

Efficacy of cryotherapy versus radiofrequency ablation in the treatment of plantar warts

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Background: Plantar warts may be refractory to any form of treatment and are associated with pain and a decreased quality of life. There are very few randomized controlled studies that focus on the treatment of plantar warts. Cryotherapy and radiofrequency ablation (RFA) have been used in the treatment of this recalcitrant condition. However, no data exists comparing the efficacy of these treatment options in the treatment of plantar warts. The aim of the study was to compare the efficacy of cryotherapy and RFA in the treatment of plantar warts.

Method: Fifty patients with a clinical diagnosis of plantar warts were included in the study. They were randomly divided into two groups of 25 patients. After paring the warts, Group A was treated with cryotherapy with nitrous oxide and Group B was treated by RFA of warts every 2 weeks for a maximum period of 12 weeks. The results of the two groups were compared at the end of 12 weeks.

Result: Fifty patients had a total of 212 warts. Eighty four percent (21/25) of the patients receiving RFA experienced subjective benefits within 2 sessions whereas in the cryotherapy group, 72% (19/25) of the patients required three to four sessions to experience subjective benefits ($p = 0.00189$). Eighty four percent (21/25) of the patients and 91.6% (121/132) of the warts in the RFA group achieved complete clearance by the end of 12 weeks whereas only 32% (8/25) of the patients and 31.25 % (25/80) of the warts receiving cryotherapy achieved complete clearance by the end of 12 weeks ($p = 0.00681$).

Conclusion: Radiofrequency ablation is more effective than cryotherapy in the treatment of plantar warts and gives quicker subjective and objective results.

Keywords: cryotherapy, plantar warts, radiofrequency ablation, treatment

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INTRODUCTION

Warts or verrucae are benign proliferations of the skin and mucosae caused by Human Papilloma Virus (HPV) belonging to the family Papovaviridae¹. Warts are extremely common, being encountered by most people at some point in their lifetime. Plantar warts are present in 7-22%

of the population². They are of three types: deep and endophytic 'myrmecia' form caused by HPV-1, smaller superficial lesions caused by HPV-2, 4, 27, and 57, and mosaic warts caused by HPV-2³. Plantar warts commonly affect the quality of life. Ciconte et al studied 85 patients with 250 common and plantar warts and found that 81.2% of the patients were moderately to extremely embarrassed

by their warts and moderate to severe discomfort was observed in 51.7% of the patients⁴. The pain caused by plantar warts is most commonly thought to derive from thick hyperkeratotic callus above the wart, acting as a foreign body which, perhaps, also makes plantar warts more resistant to treatment³.

There is much uncertainty around the optimal treatment and lack of good quality evidence on which to frame clinical decision making. Keeping in mind the morbidity associated with plantar warts⁴, there is a need to find a treatment modality which can provide quick clearance of plantar warts to decrease the associated morbidity. Thus in this study, we aimed to choose two commonly available, easy to use, and cosmetically acceptable outpatient treatment options, i.e. cryotherapy and radiofrequency ablation (RFA) and evaluate their efficacy individually and in comparison to each other.

PATIENTS AND METHODS

The study was carried out on 50 patients with plantar warts attending the Outpatient Department of Dermatology of our institution. The study was approved by the Ethics Committee of our institution. Written informed consent was obtained from each patient before enrollment. A detailed history was taken from each patient and a complete cutaneous examination was done, including the duration of the disease, associated symptoms, and number, site, size, surface, and morphology of warts. Pregnant and lactating women, patients with cold intolerance or cold urticaria, Raynaud's disease, bleeding disorders, keloidal tendency, pacemakers, patients on medications like aspirin and anticoagulants, and those who had received any form of treatment for plantar warts in the last 3 months were excluded from the study.

The patients were randomly divided into 2 groups of 25 patients, labeled as Group A and Group B. After paring, Group A patients were treated by cryotherapy employing Basco Cryosurgical Unit, Nagar, Chennai, Tamil Nadu State, India, using nitrous oxide as the cryogen. Two freeze-thaw cycles were applied to each wart at every session and the duration of the freezing time of one freeze-thaw cycle was fixed at 15 seconds. Group B patients were treated by RFA (involving electrodesiccation) of the plantar warts using Mega Surg (High Frequency

Radio Surg Unit) by DermaIndia, Erungudi, Chennai, Tamil Nadu, India. Both procedures were done in an outpatient setting. In both groups, after the procedure, patients were observed for 10-15 minutes for immediate complications like pain, bleeding, erythema, blistering, edema, etc. Topical / systemic antibiotics and analgesics, as necessary, and follow-up care were advised.

The patients in both the groups were assessed at two weekly intervals for 12 weeks and the following parameters were noted: therapeutic response, percentage of regression, treatment of the remnant part (s) of the lesion (s) if needed, and any recurrence or complication. Photographic documentation was done at each session.

At the end of the study period, response to treatment was graded as:

Good: All warts disappeared during the therapy period.

Moderate: Up to 50% of the warts disappeared.

Poor: None or few warts disappeared.

The number of sessions required for appreciation of subjective benefits by the patient and complete clearance of warts was recorded for both groups. At the end of the study, the results were statistically analyzed and p values were calculated using t-test, and chi square test. P values less than 0.05 were considered significant.

RESULTS

The baseline characteristics of the participants did not differ significantly between the two groups as shown in Table 1. Out of a total of 50 patients, 26 were males and 24 were females. The mean age of patients was 33.16 ± 17.77 years in Group A and 29.36 ± 13.54 years in Group B.

At the beginning of the study, 25 patients in group A had 77 lesions whereas 25 patients in group B had 132 lesions. The baseline characteristics of warts of both groups have been shown in Table 2. The chief complaints of patients seeking treatment for plantar warts were difficulty in walking (74%), pain and discomfort in warts even at rest (22%), and disfigurement of feet (14%). Additional causes were their concern for the increase in the number of warts, and occurrence of infection and itching in warts. At the end of 12 weeks, 5 patients (2 from group A and 3 from group B) were lost to follow-up. However, for the purpose of this

Table 1. Baseline characteristics of the patients

	Cryotherapy (n=25)	RFA (n=25)	P-value
Age, mean ± SD	33.16 ± 17.77	29.36 ± 13.54	0.192
Female n (%)	11 (44)	13 (52)	0.291
Number of warts, mean ± SD, (min–max)	3.40 ± 2.61 (1-9)	5.28 ± 4.96 (1-20)	0.098
Total number of warts	77	132	
Duration of warts, mean ± SD, years (min–max) months	1.02 ± 2.15 (2 weeks to 10 years)	1.04 ± 2.15 (3 weeks to 11 years)	0.969

Table 2. Baseline characteristics of the warts

	Group A (n=77) n (%)	Group B (n=132) n (%)	P value
Location			
Head of metatarsals	32 (41.5)	51 (38.6)	0.396
Plantar aspect of toes	11 (14.2)	32 (24.2)	0.207
Ball of great toe	13 (16.8)	9 (6.8)	0.042
Web spaces	4 (5.1)	7 (5.3)	0.981
Lateral aspect of sole	2 (2.5)	16 (13.2)	0.041
Heel	15 (19.4)	17 (12.8)	0.572
Morphology			
Myrmecia	38 (49.3)	44 (33.3)	0.089
Small isolated lesions	37 (48.2)	85 (64.4)	0.067
Mosaic	2 (2.5)	3 (2.3)	0.891
Size			
<1 cm	41 (53.24)	89 (67.42)	0.061
1-2 cm	33 (42.85)	41 (31.06)	0.095
>2 cm	3 (3.89)	2 (1.51)	0.151

study, patients who were lost to follow-up were considered to exhibit a poor response (not cured). During the study period, 3 new warts developed in patients in Group A that increased the number of warts in Group A to 80, while no new warts developed in patients in Group B. In Group B, 3 patients required local anesthesia before the procedure while none of the patients in group A required anesthesia.

Effectiveness of treatment

As the chief complaints of patients presenting with plantar warts were mostly subjective, it was important to note the number of the sessions of cryotherapy and RFA required for achieving subjective benefits including relief of pain, irritation, discomfort, and difficulty in walking. Also, the number of sessions required for complete physical clearance of the warts was recorded. A total of 20 out of 25 (80%) participants in the cryotherapy group achieved subjective benefits of whom 76% (19/25) achieved subjective benefits by 3-4 session. On the

other hand, 88% (22/25) of the patients receiving RFA achieved subjective benefits just within 2 sessions ($P = 0.00189$). Similarly, only 32% (8/25) of the patients receiving cryotherapy achieved complete clearance of warts with an average of 5.63 sessions whereas 84% (21/25) of the patients receiving RFA achieved complete clearance of warts with an average of 3 sessions ($P = 0.00482$).

At the end of 12 weeks, the percentage of warts that were completely cured was 31.25% (25/80) in the cryotherapy group and 91.66% (121/132) in the RFA group ($P = 0.00681$). Also, at the end of the study, the response of patients was graded as good, moderate, or poor, depending upon the percentage of completely cleared warts which have been depicted in Table 3.

Side effects

The participants experienced more side effects with cryotherapy than with RFA. The side effects experienced by patients in the cryotherapy group were pain (68%), cryoblisters (16%), edema, and

Table 3. Response to treatment in both groups at the end of 12 weeks

Response	Group-A (n=25)		Group-B (n=25)		P value
	No.	%	No.	%	
Good	8	32.00	21	84.00	0.0068
Moderate	9	36.00	1	4.00	0.0083
Poor	8	32.00	3	12.00	0.0966

infection, whereas pain was the only side effect recorded in the RFA group, experienced by 52% patients.

DISCUSSION

We compared the clinical efficacy of cryotherapy with nitrous oxide and RFA in the treatment of plantar warts and found that RFA had much better results, as denoted by higher cure rates (91.66% vs 31.25%) which were accomplished much more quickly than with cryotherapy, both subjectively as well as objectively.

Plantar warts are a common viral infection of the sole and a common cause of dermatology outpatient consultation. The overlying hyperkeratotic callus not only makes them painful but also refractory to treatment; as a result, plantar warts may persist for decades in adults³. Various therapeutic modalities are available for the treatment of plantar warts and the principles of treatment involve not only physical or chemical destruction of warts, but also stimulation of an immune response to the virus released from the disrupted keratinocytes⁵. The different treatment modalities include salicylic acid, cantharidin, cryotherapy, radiofrequency ablation, formaldehyde, glutaraldehyde, bleomycin, podophyllotoxin, imiquimod, and contact sensitizers like dinitrochlorobenzene and diphenyprone⁵. Topical salicylic acid treatment and cryotherapy are the most widely used treatment options^{5,6}.

Cockayne et al found that 14% of the patients receiving cryotherapy achieved complete clearance at 12 weeks after receiving up to 4 sessions of cryotherapy⁷. At the end of 12 weeks, our cure rate was higher than the cure rate reported by Cockayne et al, probably due to the more number of cryotherapy sessions given to our patients. This, therefore, indicates that with more cryotherapy sessions, a higher cure rate can be expected which reinforces the point stressed by Bourke et al⁸, who

concluded that the percentage of warts cured was related to the number of treatments. Second, the mean duration of warts in our patients was less than that included by Cockayne et al, which gave a better chance of cure to our patients. Third, a longer duration of freeze time, (15 seconds used by us versus 10 seconds by Cockayne et al) could lead to the difference.

Our cure rates with cryotherapy were, however, lower than those achieved in previous studies comparing cryotherapy with other treatment modalities⁹⁻¹¹. Bruggink et al⁹ reported a cure rate of 54% with cryotherapy in patients with plantar warts whereas Steele and Irwin¹¹ reported a cure rate of 57.7%. The difference could be due to different study populations in these studies as compared to ours. For example, Bunney et al¹⁰ included patients with hand warts alone, while Steele and Irwin excluded mosaic warts¹¹, which are generally regarded as more resistant to treatment. They also excluded patients with five or more lesions and lesions outside an average diameter of 3–9 mm while the present study included patients with mosaic warts and also 38% of warts included in our study were more than 1 cm in size¹¹. Patients were younger in the studies by Bruggink et al⁹ and Steele and Irwin¹¹, with 59% of the participants under the age of 16 in the latter, as compared with 17% in our study. The median age of the patients in the study by Bruggink et al⁹ was 15 years for cryotherapy patients compared with the median age of 22 years in our study. A higher cure rate can be expected in a younger population because of greater odds of spontaneous regression^{9,12}. Berth Jones et al, in two of their studies on cryotherapy in hands and feet warts, reported cure rates of 50% and 75%, respectively, and stressed that paring and a double freeze thaw cycle significantly improved cure rates of plantar warts achievable by cryotherapy^{13,14}.

The use of radiofrequency ablation in the treatment of plantar warts is based on the fact that temperature is an important factor in the development and treatment of warts¹⁵. Various authors have shown that the local application of heat causes the inactivation of the virus. Heat therapy with different treatment modalities such as hot-water baths^{16,17}, exothermic patches¹⁸, infrared heat^{18,19}, has been used in the past with variable results. The main disadvantage of these

studies was that the degree of temperature as well as the duration of its application could not be precisely controlled, which can be successfully adjusted by radiofrequency ablation. The results we achieved with RFA were consistent with the findings reported by Kandelwal et al, who studied the efficacy of radiofrequency ablation in the treatment of palmoplantar warts in a placebo controlled trial¹⁵. In their study, 96% of the patients and 93% of the warts were completely cured by radiofrequency ablation. Another study by Stern and Levine showed that 25 of 29 warts (86%) showed complete clearance with a radiofrequency heat generator in one to four sessions, which was consistent with the results of the present study²⁰.

The strength of our study was that our study included a predominantly adult population with persistent warts. As spontaneous regression of plantar warts occurs sooner in children than in adults²¹, having a predominantly older study population adds more advantage to the study, since the chances of spontaneous regression would be minimal and the study would represent patients requiring treatment. The main limitation of our study was the lack of follow-up. It has been suggested that a six-month follow-up is a more realistic time point to assess the success of the treatment of cutaneous warts than shorter time frames⁶. Assessment at six months not only allows for the fact that the human papillomavirus may remain dormant within epithelial cells without a visible disease but would also allow time for any response mediated by the immune system to be observed. However, we chose to assess the primary outcome in our study at 12 weeks to know the actual effectiveness of the treatment modality, ruling out any chance of spontaneous resolution. Also, we considered that 12 weeks was a reasonable time frame to expect a treatment for plantar warts to be effective. Another limitation of the study was that 5 patients were lost to follow-up during our study and they were not excluded from the study and considered to have poor response. The actual outcome of those patients was not known.

Radiofrequency ablation clearly has an edge over cryotherapy with nitrous oxide in the treatment of plantar warts. According to our findings, radiofrequency ablation produces subjective benefits in patients earlier than cryotherapy and also results in a higher complete clearance rate after fewer

sessions, irrespective of the site, size, or morphology of the warts. Therefore, radiofrequency ablation is a safe, effective, cosmetically acceptable, time saving, and convenient modality for the treatment of plantar warts.

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