International Journal of Research in Dermatology
Suganthy V et al. Int J Res Dermatol. 2019 Aug;5(3):575-579
http://www.ijord.com

DOI: http://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20193232

Original Research Article

Treatment of multiple warts: efficacy of homologous autoimplantation therapy and comparison of homologous autoimplantation therapy and cryotherapy with liquid nitrogen

V. Suganthy, G. K. Tharini*

Department of Dermatology, Government Villupuram Medical College, Mundiyambakkam, Villupuram, Tamil Nadu, India

Received: 26 February 2019
Revised: 02 June 2019
Accepted: 04 June 2019

***Correspondence:**
Dr. G. K. Tharini,
E-mail: gtrajang@gmail.com

ABSTRACT

Background: Though a multitude of therapies are available, treating warts remains a challenge, more so if multiple. Cryotherapy, a commonly used treatment, has limitations. Homologous autoimplantation is a newer therapy for multiple warts. The aims of the study were to evaluate the efficacy of homologous autoimplantation therapy and compare it with cryotherapy with liquid nitrogen.
Methods: Hundred patients with multiple warts (≥5), were randomly selected and divided into two equal groups. One group was treated with cryotherapy with liquid nitrogen and the other with homologous autoimplantation. They were followed up for six months and the time taken for clearance of the lesions, complications and recurrences were compared.
Results: Homologous autoimplantation gave a higher cure rate (78%) than cryotherapy (56%). Complications like blistering, ulceration, scarring and post-inflammatory hyperpigmentation were higher with cryotherapy (40%) than autoimplantation (6%). The recurrence rate was 4% in the cryotherapy group and none in the other. But the time taken for the resolution was lower in the cryotherapy group (2.28 weeks) than the autoimplantation group (6.46 weeks).
Conclusions: Cryotherapy with liquid nitrogen and homologous autoimplantation are safe and effective therapies for warts but the latter carried a few advantages. The cure rate was higher, complications lower and recurrence was lower. Also autoimplantation can be of help in multiple warts where physical destruction of each and every wart is cumbersome. Hard to treat lesions like periungual warts, showed good results with autoimplantation.

Keywords: Warts, Homologous autoimplantation, Cryotherapy

INTRODUCTION

Warts or verrucae are one of the common cutaneous viral infections, caused by human papilloma virus. They are benign tumours which commonly involve the skin and other epithelial tissues.[1] Warts may need differing treatments based on their type and site. Treatment of warts is difficult though many modalities are available, more so with multiple and recalcitrant warts. Cryotherapy with liquid nitrogen is a very commonly used modality and is a simple, safe and inexpensive office procedure. But it requires treatment of every individual lesion and this makes treatment of multiple warts by this technique, cumbersome. Homologous autoimplantation is a simple and novel method of treatment of warts which involves harvesting a bit of the wart tissue and implanting it subcutaneously. This, induces an immune response which leads to resolution of warts.[2] In this background, we

planned to conduct a study to compare the efficacy of cryotherapy with liquid nitrogen, the commonly used modality of treatment and homologous autoimplantation of wart, a novel method of treatment for multiple warts.

METHODS

Study design

It was an open labelled, parallel, prospective, comparative therapeutic trial conducted in the Dermatology out-patient clinic of Madras Medical College, Chennai, Tamil Nadu, a tertiary care centre in South India, between December 2011 to November 2012. The approval of the institute ethical committee was obtained. Hundred patients with multiple warts diagnosed on clinical grounds, attending there were randomly allotted into two different modes of treatment, which were, cryotherapy with liquid nitrogen and homologous autoimplantation, alternatively.

Inclusion criteria

Patients presenting with multiple warts >5 in number with a treatment free period of 4 weeks prior to joining this study.

Exclusion criteria

Patients with warts other than verruca vulgaris and palmoplantar warts, pregnancy and lactation, children <12 years of age, immunosuppressed patients, H/O cold urticaria, cryoglobulinemia, Raynaud's disease and collagen vascular diseases were excluded.

Treatment protocol and methodology

A total of hundred patients were selected after screening. There were two groups. One group was treated with cryotherapy with liquid nitrogen and the other was treated with homologous autoimplantation. Since there were no studies comparing the difference in efficacy between cryotherapy and homologous autoimplantation, the cure rate for those two procedures from different studies were taken to calculate the sample size. The cure rate for homologous autoimplantation was found to be 73% in the study on autoimplantation therapy by Shivakumar, and the cure rate of cryotherapy on multiple wart was 41.7% in a study by Kacar.[3,4] Considering the cure rate in homologous autoimplantation as 73% and cure rate of cryotherapy as 41.7% and the power of 80% and level of significance was fixed at <0.05, the estimated sample size is 44 in each group. Expecting 10% drop-out rate, the total sample size enrolled in the study was 50 in each group (100 patients totally).

As and when patients with multiple warts (>5 in number) were attending the Dermatology OPD, a treatment free period of 4 weeks was ensured and baseline evaluation done considering the inclusion and exclusion criteria, and were randomly allotted into two groups alternately (1:1 ratio). The diagnosis was made by history and clinical features by the investigator. One group was treated with homologous autoimplantation therapy and the other was treated with cryotherapy with liquid nitrogen. The patients were followed up fortnightly by the investigator for a period of 3 months, and monthly thereafter for a total of 6 months, and the time taken for clearance of the lesions, any complication that arises and recurrence were observed and recorded. Reappearance of warts at the sites of earlier lesions during follow-up was considered as 'recurrence'. The disappearance of existing lesions and absence of new lesions, within a period of 3 months from the onset of therapy was considered successful treatment. The primary parameter for effectiveness of therapy was the reduction in the number of warts (excluding the one removed for autoimplantation). The trial procedures were in accordance with the ethical standards laid by the institutional ethical committee and the Indian Council of Medical Research (ICMR). Informed consent was obtained from the patients prior to their inclusion in the study.

Statistical analysis

The data were analysed with the help of SPSS win 12 software, under the supervision of a statistician. The statistical significance was set at 0.05 level and the confidence interval at 95%. The baseline parametric variables were expressed in mean (SD) and the proportions were expressed in percentages. The statistical significant difference in cure rate, proportion of recurrence between two treatment groups was found using chi-square test and the significant difference in mean weeks for resolution was found using independent 't' test.

Procedure

Procedure of autoimplantation

A well developed verrucous papule was chosen as the donor wart. Under strict aseptic precautions and local anaesthesia, a nick was made on the wart to the level of the subcutis using a surgical blade number 11, and a chunk of the wart tissue was removed and placed on a sterile swab. Then the donor area was tightly secured using a mircopore dressing or a band-aid plaster. The recipient area was chosen on the left forearm, approximately two inches below the ante cubital crease. Under strict aseptic precautions and local anaesthesia, a small nick, upto the level of the subcutis, was made in the recipient area using a surgical blade number 11, in accordance with the resting skin tension lines. A tiny pocket was created along the nick and the harvested wart tissue was placed in it. It was then tightly secured using a micropore dressing. The patients were advised not to wet or remove the dressing at the recipient site for the next five days. Systemic antibiotics were prescribed for a period of five days. The patient was reviewed after five

days when the dressing was removed. Patients were followed up every fortnightly forthe first month, and monthly thereafter for 6 months. Resolution of warts within a period of 3 months post-procedure was considered as successful treatment.[2]

Procedure of cryotherapy

In this study, the dipstick method of application of cryotherapy was followed. In this method, first the affected area was cleaned with a disinfectant. The procedure produces pain or a stinging sensation, so local anesthesia like 1% lignocaine injection or topical anesthesia was used in children or when warts are present over sites where the procedure causes excess pain. A cotton bud was dipped into the liquid nitrogen in a container and was applied firmly on the wart till a 2 to 3 mm halo of ice was formed. Two freeze thaw cycles, each lasting 15 to 20 seconds was given. The procedure was repeated every other week, for a maximum of four treatment sessions. The patients were followed up every fortnightly during the first 2 months and monthly thereafter for a total of six months. The time taken for the resolution of warts, complications if any and any recurrence was noted. Clearance of all the warts within a period of 3 months from the onset of treatment was considered as successful treatment.[3]

RESULTS

No statistical differences were noted between the two study groups in terms of age, sex, duration, types of wart. It was observed that homologous autoimplantation gave a higher cure rate (78%) as compared to cryotherapy with liquid nitrogen (56%) with a p value of 0.19 <0.05 which is statistically significant (Table 1). On comparison of the mean of the time taken for the resolution of warts, it was found that for the cryotherapy group, it was 2.28 weeks whereas for the autoimplantation group it was 6.46 which is statistically significant with a p value of 0.002 (Table 2). So, though the cure rate was higher in the autoimplantation group, the time taken for resolution is significantly later when compared to the cryotherapy group. The recurrence rate was 4% in the cryotherapy group whereas in the autoimplantation group, there was no recurrence. It was found that the complication rate was much higher in the cryotherapy group 40% as compared to the autoimplantation group 6%. The common complications in the cryotherapy group were pain during and after the procedure, blistering (Figure 4A), hypopigmentation, hyperpigmentation (Figure 4B) and ulceration (Figure 7). In the autoimplantation group, one patient had secondary infection at the autoimplantation site, and 2 patients developed an inflammatory nodule at the site of implantation of the wart. A few patients had transient hypopigmentation (Figure 6) which disappeared in 2 weeks.

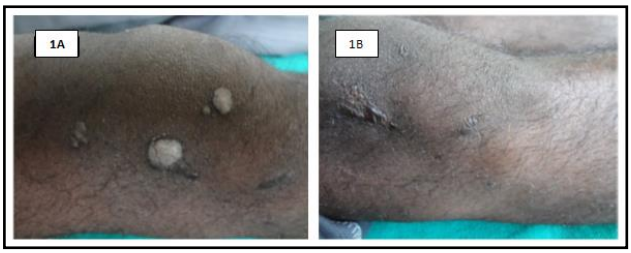

Figure 1 (A and B): Before and after cryotherapy.

Figure 2 (A and B): Before and after autoimplantation.

Figure 3 (A and B): Before and after autoimplantation.

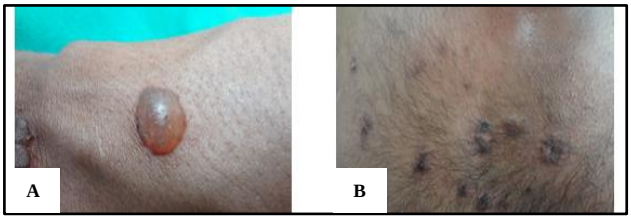

Figure 4 (A and B): Complications of cryotherapy–Blistering, hyperpigmentation.

Figure 5: Complications of cryotherapy–ulceration.

Table 1: Comparison of cure rates in the two study groups.

Result of therapy	Samples						Statistical inference
	Cryotherapy		Autoimplantation		Total		
	(n=50)	%	(n=50)	%	(n=100)	%	
Cured	28	56.0	39	78.0	67	67.0	p=0.019
Not cured	22	44.0	11	22.0	33	33.0	<0.05 Significant

Table 2: Comparison of time taken for resolution in the two groups.

Study group	Time taken for resolution (Mean in weeks)	Statistical inference
Cryotherapy	2.28	p=0.002
Autoimplantation	6.46	<0.05 Significant

Figure 6: Complication of autoimplantation–hypopigmentation.

DISCUSSION

Warts or verrucae are a common skin condition which bother the patients by their unsightly appearance and by causing pain and discomfort.[1] There are a number of therapeutic modalities for warts but none is found to be 100% effective.[5]

Basis of immunotherapy in the treatment of warts

Apart from the local immunity, systemic immunity also plays a role in the eradication of the clinical manifestations of the human papilloma virus.[1] This is evidenced by the immunological alterations occurring in a patient in whom there is spontaneous or treatment induced regression of warts.[6] In these patients, it is noticed that, viral specific antibodies are significantly increased. It is also noticed that delayed hypersensitivity reaction to HPV antigen increases in regressing warts.[7] Intradermal injection of HPV antigen also acts as a booster in the antibody response and hypersensitivity response.[8] This concept is used in the treatment of multiple warts. The various modalities of therapy for warts which act on this basis are autoimplantation therapy, autowart injection therapy and intralesional immunotherapy. In autoimplantation therapy, it is more likely that immunity against the same serotype as that of the wart that the patient has, is elicited. It works by inducing the production of Th1 cytokines of which IL1 and TNFα downregulate the transcription of HPV genes and IFNγ and IL2 stimulate cytotoxic T cells and NK cells, thus eradicating HPV infected cells.[2,6]

We compared the treatment of multiple warts with cryotherapy with liquid nitrogen and homologous autoimplantation therapy. In our study the distribution as regards to the age, sex, duration, type and number of warts was comparable to similar studies done by Srivastava et al and Shivakumar et al.[2,9]

The cure rate in the cryotherapy group was 56% while that of the autoimplantation group was as high as 78% as shown in Table 4. This correlates with the cure rate observed in the study on autoimplantation therapy by Shivakumar which was a little lower (73.3%).[2] The results of the cryotherapy group which is 56%, is lower than that of the a study which compared intralesional bleomycin and cryotherapy in the treatment of warts done by Dhar, which was 76.5%, but higher than that in another study which compared cryotherapy with topical salycilic acid in the treatment of warts which was only 14%.[10,11] A few other studies which compared cryotherapy with duct taping, cantharidin and fig tree showed showed the cure rates of cryotherapy to be 60%, 41.7% and 56% respectively.[3,12,13] Most of our patients in the autoimplantation group showed complete clearance within 8 weeks and the earliest response at 3 weeks which are in accordance with the Shivakumar's study of auto implantation therapy. The zero reccurence in the 95 autoimplantation group is comparable to the study on autoimplantation therapy by Shivakumar.[2] The complication rate too was in accordance with previous studies.

CONCLUSION

The study shows that both, cryotherapy with liquid nitrogen and autoimplantation are safe and effective in the treatment of multiple warts but the latter carried a few advantages in that, the cure rate is higher, complications

lesser and recurrence lower too. Of special mention is the point that hard to treat lesions like periungual warts, where cryotherapy is not feasible, show very good results with autoimplantation.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Drake LA, Ceilley RI, Cornelison RL, Dobes WL, Dorner W, Goltz RW, et al. Guidelines of care for warts: Human papilloma viruses. J Am Acad Dermatol. 1995;32:98-103.
2. Shivakumar V, Okade R, Rajkumar V. Autoimplantation therapy for multiple warts. Indian J Dermatol Venereol Leprol. 2009;75:593-5.
3. Savant SS. Cryosurgery. In: Savant SS, editor. Textbook and atlas of dermatosurgery and cosmetology. 2nd ed. Mumbai: ASCAD; 2005: 117-135.
4. Kacar N, Tasli L, Korkmez S, Ergin S, Erdogan BS. Cantharidinpodophylotoxin- salicylic acid versus cryotherapy in the treatment of plantar warts: A randomized prospective study. J Eur Acad Dermatol Venereol. 2012;26(7):889-93.
5. Klug A, Flinch JT. Structure of viruses of the papilloma-polyoma type. 1. human wart virus. J Mol Biol. 1965;11:403-5..
6. Briggaman RA, Wheeler CE. Immunology of human warts. J Am Acad Dermatol. 1979;1:297-304.
7. Viac J, Thivolet J, Hegaz M, Chardonnet Y, Dambuyant C. Comparative study of delayed hypersensitivity skin reaction and antibodies to human papilloma virus (HPV). Clin Exp Immunol. 1977;29:240-6.
8. Morison W. In vitro assay of cell-mediated immunity to human wart antigen. Br J Dermatol. 1974;90:531-4.
9. Srivastava PK, Bajaj AK. Autowart injection therapy for recalcitrant warts. Indian J Dermatol. 2010;55:367-9.
10. Gupta S, Malhotra AK, Verma KK, Sharma VK. Intralesional immunotherapy with killed Mycobacterium w vaccine for the treatment of ano-genital warts: An open label pilot study. J Eur Acad Dermatol Venereol. 2008;22:1089-93.
11. Dhar SB, Rashid MM, Islam A, Bhuiyan M. Intralesional bleomycin in the treatment of cutaneous warts: A randomized clinical trial comparing it with cryotherapy. Indian J DermatolVenereol Leprol. 2009;75:262-7.
12. Cockayne S, Hewitt C, Hicks K, Jayakody S, Kang'ombe AR, Stamuli E, et al. Cryotherapy versus salicylic acid for the treatment of plantar warts (verrucae): A randomized control trial. BMJ. 2011;342:d3271.
13. Focht DR 3rd, Spicer C, Fairchok MP. The efficacy of duct tape versus cryotherapy in the treatment of verruca vulgaris (the common wart). Arch Pediatr Adolesc Med. 2002;156(10):971-4.

Cite this article as: Suganthy V, Tharini GK. Treatment of multiple warts: efficacy of homologous autoimplantation therapy and comparison of homologous autoimplantation therapy and cryotherapy with liquid nitrogen. Int J Res Dermatol 2019;5:575-9.