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EFFICACY OF INTRALESIONAL BLEOMYCIN IN RECALCITRANT WARTS A STUDY AT TERTIARY CARE CENTRE

Balaji Ganesh J., Kaviarasan PK*., Prasad PVS., Kannambal K and Poorana B

Department of Dermatology, Venereology and Leprosy, Rajah Muthiah Medical College and Hospital, Annamalai University, Chidambaram, India – 608002.

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A B S T R A C T

Background/Aim: Warts are rough verrucous spiny papules or nodules that can be found on any cutaneous surface. In few patients warts spontaneously regress, whereas others show persistence and progression leading to physical and emotional stress. Several therapeutic approaches like electrosurgery, cryotherapy, keratolytics, vaccines have been used in treating warts, but resistance and recurrences to these therapies has been reported. Bleomycin is an anticancer drug having antitumor, antibacterial and antiviral activity showing promising efficacy in the management of recalcitrant warts. It has gained increasing popularity in the recent past for treatment of warts particularly in palmoplantar and periungual regions as other modalities are not very effective. Hence we evaluated the role of intralesion albleomycin in recalcitrant warts.

Material And Methods: The study group consisted of 30 cases of multiple cutaneous warts. We administered bleomycin which was mixed with 2% lignocaine and injected intralesionally into the warts at an interval of every 3 weeks till the clearance in 30 patients who attended DVL out patient clinic at RMMCH. Ethical clearance was obtained as well as informed consent from all patients.

Results: After completion of 3 sittings at the interval of 3 weeks we observed that the response in common warts was 90%, periungual warts was 85%, while the response in palmar warts was 90% and plantar warts was 76 %.

Conclusion: Our study showed that intralesion albleomycin injection was safe and efficacious in the treatment of multiple recalcitrant cutaneous warts and the bleomycindose for periungual warts needs more visits than cutaneous and palmar warts.

INTRODUCTION

Warts are benign cutaneous and mucosal epithelial proliferations caused by Human papilloma viruses (HPV). More than 100 HPV types have been recognised.[1]The common warts are caused by HPV types 1, 2, 4, 27 and 57. HPV infection occurs through inoculation of virus into the viable epidermis through defects in the epithelium. They infect different areas of skin and mucous membranes. Warts can appear at any age. In few patients, warts may spontaneously regress, whereas others show persistence and progression with spread to other body sites, leading to physical and emotional stress. Several therapeutic approaches like electrosurgery, cryotherapy, keratolytics, vaccines have been used in treating warts, but resistance and recurrences to these therapies has been reported. Bleomycin is an anticancer drug. In the recent times it has been showing promising efficacy in the management of recalcitrant warts.

The Role of bleomycinin recalcitrant warts

Bleomycin is an anticancer drug that is derived from *Streptococcus verticillus*. It inhibits cell cycle at G2phase and causes destruction of the tumor cells by DNA fragmentation, RNA degradation, and simultaneous freeradicals production. It has an antitumor, antibacterial and antiviral activity which may be related to its ability to bind with deoxyribonucleic acid (DNA), causing bleomycin strand scission and elimination of pyrimidine and purine bases. The bleomycin hydrolase enzyme which is known to inactivate bleomycin is normally found in all the body tissues but it is present in very small amounts in skin.[2] Thus, after injecting it intralesionally, a significant amount of the active drug is available for the action at the site, and so even a small amount is enough for treatment of warts. Numerous reports have been published on the use of intralesion albleomycin for the treatment of warts, with cure rates ranging from 14% to 99%. Another

Corresponding author:* **Kaviarasan PK
Department of Dermatology, Venereology and Leprosy, Rajah Muthiah Medical College and Hospital, Annamalai University, Chidambaram, India – 608002.

administration procedure of bleomycin is utilising multipuncture technique which is also thought to be safe and effective in recalcitrant periungual warts.[3]

MATERIALS AND METHODS

The present clinical study was conducted between October 2016andfebruary 2017 in the Department of Dermatology. A written informed consent was obtained from all the patients and ethical clearance was obtained from the institution. Thirty patients with multiple common warts, palmar, plantarand periungual warts of more than 3month duration, age ranging from 18 to 65 years were included in the present study. Pregnant women and immunosuppressed patients were excluded from the study. Diagnosis was made on the basis of history and visual diagnosis. Patients were categorized into two groups (groups A and B) of 30 each. Alternate patients were included in groups A and B which were treated with intralesional bleomycin and normal saline (control), respectively. Bleomycin for injection is available in vials containing 15 mg powder. It was diluted first with 5 ml distilled water to prepare the stock solution. Two parts of 2% lignocaine and one part of the bleomycin stock solution was taken in ainsulin syringe, so that the final concentration became 1 mg/mL. Each wart and the adjacent skin was cleansed with isopropyl alcohol. The fresh solution was injected strictly intralesionally till blanching of the lesion occurred. The amount of the injection given depends on the size of warts: warts up to 5 mm, 10 mm and more than 10 mm received 0.2 mL, 0.5 mL and 1.0 mL, respectively.[4]After 2 weeks of bleomycin injection, a black, ecchymosed eschar developed which was pared and residual warts if present were injected a second time. In the controlled group, normal saline was injected in a similar manner as the bleomycin solution. The patients were followed up weekly for first month, fortnightly up to 3 months and then quarterly up to 1 year. A chi-square test was applied for statistical analysis. Routine haemogram, liver function tests, renal function tests and X-ray of the chest were done before and after 3 months of treatment.

RESULTS

Two hundred and forty nine warts (249) were present in 40 patients which were included in the present study. There were 28 males and 12 females whose mean age was 30.75 years and 31.05 years, respectively. Group A and B patients were having 139 and 110 warts, respectively [Table 1]. The baseline parameters (age, sex, distribution of warts) between the two groups were statistically comparable, and no significant statistical difference was observed. A total of 124 out of 139 warts treated with intralesional bleomycin in a dosage of 1 mg/mL in group A showed complete resolution after three injections within 9 weeks. The response in common warts was 90%, periungual warts was 85%, while the response in palmar wartswas 90% and plantar warts was 76 % at visit 3 [Table 2]. Warts regressed with a slight hyperpigmentation that gradually faded during the follow-up of 1 year [Figure 2], Of the 110 warts treated with normal saline (group B), only 10 (9.09%) showed disappearance of the lesion within 9 weeks [Table 2],. The difference in the resolution rate at the end of 12 weeks was statistically highly significant ($P = 0.001$) between groups A and B.Most patients in group A experienced moderate pain during injection that was of short duration and was overcome by mixing with xylocaine. There was no effect on nail growth following intralesional injection around the nail. None of the patients experienced any systemic toxicity.

Table 1

Groups	Common wart	Palmar	Periungual	Plantar	Total
Group A IL Bleomycin					
No of pts	11	5	2	2	20
No of lesions	77	42	7	13	139
Group B Control					
No of pts	10	5	1	4	20
No of lesions	52	34	1	23	110

Table 2

Type of wart	Group A IL Bleomycin						Group B Control					
	Visit 1		Visit 2		Visit 3		Visit 1		Visit 2		Visit 3	
	N	%	N	%	N	%	N	%	N	%	N	%
Common	77	55.4	52	37.4	7	5.0	52	47.3	52	47.3	45	40.9
Palmar	42	30.2	24	17.3	4	2.9	34	30.9	34	30.9	33	30.0
Periungual	7	5.0	5	3.6	1	0.7	1	0.9	1	0.9	1	0.9
Plantar	13	9.4	8	5.8	3	2.1	23	20.9	23	20.9	21	19.1
Total	139				15		110				100	

Groups	Mean	SD	P Value
Group A	20.25	24.18	0.001
Group B	26.67	18.59	(P<0.01)

P<0.01 Significant at 0.01 level

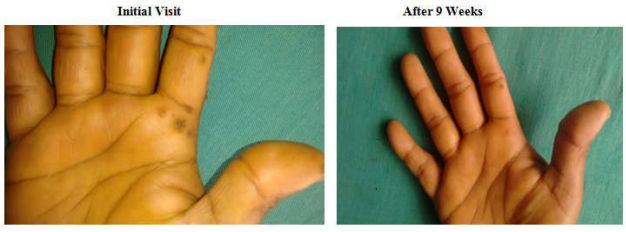

Figure 1

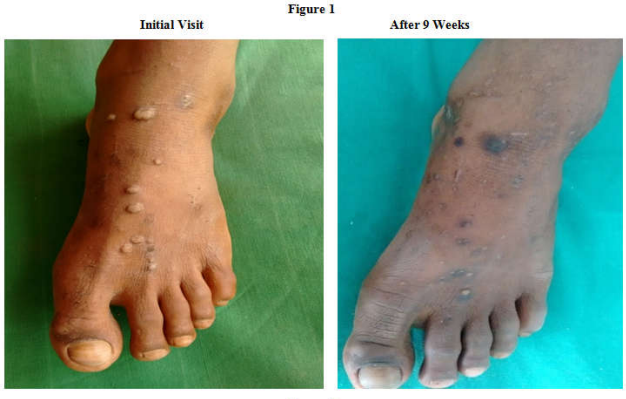

Figure 2

DISCUSSION

Warts can extremely affect patient's quality of life by causing embarrassment and frustration. It is known for its persistence and recurrence. Most of them are resistant even after repeated treatment with various physical modalities.[5] Bleomycin when used in high doses (>450 units) as in cancer chemotherapy can cause pulmonary fibrosis. For a very low dose (1 mg/mL), used in clearance

of warts, no systemic side effects have been observed.[6] This study was undertaken with the aim to evaluate efficacy of intralesional bleomycin in the management of recalcitrant warts.

We determined the efficacy of bleomycin in the treatment of common, periungual and palmar and plantar warts which were difficult to treat with other modalities.

Our results have shown a 83% cure rate in palmo-plantar warts which is comparable to 87% cure rate in a similar study conducted by Salk and Douglas.[7]

In 1983, Shumer and O'Keefe conducted a double-blind placebo-controlled study and treated 151 warts with intralesional bleomycin and 55 warts with normal saline as placebo. Their study showed a 60% cure rate for plantar warts and a 94% rate for periungual warts.[2]The present study has shown a76% clearance rate of plantar warts and 84% clearance rate for periungual warts with intralesional bleomycin. Plantar warts clearance was higher in the present study when compared to the abovementioned study. The cure rate of periungual warts was 10% lower than the above study. Our study has shown an9.09% cure rate at the end of 9 weeks.

Olson made a study on plantar warts and found complete response in 18 of 25 (72%) patients with bleomycin and 5 of 21 (27%) patients treated similarly with placebo.[8] while our study showed a cure rate of 85 % and 9.09 % for the warts treated with bleomycin and normal saline as placebo, respectively, in 9 weeks.

Hayes and O'Keefe demonstrated a cure rate of 78%, much lower than that in the present study.[9]Bremner treated 142 warts in 24 patients with intralesional bleomycin and reported a 63% cure rate which is lower than that in our study.

Shelly and Shelly used multiple-puncture technique using a bifurcated vaccination needle to introduce bleomycin in warts and mentioned a success rate of 92%.[3]

Potential side effects include scarring, nail damage and Raynaud's phenomenon were observed in few studies. But they were not observed in our study. Hyper pigmentation over intralesional injection site was noticed in 40% pts. Bleomycin dose for periungual warts needed more visits than cutaneous and palmar warts.

Our results have shown bleomycin to be highly effective in the treatment of common, palmo-plantar and periungual warts. The bleomycin was diluted with 2% lignocaine which reduced localized pain during and after injection.

CONCLUSION

This study is being presented to highlight the efficacy of intralesional bleomycin in recalcitrant warts. Bleomycin therapy requires less equipment. Easy pain management and shorter pain period is a winning edge of bleomycin compared to other modalities. We conclude that intralesional bleomycin injection is safe and efficacious in multiple recalcitrant cutaneous warts.

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