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Original Research Article

Comparative Clinical Study of Immunotherapy between MMR Vaccine Versus BCG Vaccine in Cutaneous Warts

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Abstract

A hospital based comparative study done in 40 patients with multiple *verruca vulgaris* who attended DVL department. All patients randomly assigned into 2 groups: Group A: 20 patients subjected to 0.3 ml of intralesional MMR (into the largest verruca) and Group B: 20 patients subjected to 0.1ml of intralesional BCG (into the largest verruca). Clinical response was graded into complete cure, partial cure and no response. Out of the 40 patients, 21(52.5%) showed complete response and 6 (15%) showed partial response while 3 patients (%) showed no response. On comparing the treatment responses at the lesional site by the end of 3rd month, we observed no statistically significant difference between MMR & BCG group. While the treatment responses at distant site, there was significant difference in clearance rate where MMR showed higher efficacy compared to BCG group. Study conclude that intralesional MMR vaccine is an important modality for the treatment of palmoplantar warts, with better cure rates and excellent safety profile. It is a simple, cost-effective, and non-destructive treatment option with good tolerability.

Keywords: Multiple *verruca vulgaris*, MMR vaccine, BCG vaccine.

Introduction

Warts are benign epidermal tumours caused by HPV, a ds-DNA virus. They show tropism for epithelial cells, causing mucocutaneous manifestations. It affects skin and mucous membranes with more than 200 types and more had been identified [1]. Cutaneous warts manifests as *verruca vulgaris*, plane, plantar, myrmecia, mosaic, filiform or digitate and periungual[2]. Current therapies are mainly divided into two groups: destructive therapies and immunomodulators. Destructive therapies include salicylic acid, podophyllin, trichloroacetic acid, 5-fluorouracil, retinoids, bleomycin, cantharidin, and formaldehyde, as well as physical modalities such as surgical excision, electrodessication, cryotherapy, and different types of lasers. Immunomodulators involve interferon, imiquimod, cidofovir, and vaccines [3].

Immunotherapy is becoming more and more popular, especially in the treatment of refractory warts. Immunotherapy is defined as a type of biological therapy that uses substances to stimulate or suppress the immune system to help the body fight cancer, infection, and other diseases. Some types of immunotherapy only target certain cells of the immune system. Others affect the immune system in general [4].

The exact mechanism of action of intralesional immunotherapy is still unclear. Proposed mechanisms include induction of a delayed-type hypersensitivity reaction, a strong non- specific inflammatory response against HPV infected cells [5]. Antigen injection may be associated with proliferation of peripheral blood mononuclear cells that promote Th1 cytokine responses which include IL-2, INF-gamma and TNF-alpha. This further activate cytotoxic T cells and natural killer cells to eradicate HPV- infected cells [6]. This stimulated immune response could then subsequently destroy all lesions on the body, rather than the locally treated lesion [7-9].

Materials and Methods

This is a hospital based comparative study done from February 2022 to 2023 which included 40 patients who attended DVL department, Mamata General Hospital, Khammam. All these patients gave informed consent to participate in this study. They were randomly assingned into two groups:

Group A: 20 patients subjected to 0.3 ml of intralesional MMR (into the largest verruca)
Group B: 20 patients subjected to 0.1ml of intralesional BCG (into the largest verruca)

Inclusion criteria

a. Patients with multiple *verruca vulgaris* (more than one)
b. Age more than 15 years
c. No concurrent treatment for verruca

Exclusion criteria

a. Patients with fever or signs of any inflammation or infection.
b. Children < 12 years.
c. Pregnancy.
d. Lactation.
e. Immunosuppression.
f. Anogenital/palmoplantar/planar warts.
g. Patients who received any other treatments for verruca in the last month before enrolment.
h. Past history of asthma, allergic skin disorders, meningitis or convulsions.

Demographic details including age and sex were noted. Photographic documentation was done. Written consent was obtained from all of the patients. The MMR vaccine was reconstituted and a volume of 0.3 ml was injected with insulin syringe into the wart or into the largest wart in patients with multiple warts.

This intralesionally in one of the largest wart or in multiple wart lesions. This was repeated every 3 weeks until complete clearance of all the warts or for a maximum of 4 treatment sessions. Patients were assessed at the beginning of the study and during each treatment session to record the reduction in the size and number of warts, side effects like pain, hypopigmentation or flu like symptoms.

The clinical response was graded into complete (complete cure), partial (if there was decrease in the size or decrease in the number of warts) and no response (no change in size and number of warts). The patients were followed up every 2 months for a period of 6 months to detect any recurrence.

Ethics Statement

A clearance certificate was obtained from the Institutional Ethical Committee before initiation of the study.

Results

A total of 40 patients were included in the study, of which 4 patients lost follow-up during the study. There were 28 males and 12 females with M: F ratio of 2.3:1. The patients were aged between 18 and 60 years with a mean age of 28.4. Majority of the patients (32 patients) had multiple warts. Only 8 patients had single wart. The duration of warts ranged from 20 days to 9 months, with a mean of 3 months 20 days.

Table 1: Baseline characteristics of the patients

Age in years	18-60 years	Mean – 28.4
Male/female ratio	28:12	2.3:1
No of warts :		
Single	8	21.2
Multiple	32	44.3
Duration of warts :		
Less than 1month	4	8.5
3-6 months	11	24.3
6-9 months	25	52.7

MMR group includes 16 (80%) of males and 4 (20%) of females with 4 (20%) members included under < 20 years, 15 (75%) included under 20-40 years, and 1 (5%) member under 40- 60 years. BCG group includes 12 (60%) males and 8(40%) females with 5 (25%) members included under <20 years, 13 (65%) members included under 20-40 years, 2 (20%) under 41-60years. Out of the total 40 patients, 21(52.5%) showed complete response and 6 (15%) showed partial response while 3 patients (%) showed no response (Figure 1).

Table 2: Response to treatment

	Complete response	**Partial response**	**No response**
No of patients	21	6	3
% of patients	52.5	15	7

On comparing the treatment responses at the lesional site by the end of 3rd month, we observed no statistically significant difference between MMR & BCG group. While the treatment responses at distant site, there was significant difference in clearance rate where MMR showed higher efficacy compared to BCG group.

In MMR group, only one patient (6%) showed erythema around lesion and 4(26.6%) showed hyperpigmentation whereas in BCG group, 9 (60%) patients showed lesional ulceration 5 (30%) showed flu like symptoms and 8(53.3%) showed hyperpigmentation.

Table 3: Side effects

MMR	BCG
Erythema	Lesional ulceration
Hyperpigmentation	Flu like symptoms
	Hyperpigmentation

Local side effects like pain and erythema were noted in 6 of the patients in the BCG group which subsided on the fourth day of injection. Flu like symptoms were noted in 2 patients which on treatment with Paracetamol, subsided on third day of injection. There were few adverse effects in the MMR group.

Figure 1: Clinical Pictures before and after the treatment

Discussion

Treatment of multiple cutaneous warts has been a therapeutic challenge for every physician. Immunotherapy has emerged as a promising modality for treating them in the recent years.

In 2010, Nofal and Nofal [10,11] conducted a case control study taking 135 patients with single and multiple common warts giving intralesional MMR vaccine to the first group and intralesional normal saline to the second group. Among MMR group, complete response was achieved in 80% and 84.6% of patients presenting with recalcitrant and multiple warts respectively. According to this study there was a significantly higher grade of improvement in the MMR group when compared with the BCG treated group.

In 2019, in a study by Jaisinghani et al [12] BCG immunotherapy was used for recurrent multiple warts. They found that complete clearance was seen in 70% of the patients. The resuts obtained here were inferior to the above mentioned study.

In a study by Munnangi et al [13], they have compared the efficacy of MMR vs BCG given intralesionally in multiple warts, taking 15 patients each in two groups treated with either vaccines. They noted that there was statistically significant difference both at lesional site and distant site where higher efficacy was seen with MMR compared to BCG.

The major aim in this work is to evaluate the effectiveness of two variants of immunotherapy that is intralesional MMR and intralesional BCG and also to compare between them in treatment of common warts.

In our study MMR group showed complete remission in 21(52.5%), partial response in 6(15%) and no response in 3(7%) at the lesional site by the end of 4th month, these results were in concordance with Nofal et al study, Dhope et al study, Saini P et al study, Raju et al study, Naseem et al study, which shows complete response in 57 patients (81.4%), partial response in seven patients (10%), and no response in six patients (8.6%)[15,16].

In Dhope et al study (n=20) MMR group showed pain in 85% patients and erythema, swelling, and flu-like symptoms in almost some numbers of patients, i.e., 25%, 20%, and 10%, respectively[14] whereas in our study MMR group showed fewer side effects. In Kenawi et al., study (n=30) BCG group showed flu like symptoms in all patients and lesional ulceration in 26.7% with necrosis in 16.7% [17] where as our study showed flu like symptoms in 2 patients, pain, erythema and lesional ulceration in 6 patients.

Conclusion

Immunotherapy for warts with various agents has shown significant results in terms of safety and efficacy. Intralesional MMR vaccine is an important modality for the treatment of palmoplantar warts, with good cure rates and excellent safety profile. It is a simple, cost-effective, and non-destructive treatment option with good tolerability. Combination of immunotherapy with other destructive modalities has shown an increased therapeutic response in recalcitrant and recurrent cases.

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