 weeks (with the intention to treat clearance rate of 61.5% (48/78); clearance rate per treatment completion was 90.6% [48/53]; Table 2), similar to existing microwave treatment data and other standard wart treatment patterns and time frames reported in the literature (Figure 4).^{9–14} Clearance rates (per ITT) were numerically higher in patients who received one or two additional treatment sessions after the primary session (χ^2 [2, $N=78$]=2.07, $p=0.36$), with up to 71.0% (22/31) achieving the treatment end point after completing the third session, compared with 55.3% (16/30) and 58.9% (10/17) for the first and second session, respectively (Table 3).

In the overall study population, there were no statistically significant differences in the clearance rate of patients with nonrecalcitrant warts versus recalcitrant warts, where recalcitrance was defined by warts lasting for ≥ 24 months (63.5% nonrecalcitrant [40/63] vs. 50% recalcitrant [11/22]) (χ^2 [1, $N=85$]=1.24, $p=0.27$), or where recalcitrance was defined by prior inadequate response to ≥ 2 treatments (58.9% nonrecalcitrant [33/56] vs. 62.1% recalcitrant [18/29]) (χ^2 [1, $N=85$]=0.079, $p=0.78$). Compared with the overall population, patients requiring between four and seven sessions exhibited a much higher proportion of recalcitrance based on warts lasting for ≥ 24 months, and prior inadequate response to ≥ 2 treatments, compared with patients with three or fewer treatments (Table 1); the relatively low response rate of 42.9% (3/7) for 4–7 treatments versus three or fewer treatments could be attributed to continuing or developing recalcitrance in this sample set (Table 3). Most notably, one patient with two verrucae persisting for 84 months, and 11 prior failed treatments, did not achieve the treatment end point after the fourth microwave session. However, another patient with 31 prior failed treatments, and verruca persisting for 24 months, achieved clearance of verrucae plantaris after the fifth treatment session.

Efficacy analysis by age groups found clearance rates for children (≤ 18 years) and adults (>18 years) at 61.0% (25/41) and 59.1% (26/44), respectively (Table 4). No statistically significant differences were observed (χ^2 [1, $N=85$]=0.03, $p=0.86$).

3.3 | Pain assessment

Patient-reported wart pain scores at matching pretreatment, during the treatment visit period, and post-treatment time points were available for 53 patients who completed between one and three sessions. The mean wart pain scores were 3.3 (SD: 1.0; range: 2–7), 3.1 (SD: 0.9; range: 0–5), and 0.08 (SD: 0.4; range: 0–3) for pretreatment, during treatment and post-treatment periods,



FIGURE 2 Patient presenting with recalcitrant plantar warts achieving complete resolution after microwave treatment. A 14-year-old male, with no known history of diabetes, presented with mosaic lesions on the hallux and second toe of the right foot. Lesions have persisted for 3 years, prior treatments were unsuccessful including salicylic acid, cryotherapy, and imiquimod. The patient subsequently received two sessions of microwave treatment at 4 weeks apart. Photographic assessment of the hallux was conducted at (A, C) baseline and (B, D) 12-week review.

TABLE 2 Efficacy of microwave treatment in patients with verrucae plantaris shown as per standard treatment pattern of up to three sessions, and in all patients who received one or more sessions.

Microwave sessions	Completed/lost to FU (n/n)	Clearance rate per ITT ^a % (n)	Clearance rate per treatment completion ^b % (n)
Up to 3 sessions (n=78)	53/25	61.5 (48/78)	90.6 (48/53)
≥ 1 session (n=85)	59/26	60.0 (51/85)	86.4 (51/59)

Abbreviations: FU, follow-up; ITT, intention-to-treat.

^aMissing data were analyzed as “nonresponders” (i.e., treatment failure).

^bMissing data were excluded from the analysis.

respectively. Compared with pretreatment, no statistically significant changes in pain levels were observed during treatment, while pain levels significantly decreased post-treatment regardless of

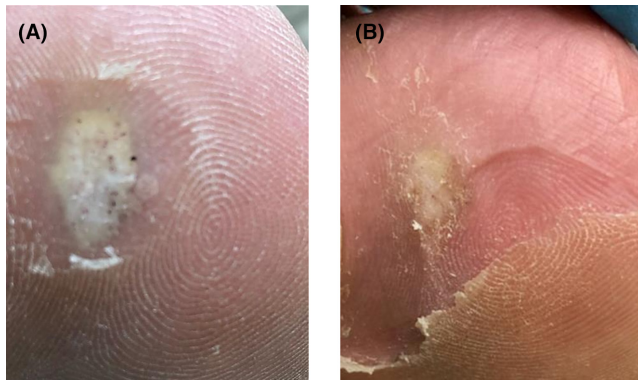


FIGURE 3 Patient presenting with a large recalcitrant plantar wart achieving partial resolution after microwave treatment. A 44-year-old healthy, athletic male, with no know history of diabetes, presented with a large (2.5 × 1 cm) lesion on the right foot. The lesion has persisted for 2 years, prior treatments consisting of salicylic acid, cryotherapy, imiquimod, debridement, and needling were unsuccessful. The patient subsequently received four sessions of microwave treatment at 4 weeks apart, and two additional sessions at 8 weeks apart. Photographic assessment was conducted at (A) baseline and (B) 36-week review.

the number of sessions ($p < 0.0001$; Figure 5). All patients with total clearance of their warts, and all patients who completed one or two sessions, reported pain scores of 0 at follow-up. Two patients who did not achieve clearance after three sessions reported pain scores of 1 and 3.

3.4 | Safety

One adverse event of ulceration, following the administration of local anesthetic prior to microwave treatment, was reported. A previous survey study of patients who had received Nd:YAG laser for wart treatment reported an ulceration rate of 40% (4/10) in patients who underwent local infiltration of the lesion prior to laser application.¹⁵ It is possible that injections of anesthetic in the tissue increases local fluid content, which creates a greater target for microwave with subsequently increased heating of the area undergoing treatment. Additionally, patient feedback on pain would be absent, leading to an increased risk of overtreatment, and hence ulceration. In the current study, only one patient received pretreatment local anesthesia. This patient subsequently developed ulceration at the treatment site, which led to the cessation of any local anesthesia administration at subsequent visits and no further ulceration was observed. There were no other adverse reactions.

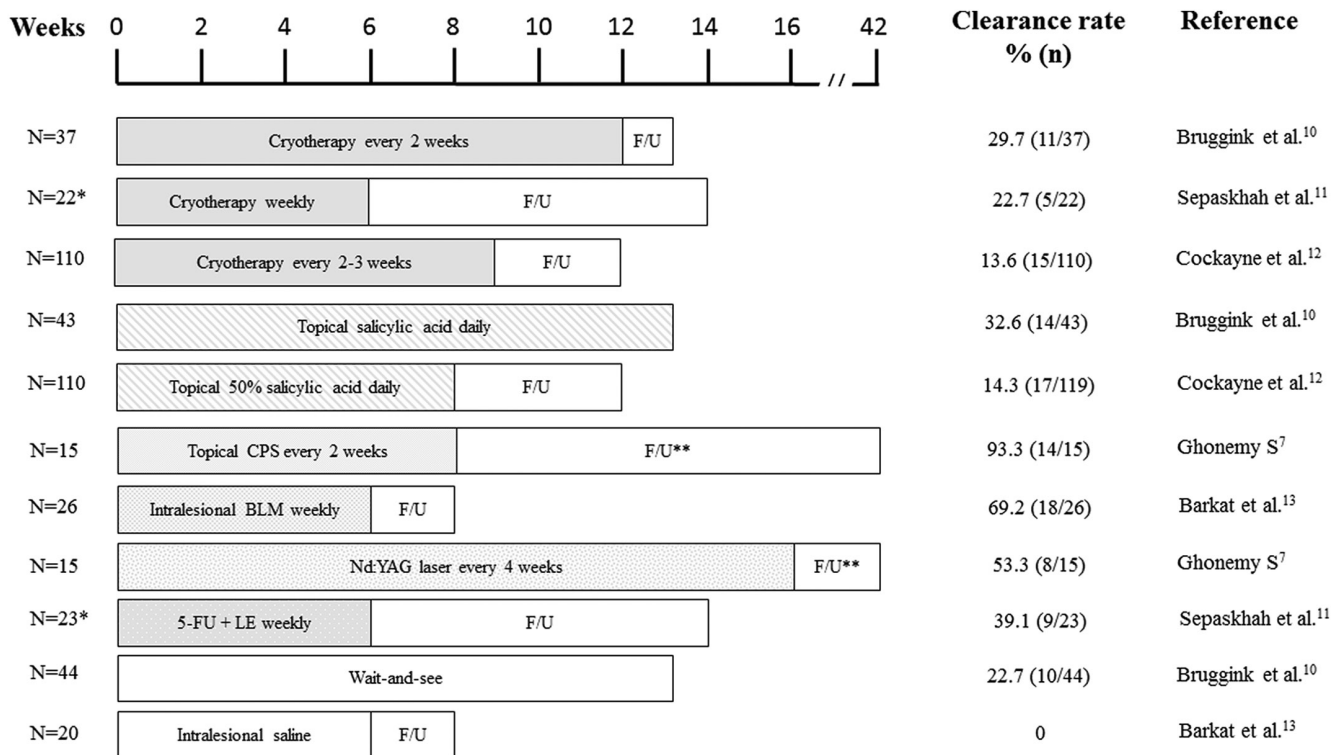


FIGURE 4 Previously reported clearance rates of other treatment modalities for verrucae plantaris. Clearance rates, defined as the complete visible clearance of warts with or without dermoscopic evaluation, were extracted from five studies treating patients with cryotherapy, salicylic acid, 5-fluorouracil, and/or bleomycin.¹⁰⁻¹⁴ Data from matching control or placebo groups were also extracted if available. *Mixed patient cohort of common and plantar warts. **Follow-up assessment was conducted 6 months after the end of study. BLM, bleomycin; CPS, 1% cantharidin, 20% podophyllin resin, and 30% salicylic acid; F/U, follow-up; 5-FU + LE, intralesional 5-fluorouracil injection admixed with lidocaine and epinephrine.

Microwave sessions	Completed/lost to FU (n/n)	Clearance rate per ITT ^a % (n)	Clearance rate per treatment completion ^b % (n)
1 Session (n=30)	16/14	55.3 (16/30)	100.0 (16/16)
2 Sessions (n=17)	10/7	58.9 (10/17)	100.0 (10/10)
3 Sessions (n=31)	27/4	71.0 (22/31)	81.5 (22/27)
4+ Sessions (n=7)	6/1	42.9 (3/7)	50.0 (3/6)

Abbreviations: FU, follow-up; ITT, intention-to-treat.

^aMissing data were analyzed as “nonresponders” (i.e., treatment failure).

^bMissing data were excluded from the analysis.

TABLE 4 Efficacy of microwave treatment in patients with verrucae plantaris stratified by age groups.

Age group	Completed/lost to FU (n/n)	Clearance rate per ITT ^a % (n)	Clearance rate per treatment completion ^b % (n)
≤18 years (n=41)	26/15	61.0 (25/41)	96.2 (25/26)
>18 years (n=44)	33/11	59.1 (26/44)	78.8 (26/33)

Abbreviations: FU, follow-up; ITT, intention-to-treat.

^aMissing data were analyzed as “nonresponders” (i.e., treatment failure).

^bMissing data were excluded from the analysis.

4 | DISCUSSION

The results from this work demonstrate a significant clearance rate of verrucae plantaris in a group of patients of varying age, disease severity, and treatment histories, using microwave therapy. We found that 60% (51/85) of patients achieved clearance after an average of 2.3 sessions, and the rate was higher in patients who completed three sessions (71.0% [22/31]). However, these ITT results are a “worst-case” estimate which likely underestimates the true microwave response potential, based on comparison with the clearance rates per treatment completion. Nonetheless, the ITT results compare favorably to other treatment modalities (Figure 4), and corroborated findings from a pilot UK study treating plantar warts with up to four microwave sessions.^{10–14,16} In contrast to patients treated with cryotherapy or salicylic acid, we found no significant differences in clearance rates between children and adults (61.0% [25/41] vs. 59.1% [26/44]).¹³ Other factors potentially affecting treatment outcomes may include the number and size of lesions, inclusion of patients with recalcitrant warts, hands warts or history of self-treatment, as well as energy settings of the microwave device.^{9,13,16}

Analysis of the patient's wart pain scores revealed that all patients, regardless of final outcome, experienced significant pain reduction post-treatment whereby average pain scores reduced from 3.3 to 0.08 (Figure 5). The effect of microwave reducing verrucae pain was demonstrated in a similar manner in the UK study with a reduction in the mean pain scores noted prior to and at the conclusion

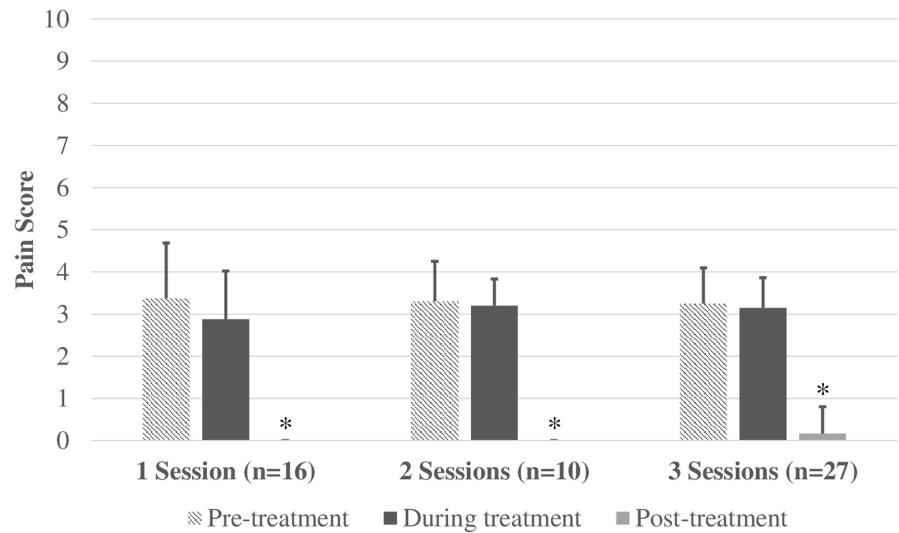
of treatment (2.85 to 0).¹⁶ A similar reduction in pain has also been observed in patients undergoing microwave treatment for their painful corns.¹⁷ The reasons for this effect are unclear although it has been suggested that heating of the nerve endings in the skin may lead to nerve desensitization with an increase in the pain threshold, leading to a subsequent drop in pain experienced by the patient.¹⁸ Similarly, microwave-induced hyperthermia has been reported to give pain relief to patients with tendinopathy, osteoarthritis, or carpal tunnel syndrome, further supporting the notion that microwave treatments may exert an effect on local pain mechanisms.^{19–21}

A previous survey found more than half of physicians (66.2% [47/71]) apply pain mitigation measures during microwave treatment sessions, including anesthesia, gating or distraction techniques, as well as nitrous oxide.⁹ In this study, we observed no significant increases in pain levels at the lesion site during treatment (Figure 5). This difference may be attributed to the energy setting of the microwave device (8W for 2s corresponding to 16 Joules in this study compared with 16–20 Joules as previously reported).⁹ One case of ulceration at the treatment site was reported in a patient who received a local anesthetic, and this observation led to the cessation of local anesthesia at the physician's discretion. No other patient received local anesthesia for the duration of this study, and no additional cases of ulceration were reported. Other previously reported adverse reactions in response to microwave treatment not observed in this study included poor healing and blistering.⁹

Comparison with previous reports on traditional treatment modalities, such as cryotherapy and salicylic acid, as well as investigational agents including bleomycin and 5-fluorouracil, showed varying degrees of efficacy in inducing the complete clearance of plantar warts (Figure 4). The clearance rate of plantar warts in our study was 60.0% (51/85), which is notably higher compared to patients treated with cryotherapy (13.6% [15/110] to 29.7% [11/37]) or topical salicylic acid (14.3% [17/119] to 32.6% [14/43]).^{11–13} Intralesional bleomycin injection, although effective with 69.2% (18/26) of patients achieving clearance at week 8, may have limited utility due to pain at the injection site; especially for patients with multiple warts.^{12,22} With intralesional bleomycin injection one case of hemorrhagic eschar was also reported.²² Similarly, another study reported a 93.3% (14/15) clearance rate in patients treated using a solution of 1% cantharidin, 20% podophyllin resin, and 30% salicylic acid following surgical delamination of plantar warts.¹⁰ Its side

TABLE 3 Efficacy of microwave treatment in patients with verrucae plantaris stratified by the number of treatment sessions administered.

FIGURE 5 Pain scores reported in patients completing up to three microwave treatment sessions at pretreatment, during treatment, and post-treatment time points. * $p < 0.0001$ compared with pretreatment.



effects profile, including pain, bulla, and hemorrhagic bulla, may also limit its utility.¹⁰

The high clearance rate demonstrated by the microwave application may arise as an effect of heating HPV infected cells. The unit delivers microwave radiation into the skin which leads to the rapid elevation of the treated area into the hyperthermic or heat shock range of 41–45°C, a few degrees above body temperature (37°C). Previous research has shown that elevating body tissues to within this range can modulate a range immune processes without causing significant tissue damage.²³ Hyperthermic temperatures applied to HPV infected skin can amplify wart resolution by positively affecting many facets of the immune response.²⁴ If tissue is exposed to temperatures above 41°C for prolonged periods, cell damage and death is likely. However, cells placed under stress from microwave heating of a few seconds produce molecules known as heat shock proteins (HSPs).²⁵ These have evolved to protect cells in extreme stress conditions from cell death. HSPs have a number of functions—first and foremost as protein chaperones that are involved with the folding, shape regulation, and degradation of intracellular proteins.⁶ Moreover, HSP-70 has been shown to induce the maturation of Langerhans cells and enhance their migration to the lymph nodes. When comparing normal skin to HPV infected skin, it was discovered that the migratory response was more marked in the HPV infected skin.²⁶ HSP release also has been shown to stimulate cytokine release from antigen presenting cells, as well as nitric oxide, chemotactic factors from macrophages and to stimulate antitumor activity by the immune system.²³ Additionally, microwave treatment appears to have a more direct effect on HPV infected keratinocytes by disrupting viral protein expression and cell apoptosis.^{25,27}

Some limitations of our study include the retrospective study design and lack of head-to-head comparisons with other treatment modalities. This study is among the first to assess the utility of microwave devices in patients with verrucae plantaris, including those with prior failed treatments and lesions persisting for ≥ 2 years characteristic of recalcitrant warts. Further studies are warranted to confirm our findings, and to further elucidate the mechanism of action of microwave treatment.

5 | CONCLUSIONS

The application of microwave energy in the treatment of verrucae plantaris has demonstrated a high clearance rate of 60% (51/85) in a cohort of 85 patients following one course of treatment. The clearance rate was 86.4% (51/59) in patients who completed treatment. Patients who received three sessions achieved a higher clearance rate (71.0% [22/31]). Clearance rates were similar between children (61.0% [25/41]) and adults (59.1% [26/44]). A notable number of patients with recalcitrant warts also achieved clearance after four or more sessions (42.9% [3/7]). Significant improvements in pain associated with lesions were seen in patients who completed treatment (post-treatment pain score of 0.08 [0.4], $p < 0.0001$ relative to pretreatment); no other adverse events were observed. Microwave treatment, in this series of patients, has demonstrated to be a safe and effective means of treating verrucae plantaris, where other treatment modalities may have failed or demonstrated poor efficacy.

AUTHOR CONTRIBUTIONS

IRB, RMC, and AKG were involved in conceptualization; TW, EAC, IRB, and RMC were involved in data curation; TW, EAC, IRB, and RMC were involved in formal analysis; RMC was involved in investigation; RMC, AKG, IRB, EAC, and TW were involved in methodology; AKG and EAC were involved in project administration; AKG and RMC were involved in resources; AKG, EAC, and IRB were involved in supervisions; AKG and RMC were involved in validation; TW was involved in visualization; TW, RMC and IRB were involved in writing—original draft preparation; AKG and EAC were involved in writing—review and editing.

CONFLICT OF INTEREST STATEMENT

AKG, TW, and EAC report no competing interests to declare. IRB is a consultant for Emblation Limited, UK. RMC is a consultant for Emblation Inc, USA.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL STATEMENT

Not applicable. The authors declare that human ethics approval was not required for this article.

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