ORIGINAL ARTICLE

TO COMPARE EFFICACY BETWEEN CRYOTHERAPY AND MITOMYCIN MICRONEEDLING FOR THE TREATMENT OF PLANTAR WARTS

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Background: Cryotherapy is a common destructive treatment modality for treating plantar warts that results in blistering and scarring. Mitomycin an antitumor drug with antiviral property is a safe, better and a promising option for treating plantar warts. Objective was to compare efficacy of cryotherapy and mitomycin microneedling in the management of plantar warts. It was a randomized controlled trial conducted at the Skin Department CMH Abbottabad from 1st May to 31st December 2021. **Methods:** The study included 60 patients with plantar warts. Each group with 30 patients. Random tables were used to determine the distribution of patients within each group. Group A received mitomycin microneedling (1u/ml) repeated every 3 weeks. Group B was prescribed liquid nitrogen cryotherapy. The freeze-thaw cycle was 20 secs and repeated every 2 weeks. Both groups were treated for 4 months duration. For analysis of data, SPSS version 21.0 was used. Efficacy was compared by the application of Chi-square test between the two groups. $p \leq 0.05$ was considered statistically significant. **Results:** Mitomycin microneedling completely cured 76.7% of patients, while cryotherapy was effective for only 56.7%. Complete remission was observed after two to three sessions of mitomycin microneedling while average of 4 sessions of cryotherapy were required for complete remission. In general, microneedling with mitomycin had better tolerance, pain being the commonest adverse effect. **Conclusion:** Plantar warts can be effectively treated with mitomycin microneedling. Treatment of plantar warts with this method is more effective, requires fewer sessions, and may take less time to complete.

Keywords: Mitomycin; Microneedling; Cryotherapy; Plantar wart

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INTRODUCTION

Plantar warts, also known as verrucae plantaris, are benign tumours caused by human papillomavirus (HPV). Most infections are asymptomatic which are frequently controlled or cleared by our immune system. The HPV shedding from plantar warts can be spread to other contact sites on the sole or other individuals.[1] HPV has various strains. The genotypes detected in plantar warts are HPV-57, HPV-27, HPV-2, and HPV-65.[2] The overall annual incidence is about 14%. The main risk factors are people with immune-compromised conditions, those walking barefoot on public surfaces, persons with infected family members, and those with a history of plantar warts.[3] Increased sweating and peripheral cyanosis facilitate infection.

Plantar warts typically exhibit capillary haemorrhage, clinically presented as black dots.[4] Mosaic plantar warts are a cluster of several small warts growing closely together in one area. They are more challenging to treat than solitary warts. Myrmecia warts are deep round painful warts that often appear on weight-bearing sites.

A variety of treatments are available, including caustic acid (phenol trichloroacetic acid), electrocautery, cryotherapy[5], surgery, ablative laser therapy, interferon, intralesional injections of bleomycin. Immunotherapy with mumps, measles, rubella (MMR) vaccine and purified protein derivatives (PPD), glutaraldehyde, formalin, topical 5 fluorouracil, retinoic acid, vitamin D analogues, photodynamic therapy, zinc and imiquimod. Even though most lesions resolve spontaneously, treatment is performed for pain upon walking or for cosmesis. It is ideal for the treatment to be simple and cause the fewest side effects. The action of salicylic acid is slow and requires frequent application up to 12 weeks to be effective.

Alternatively, cryotherapy is effective and favourable for most patients, treating 50–70% of lesions after three to four cryotherapy sessions.[6] Different dermatologists follow different protocols. Jihan M. Muhidat *et al.*; Department of Dermatology, Jordan have discussed in their study that freezing time of l0 secs with two weekly intervals between sessions resulted in 77.8% cure rates as compared with 20 seconds freezing time with four weekly intervals, i.e.,

54.3%. Mitomycin microneedling is another current treatment. It belongs to an anti-neoplastic antibiotic that includes bleomycin. It acts by cross-linking the complementary strands found in the DNA, thereby inhibiting its synthesis. The systemic adverse effects are nausea, fever, vomiting, bone marrow suppression, and haemolytic uremic syndromes.

Using insulin syringes containing mitomycin, multiple punctures are made on the wart surface, and mitomycin is applied topically. To determine the endpoint of micro-needling, grey-white discoloration is observed.[7] Ha, Ryeong *et al*. concluded average lesional diameter treated either with cryotherapy or bleomycin microneedle patch was equally reduced at weeks 8 and 16. Cryotherapy was significantly more painful (p<0.0001) than bleomycin microneedle patch treatment. This research aimed to investigate the effectiveness of two treatment options, including cryotherapy and mitomycin microneedling, to treat plantar warts and obtain the best result with minimum side effects and high levels of patient satisfaction.[8]

MATERIAL AND METHODS

After taking full informed consent sixty patients having warts were enrolled in the research. From May 2021 to December 2021, all patients from the Dermatology Department of the CMH, Abbottabad, were included. The Ethical Committee of the CMH, Abbottabad, approved the study protocol (CMHAtd-ETH-28-Derm-22). For two proportions, the sample size was estimated using a WHO calculator, taking the significance level 5%. The calculated sample size was 60 (30 in each group). Non-probability consecutive sampling technique was used. Patients in each group were allotted using random tables. In order to deliver mitomycin (1u/ml) insulin syringe was used. Multiple punctures were made on surface of wart until an endpoint of grey white discolouration was observed.

Both males and females age older than 15 years of age having Myrmecia and mosaic plantar warts who did not get any treatment in the last three months were included. Myrmecia wart was defined as deep, painful warts mainly on the weight-bearing sites, while mosaic warts meant a cluster of several small warts.

The following groups of people were excluded from procedures; pregnant women, nursing mothers, children under 15 years, those with immune deficiencies, HIV-infected patients, those with high sensitivity to mitomycin or those who have had a wart treated within the past three months. At the beginning of the study, patients were evaluated and they were also assessed at subsequent visits for the number and severity of warts. Each session was scheduled at two weekly intervals. Majority of patients in cryotherapy group required four sessions while in mitomycin group frequency of session was two to three. The treatment response was assessed by observing the number and reduction of lesional areas. An acceptable therapeutic response was one in which the size of a large wart was reduced by at least 75%, in addition to treating all lesions of warts. As a "negative" response, warts whose resolution rates were less than 25% were noticed in both groups. A partial response (a wart that shrinks between 25 and 75%) is regarded as a negative result. During treatment, the severity of adverse reactions for each patient was recorded.

RESULTS

In this study, sixty affected individuals were enrolled. The demographics of the affected individuals in both groups are shown in Table-1. Patients responded to cryotherapy much better at the end of the treatment course (p=0.023), suggesting that mitomycin microneedling is more effective. In cryotherapy group complete response among patients was observed after 4th session while there was partial response after two sessions and no response after 1st session whereas in mitomycin treated patients' complete remission was mostly observed after 3rd session while after 1st and 2nd session response was nil and partial respectively. In addition, 76.7 percent of patients with multiple warts in the mitomycin group experienced complete remission. (Table-2).

Patients who received mitomycin were entirely cured in 23 (76.7%) cases, while patients who had cryotherapy were wholly cured in 17 (56.7%) cases. Mitomycin microneedling and cryotherapy respectively failed to treat six (20.07%) and twelve (39.97%) patients. One (3.33%) showed partial treatment response among the patients in each group. (Figure-1, Figure-2)

During the treatment, all the observable adverse effects were also recorded. Pain in the liquid nitrogen treated category was commonly noticed, i.e., 27 patients out of 30 (90%) while only a few individuals developed blisters i.e 5 patients out of 30 (16 %). In the mitomycin group, pain during microneedling was commonly observed, i.e., 25 out of 30 patients (83.3%).

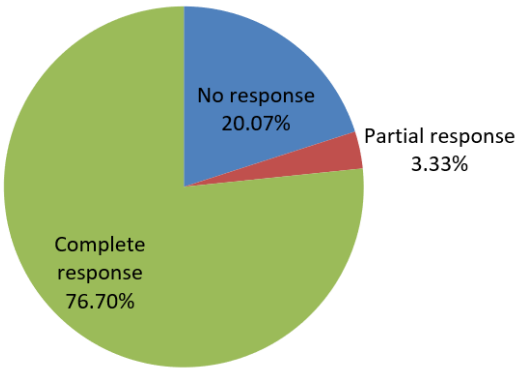

Figure-1: Mitomycin

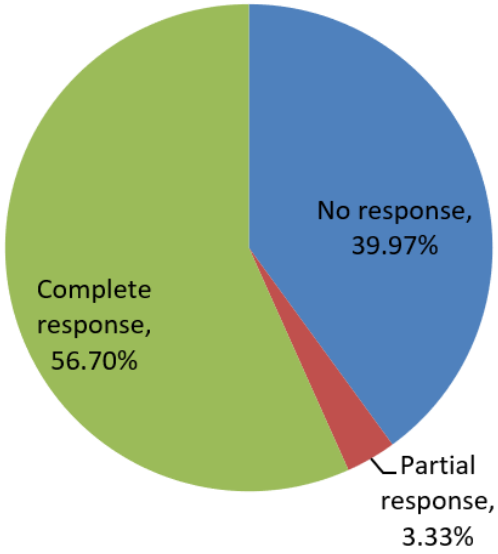

Figure-2: Cryotherapy

Table-1: The demographic characteristics of both groups of patients.

	Mitomycin Group	Cryotherapy Group
Total patients	30	30
Age (mean SD)	20.13±2.23	25.31±3.93
Gender		
Male	22	21
Female	08	09
Types of warts		
Myrmecia	09	07
Mosaic	18	15
Both	03	8
Number of warts	3.50±1.08	3.47±1.09
The surface area of the	429.37±126.875	298.96±122.120
warts (square millimeters)		
Subjects with multiple warts	22 (73.3%)	21(70%)

Table-2: Percentage of subjects cured after receiving treatment. Each session was repeated after 2 weeks in cryotherapy group and after 3 weeks in mitomycin group.

	Mitomycin Group	Cryotherapy Group	*p*-value
≤ 1 month	1 (50%)	Not applicable	0.031
1–2 months	1 (50%)	4 (70%)	
2–3 months	7 (98%)	6 (96%)	
≥ 3 months	12 (59.7%)	7(34.4%)	
Wart size reduction (%)			
After 1/3 of sessions	19.98±19.51[a]	16..01 ± 16.12	0.075
After 2/3 of sessions	67.02±22.27	59.44±43.16	0.062
After 4 sessions	78.01±33.79	70.01±20.032	0.012
Number of sessions needed for complete resolutions [b]	2.17±0.85	3.82±2.481	0.040

[a]Mean ± standard deviation.
[b]Number of sessions that resulted in the complete treatment of all lesions.

DISCUSSION

Plantar warts are common viral cutaneous infections characterized by skin-colored hyperkeratotic papules and plaques on the soles.

In our study cryotherapy was efficient in 56.7% of the patients. Cockyane *et al*. discussed in the study that cryotherapy showed 85% cure rates in patients whereas treatment related adverse effects were few only two participants in cryotherapy group developed unusual large blisters.

Mitomycin microneedling in this research was safe and effective in 76.7% of patients. Soni P *et al*. concluded in their study that the intralesional bleomycin is highly effective, safe and non-toxic in treating palmoplantar warts. A total of 82 patients (96.47%) out of 85 patients treated with intralesional bleomycin in a dosage of 1mg/ml responded after one or two injections within 12 weeks.

Other topical therapies may be used, i.e., Intralesional Vitamin D3, intralesional 5-Fluorouracil and trichloroacetic acid with different randomized controlled trials supporting their use in treating verruca plantaris.[9]

Modern treatment of plantar warts includes intralesional immunotherapy. Some patients may benefit from pulsed dye lasers, although more research needs to be conducted.

CONCLUSION

For plantar warts, mitomycin microneedling is a better treatment option. There were no adverse effects reported with this treatment. It can treat different clinical subtypes of plant warts. It requires few doses and has an excellent therapeutic response.

Conflict of interest: None
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AUTHORS' CONTRIBUTION

FA: Literature search, data collection, write-up. MH: Literature search, conceptualization of study design. BM: Data collection, data analysis, data interpretation. MS: Literature search, write-up, proof reading. SA, SUH, NA: Proof reading, write-up.

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