Original Research Paper

Volume - 14 | Issue - 09 | September - 2024 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Dermatology

A COMPARATIVE STUDY TO EVALUATE THE EFFICACY AND SAFETY OF INTRALESIONAL MMR VACCINE VERSUS INTRALESIONAL VITAMIN D IN PATIENTS OF EXTRAGENITAL WARTS

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ABSTRACT **Background:** An armamentarium of treatments is available for warts yet there is no single treatment modality, with ideal efficacy and cure rates up to present time making treatment of warts a great challenge. Recently immunotherapy has proved efficacy in treatment of warts by induction or boosting of a systemic immune response which can also result in clearance of distant warts with minimal recurrence. **Objective:** To compare Efficacy of Intralesional MMR Vaccine V/S intralesional Vitamin D in extragenital warts. **Methods:** 50 patients with extragenital warts were randomly divided into two groups of 25 patients each; Group A received intralesional MMR vaccine in largest wart, and Group B received intralesional Vitamin D into maximum of 4 lesions per session. Sessions were performed at 2-week intervals until complete clearance or for a maximum of four sessions, whichever was earlier. Follow-up was done at 6 months to detect any recurrence. **Results:** In Group A: complete response was observed in 19 patients (76%), partial response in 5 (20%) and no response 1(4%) patient. In Group B: complete response in 18(72%) patients, partial response in 4(16%) and no response in 3(12%) patients. Mean 2.73 and 3.11 no. of injections required for complete response in Group A and B respectively. **Conclusions:** Both intralesional MMR vaccine and vitamin D3 are simple, safe, efficacious and cost- effective treatment modalities for extragenital warts with minimum recurrences and scarring.

KEYWORDS : MMR Vaccine, Vitamin D, Warts, Immunotherapy

INTRODUCTION

Warts are common cutaneous infection caused by invasion of keratinized and non-keratinized epithelia with Human papilloma viruses (HPV). Till date, about 226 HPV genotypes that cause both genital and cutaneous warts have been completely classified.[1] Warts are usually asymptomatic but causes considerable psychological morbidity. The infection may clear spontaneously but time taken is long and varies greatly.

A plethora of conventional treatment modalities exist for treating warts including keratolytics, chemical cauterisation, cryotherapy, electrosurgery, radiofrequency and laser ablation. These destructive therapies are limited by side effects like pain, scarring and recurrence. Recently, various intralesional immunotherapeutic options are being used for warts like measles, mumps, and rubella (MMR) vaccine, tuberculin purified protein derivative (PPD), Bacillus Calmette and Guerin (BCG) vaccine, Mycobacterium w (Mw) vaccine, Candida albicans antigen, Vitamin D. Intralesional MMR mounts Th1 immune response, increases TNF α, IL-2, IL-4, IL-5, and IFN-γ and induces a delayed hypersensitivity reaction that recognizes the injected MMR antigen as well as HPV, and hence enhances the ability of the immune system to recognize and clear HPV.[2]

The vitamin D acts via vitamin D receptors (VDRs) exerting multiple physiological and pharmacological effects.VDR activators inhibit cell replication and have immunomodulatory properties. Vitamin D derivatives regulate epidermal proliferation, inhibits hyperkeratosis and induce apoptosis. It down regulates IL-1a, IL-6, and activates the toll-like receptor of human macrophages, which induce antimicrobial peptide formation in injected and distant warts.[3]

MATERIALS AND METHODS

STUDY DESIGN

This hospital-based, prospective study was conducted in the Department of Dermatology, venereology and leprosy at Jawahar Lal Nehru hospital, Ajmer, over a period of 1 year among 50 patients attending outpatient department. Informed consent was obtained from all patients to be a part of the study.

INCLUSION CRITERIA

1. Patients clinically diagnosed as extragenital warts.
2. Either Age and Sex.
3. Patients with no prior treatment for at least 6 months.
4. Patients willing to involve in the study.

EXCLUSION CRITERIA

1. Patients with Genital Warts.
2. Keloidal tendency and history of keloid.
3. Pregnancy and lactation.
4. Patients on immunosuppressive therapies.
5. HIV, Hepatitis B, Hepatitis C.
6. Patients with prior allergy to any component of MMR vaccine or Vitamin D injection.

STUDY SUBJECT-

The study included 50 patients with extragenital warts randomly divided in two groups of 25 each. Baseline characteristics of the warts (site, number, duration, previous treatment taken) were recorded. Relevant laboratory investigations including Complete hemogram, Random blood sugar, RFT, LFT, Urine pregnancy test, HIV, HBsAg, VDRL were advised after taking detailed history and examination.

PROCEDURE

Group A patients received intralesional MMR vaccine after testing for existing immunity by intradermal injection of 0.1 ml MMR vaccine into the skin of forearm in the volar aspect. A 5 mm+ erythema and induration by 48–72 hours was considered positive .Only positive response patients were included. Vaccine was reconstituted with 0.5 ml distilled water and then injected with insulin syringe into the largest wart in the dose of 0.3 ml if test site induration was 5–20 mm, 0.2 ml if it was 21–40 mm, and 0.1 ml if it was >40 mm. Group B patients received intralesional Vitamin D3 (600000 IU, 15mg/ml) in a dose of 0.3 ml in maximum of 4 warts per session. In both groups injections were repeated every 2 weeks till a maximum of 4 injections or till the complete clearance of warts, whichever was achieved first.

FOLLOW- UP

Follow up was done every 2 weeks till clearance of lesions and then at 6th month. Warts' number, appearance of new lesions, adverse events, recurrence were assessed during this period.

ASSESSMENT

In both groups concurrent photographic documentation was done at baseline and at every follow up visit. The responses were graded as under

CR (Complete response) – 100 % reduction in number
PR (Partial response) – 50-99% reduction in number
NR (No or Inadequate response) – <50% reduction in number

RESULTS

Demographic and clinical data of patients of both groups (Table 1) was comparable without any statistically significant difference.

Regarding the response of warts at the end of therapy (Table 2), in Group A, 19(76%) patients had complete response, 5(20%) patients had partial response and 1(4%) patient had no response. In group B complete response was found in 18 (72%) patients, partial response in 4(16%) and no response in 3(12%) patients. Response observed was slightly higher in Group A than in Group B (p-value=0.566, not significant). Mean 2.73 and 3.11 no. of injections were required for complete response in Group A and B respectively.

The side effects observed were minimal and well tolerated. Pain during injection and bleeding at injection site was a universal complaint which resolved spontaneously. In group A, injection site swelling and flu like symptoms were observed in 1(4%) patient each; pruritus noted in 2(8%) patients. In Group B, side effects noted were transient erythema in 2 (8%) patients, pain and swelling upto around a week in 3(12%) patients. Recurrence was found in 1 patient in Group A and in 3 patients in Group B upon 6 months follow up.

TABLE – 1 Demographic and clinical Data of studied groups

	Group A(MMR)	GroupB (Vitamin D)
Age (years)		
<25	15(60%)	16(64%)
25-40	8(32%)	6(24%)
>40	2(8%)	3(12%)
Mean+SD	23.8 + 11.65	24.84+10.82
Min-Max	9-60	9-50
Gender		
Male	16(64%)	15(60%)
Female	9(36%)	10(40%)
Mean no. Of lesions	12.00 + 6.64	11.72 + 6.84
Mean duration of lesions (months)	9.24 + 7.83	10.08 + 7.92
Previous treatment		
Yes	15(60%)	14(56%)
No	10(40%)	11(44%)
Type(warts)		
Palmoplantar	13(52%)	11(44%)
Vulgaris	9(36%)	10(40%)
Periungual	1(4%)	2(8%)
Plana	2(8%)	2(8%)

TABLE – 2 Comparison of response between studied groups

Response at the end of therapy	No. Of patients	
	Group A (MMR)	Group B (Vitamin D)
Complete response	19 (76%)	18 (72%)
Partial response	5 (20%)	4 (16%)
No response	1 (4%)	3 (12%)
Total patients	25 (100%)	25(100%)

DISCUSSION

Cutaneous warts are common skin lesions caused by infection of epithelia with Human papilloma viruses (HPV). There is no single efficacious treatment modality, with ideal efficacy and cure rates up to present time making it a great challenge in treatment of warts.

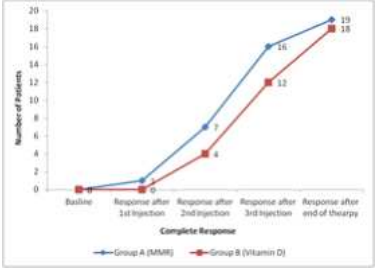

Fig. 1- Comparison of complete response in both groups

A novel approach to treating warts is by induction or boosting of an immune response by immunotherapy. Since immunotherapy triggers the systemic effects of the immune response, it also leads to clearance of distant warts.

In group A (MMR) complete response was seen in 76% patients. The results were similar to study by Shaheen et al[4], they observed a complete response in 80% patients. Chauhan et al5 and Nofal et al6 observed complete response in 82.4% and 81.4% patients respectively. These figures were higher than our study, probably due to more no. of patients and treatment sessions in those studies. We observed complete response in 1 patient after first dose as compared to 4 patients by Chauhan et al.[5]

In group B (Vitamin D) complete response was seen in 72% patients. These results were almost similar to the studies by Kavya et al7 (78.57%) and Aktas et al[8] (80%).

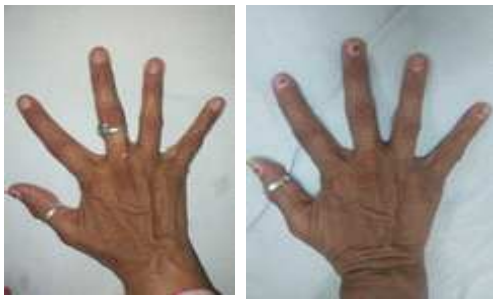

Fig.2 – Verruca Vulgaris (Before and after intralesional therapy)

We observed recurrence in 1 and 3 patients in group A and B respectively. Lesser recurrence represents advantage of immunotherapy associated with acquisition of long term immunity to HPV. Similar recurrence rates were seen by Nofal et al.[9], and Kavya et al[7]

CONCLUSION

Both intralesional immunotherapies (MMR vaccine and Vitamin D) in warts are effective, well tolerated, with minimal recurrence and without any serious side effects. These are novel, easily available and cost effective treatment options. They have an added advantage of non requirement of treating each lesion separately, therefore time saving and non scarring treatment modalities.

DECLARATION OF PATIENT CONSENT-

Written consent was taken from the patients or parents of patients about procedure and for images and other clinical information reported in the article.

FINANCIAL SUPPORT AND SPONSORSHIP

Nil

CONFLICTS OF INTEREST

None

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