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A COMPARATIVE STUDY BETWEEN INTRALESIONAL BLEOMYCIN VERSUS MEASLES, MUMPS, RUBELLA VACCINE IN TREATMENT OF VIRAL WARTS

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ARTICLE INFO	A B S T R A C T	
<i>Article History:</i> Received 13 th November, 2018 Received in revised form 11 th December, 2018	Background- The currently available treatments for warts, including cryosurgery, laser surgery, electrosurgery, and topical keratolytic applications, are often very painful and can induce disfiguring scars. Recently, intralesional bleomycin and MMR vaccine has been shown to be effective in the management of warts.	
Accepted 8 th January, 2018 Published online 28 th February, 2019	Aim- our aim was to compare the efficacy of intralesional bleomycin with intralesional MMR vaccine in treatment of cutaneous warts.	
Key words:	received either intralesional bleomycin or MMR vaccine for maximum of 4 treatment 2 weeks apart. Patients had their warts measured at base line and with each return visit	
warts,bleomycin,MMR vaccine	including a post treatment follow up at 6 week apart from last treatment taken. Results -our results have shown a 96 % cure rate with intralesional bleomycin and 80% cure rate with MMR vaccine in cutaneous warts	
	Conclusion -Intralesional bleomycin was significantly more effective than intralesional MMR vaccine for treatment of cutaneous warts.	

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INTRODUCTION

Warts are scaly, rough, spiny papules or nodules that can be found on any cuteneous surface. Cuteneous warts are cuteneous manifestation of human papilloma (HPV) infection. The clinical appearence of warts is variable and depends to some extent on the type of HPV involved and the site of infection. Diagnosis of warts is usually based on clinical examination.

There is no treatment which is 100% effective for warts .Warts were earlier treated by destructive modalities namely cryotherapy, electrocoagulation, topical salicylic acid, topical 5-fluorouracil, laser surgery etc. All of these treatments are essentially painful, time consuming, expensive and recurrence is common. [1]

Numerous reports have been published on the use of intralesional bleomycin for the treatment of warts, with cure rates ranging from 14% to 99%. Bleomycin 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[2]. 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.

**Corresponding author:* Amardeep Kumar Department of Dermatology, Venereology and Leprosy, SN Medical College, Agra, India 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.

In some of the previous studies, it has been shown that mumps-measles-rubella (MMR) vaccine results in regression of warts via immunomodulation and induction of immune system.[3,4] This method can be used in larger populations because of vaccine availability and safety.Due to the high prevalence of warts in various populations, especially in children.[4]

MATERIAL AND METHODS

The present clinical trial was conducted between august 2017 and august 2018 in the Department of Dermatology. A written informed consent was taken from all the patients and ethical clearance was obtained from appropriate authorities of the college.

Fourty four patients were included in the study with age range from 12 - 65 years. Patients with different types of warts (common, plantar, periungual warts) were selected from the outpatient department of skin and V.D. from S.N. Medical college, Agra.

Inclusion criteria

A minimum age of 12years, acceptable pretreatment laboratory studies (complete blood cell count, serum chemistries, urine analysis, and pregnancy test) and a written consent was taken from each patient before the study.

Exclusion criteria

Patients who were not willing and not consenting for the study. Pregnant and lactating women.

Patients who received prior treatment for warts and Children below 12 years of age.

The selected patients were randomized into two treatment groups where group(A) received intralesional bleomycin available in vial containing 15 IU powder .It was diluted first with supplied 5 ml diluents (distilled water) with the package. Before injecting it was further diluted by adding 2% lidocaine, double the amount taken from the vial, so that the concentration become 1 mg/1 mL (0.1% or 1 unit/mL). This was injected into the base of the wart, using a 100-unit insulin syringe at biweekly intervals till complete clearance of the warts. In group (B) Measles-Mumps-Rubella Vaccine was injected 0.5 ml into the largest wart at 2-week intervals until complete clearance was achieved or for a maximum of 4 treatments.

Evalution

In both groups all patients were examined and photographed before each injection noting the number and surface area of warts. During follow up the presence or absence of response to treatment and approximate decrease in the size of warts in patients were recorded. The response was evaluated as:

Complete response which is defined as the complete absence of clinically apparent wart.

Partial response was defined as decrease in size >25%. No response was defined as <25% decrease in size.

Patients were evaluated every 2 weeks and were follow up for a period of 6weeks.

Statistical analysis was done by chi square test.Patients had their warts measured at base line and with each return visit.

RESULTS

2 patients from group B were excluded due to infrequent follow up. So ultimately, there were 22 patients(52%) in group A,20(48%) in group B and in all there were 42patients.In group A, among 22 patients 18(82%) patients show complete response,3(14%) show partial and 1(4%) patient show no response. Among group B 9(45%) patients show complete,7(35%) partial,4(20%) no response. Table 1

Table 1 Clearance of warts in two groups

Groups MMR		Bleomycin Total	
Complete response	18(82%)	9(45%)	27(64%)
Partial response	3(14%)	7(35%)	10(24%)
No response	1(4%)	4(20%)	5(12%)
Total	22(100)	20(100)	42(100)

The statistical difference between Group A and Group B was significant $p{=}0.042445 (p{<}0.05)$

No statistical significant difference was observed between the two groups in terms of age, sex, diagnostic subcategory of warts, distribution of number of warts and their surface area during enrolment.

At the end of the treatment, 96% of group A patients, warts were clear. In group B 80 % of patients warts were clear.

Statistically significant difference was observed between the two groups.

Results of both group A and B shown in Figure 1, Figure 2, Figure 3, Figure 4



Figure 1 warts before and after treatment with bleomycin



Figure 2 warts before and after treatment with bleomycin



Figure 3 warts before and after treatment with MMR vaccine



Figure 4 warts before and after treatment with MMR vaccine

DISCUSSION

We determine the efficacy of intralesional bleomycin in treatment of warts.

Our results have shown a 96% cure rate in warts which is higher than that(87%) in a similar study conducted by salk and douglas[5] .Numerous reports have been published on the use of intralesional bleomycin for the treatment of recalcitrant warts with cure rate ranging from 14% to 99%.

Dhar *et al.* conducted a randomized clinical trial treated 39 patients with bleomycin with 34 treated with cryotherapy. Their study showed a 94.9% clearance rate.[6]

Bremner treated 142 warts in 24 patients with intralesional bleomycin and reported a 63% cure rate which is lower than that in our study.[7]

In this study intralesional MMR vaccine shown a 80% cure rate in cuteneous warts which is greater than Anuja dhope *et al.* who reported 65%.[8]

Nagat Sobhy Mohamad et al. obtained clearance rate of 82%[9]

In our study, there were only local side effects such as pain, necrosis and hyperpigmentation with intralesional bleomycin and local side effects such as pain, erythema and swelling with intralesional MMR vaccine similar to previous studies and no systemic adverse events were observed.

Bleomycin when used in high doses (>450 units) as in cancer chemotherapy can cause pulmonary fibrosis. For a very low dose (1 mg/mL), no systemic side effects have been observed.[10]

CONCLUSIONS

At the end of the study period, the following conclusions were drawn that the overall clearance rate of warts with intralesional bleomycin was 96% versus 80% with intralesional MMR vaccine.

Therefore bleomycin is found to be safe and effective for treatment of warts as compare to intralesional MMR vaccine in our study.

Bleomycin treatment does not require any special equipment or setup, it has short course of therapy ,reducing patient time and low recurrence rate.

Treatment has good safety profile as well as a high cure rate of more than 90%.Side effects are few and rare.Not much study has been carried out to compare efficacy of intralesional bleomycin versus intralesional MMR vaccine in warts till now.

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