Section: Dermatology

Original Research Article

THERAPEUTIC OUTCOME OF INTRALESIONAL IMMUNOTHERAPY IN VERRUCA VULGARIS USING MMR VACCINE- AN INTERVENTIONAL STUDY

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Abstract

Background: Verruca vulgaris, commonly known as warts is a viral skin infection caused by the human papillomavirus (HPV). Conventional treatments for verruca vulgaris often have limitations in terms of efficacy and recurrence rates. In recent years, intralesional immunotherapy using the MMR vaccine has shown promising results in the management of warts. **Aims and objectives:** To evaluate the efficacy and safety of the intralesional MMR vaccine in the treatment of verruca vulgaris. **Material and Methods:** A prospective interventional study was conducted on 50 patients diagnosed with verruca vulgaris over 7 months. 0.3ml of the MMR vaccine was administered at regular intervals into the largest wart once every 2 weeks until complete clearance or a maximum of 5 doses. Clinical assessments were performed at baseline, during treatment, and during follow-up visits to monitor lesion size, resolution, and side effects. **Results:** Only 44 patients completed the study & and 17 (38.64%) showed complete warts clearance. In 5 (11.36%) patients the warts subsided completely after one dose itself. Injection site pain followed by bleeding in some cases were only adverse effects. There was no recurrence of warts among the cured. **Conclusion:** Intralesional immunotherapy using the MMR vaccine appears promising and effective therapeutic for treating verruca vulgaris. The results of this interventional study suggest that MMR vaccine immunotherapy may offer a safe and well-tolerated alternative to conventional treatment.

INTRODUCTION

Common warts, scientifically known as Verruca vulgaris, are a type of keratotic papilloma that occurs mostly in young people. They are caused by a localized infection of the epidermis by the human papillomavirus and can pose a significant burden to both patients and physicians due to their high recurrence rates and the difficulty in treating them.[1] Despite various therapeutic modalities being employed to manage these warts, complete resolution remains difficult in many cases.[2] However, immunotherapy has shown promise in targeting and eliminating the HPV-infected cells within the warts by harnessing the body's immune system.[3] Various intralesional agents are used for immunotherapy of warts, including Mycobacterium w vaccine (Mw), Bacillus Calmette-Guerin vaccine (BCG), tuberculin purified protein derivative vaccine (PPD), measles, mumps, and rubella vaccine (MMR), candida albicans antigen, trichophyton antigen, vitamin D3, interferon alpha 2B, 5-fluorouracil and imiquimod.[2,4-9]

These vaccines are believed to induce a strong nonspecific T-cell inflammatory response against HPV-infected cells. The injection of antigens may lead to the proliferation of peripheral blood mononuclear cells that promote Th1 cytokine responses. These responses include IL-2,4,5,8, INF-gamma, and TNF-alpha, which further activate cytotoxic T cells and natural killer cells to eliminate HPV-infected cells.[10-11]

The immune response stimulated by these agents clears locally treated lesions as well as all lesions on other body sites.[9]

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Our study aimed to determine how effective the MMR vaccine is in completely resolving verruca vulgaris lesions. Along with assessing its efficacy, we also monitored the safety and tolerability of this new treatment approach for any potential adverse effects.

MATERIALS AND METHODS

A prospective, interventional, hospital-based study was conducted from January 2023 to July 2023 at the dermatology OPD of Varun Arjun Medical College & Rohailkhand Hospital, Shahjahanpur, Uttar Pradesh. The study involved 50 patients who were diagnosed with verruca vulgaris. All patients provided informed consent to participate in the study.

Subject selection criteria

Inclusion Criteria

- Patients who had been diagnosed with verruca vulgaris.
- Patients of both sexes, who were over 12 years old.
- Patients who were willing to take part in the study and had provided informed consent.
- Patients who were not going under concurrent treatment for verruca.

Exclusion Criteria

- Pregnancy or lactation.
- Immunocompromised individuals.
- Children under the age of 12 years.
- Patients having fever or showing signs of any infection or inflammation.
- Patients who received other treatments for verruca within the month before enrolling in the study.
- Patients having genital or perianal warts.

Each participant provided informed consent before their baseline demographic data and detailed medical history were collected. The size, number, type, and presence or absence of distant warts were recorded during the clinical examination. Approval was obtained from the Ethics committee before the study. The MMR vaccine was reconstituted with 0.5 mL of provided diluent (distilled water). Each enrolled patient received an intralesional injection of 0.3 mL of MMR vaccine in their largest wart using a 30G insulin syringe. This injection was given every 2 weeks until complete clearance or a maximum of 5 doses. Photographic documentation was taken at each visit, including before treatment (at baseline). The response was graded as complete clearance, partial, or no response. Patients were followed up every 4 weeks for an additional 2 months to assess therapeutic response, side effects, and recurrence. The Friedman test was used to analyze the relationships between variables, and a mean rank table was established to assess the study's outcome.

RESULTS

The study involved 50 patients with verruca vulgaris, but 6 of them were lost to follow-up. Therefore, only 44 cases (88%) were included in the study. The patients' ages ranged from 12 to 50 years. Among the 44 patients, 34 (77.27%) were males and 10 (22.72%) were females, resulting in a male-to-female ratio of 1.2:1. [Table 1]

The majority of cases had warts for six months or less, specifically 33 out of 44 (75.01%) cases. [Table 2]

Shows that verruca vulgaris commonly occurs on the face, neck, and hands, with 12, 18, and 11 cases respectively. [Table 3]

The therapeutic response to the MMR vaccine was measured at each follow-up and analyzed at the end [Table 4 and Figure 1]. The response was classified into four grades: Grade 1 for no improvement, Grade 2 for less than 50% improvement, Grade 3 for more than 50% improvement, and Grade 4 for complete improvement.

The study assessed patient satisfaction using a Likert scale. [Table 5]

The study showed that immunotherapy was effective in treating verruca vulgaris. The results of the Friedman test were significant, with a significant increase in the mean rank after each vaccination visit ($\chi 2$ = 82.17, p-value = 0.001). The median treatment response was highest on the third visit (median = 11) and lowest on the first visit (median = 9). Additionally, the response was greater with more MMR vaccine injections. [Table 6]

During all visits, injection site pain was reported by everyone (100%). Bleeding was observed in 11 cases (25%). No systemic adverse effects were detected. Patients who had complete clearance of warts at the end of the study period did not experience any recurrence. The results of some patients, including clinical pictures before and after therapy, are displayed in the following figures.

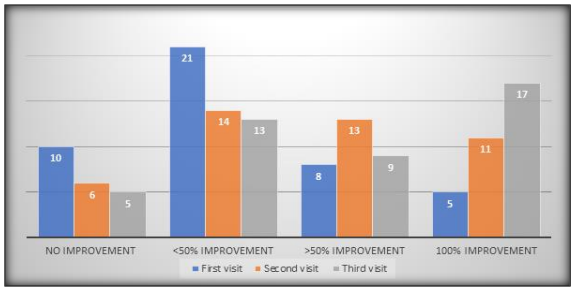

Figure 1: Treatment response at the end of the study

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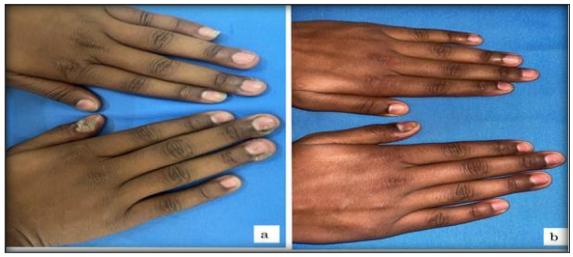

Figure 2: Multiple common warts over digits (a) before and (b) complete clearance of treated and other warts after five doses: The largest wart over The thumb was treated with the intralesional MMR. Vaccine

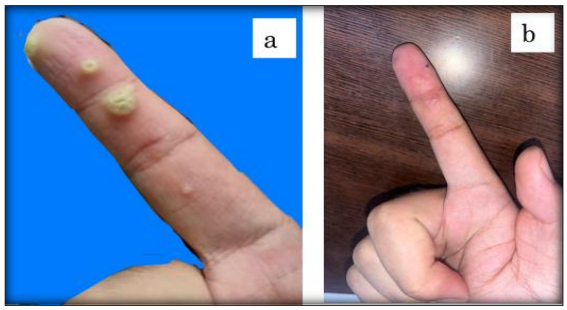

Figure 3: Multiple palmar warts over index finger (a) before and (b) complete clearance of treated and other warts after five doses: The largest wart over the index finger was treated with the intralesional MMR vaccine

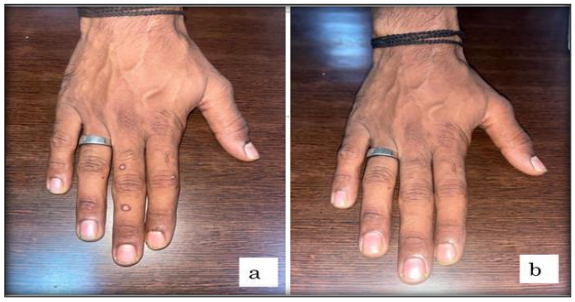

Figure 4: Multiple common warts over digits (a) before and (b) complete clearance of treated and other warts after five doses: The wart over the middle finger was treated with the intralesional MMR vaccine

Table 1: Age & Sex wise distribution of verruca vulgaris patients

Gender	Age groups of patients (years)				Total cases (n=44) (%)
	≥ 12 and ≤ 20	21-30	31-40	41-50	
Male	10	6	15	3	34 (77.28%)
Female	4	1	3	2	10 (22.72%)
Total	14	7	18	5	44 (100%)

Table 2: Distribution of cases based on the duration of verruca vulgaris

Sr no.	Duration in months	Number of cases (n=44) (%)
1	1-6	33 (75.01%)
2	6-12	9 (20.45%)
3	13-18	1 (2.27%)
4	19-24	1 (2.27%)

Table 3: Distribution of cases based on site of verruca vulgaris

Sr No.	Site of lesions	No of patients
1	Face	12
2	Neck	18
3	Hand	11
4	Elbow	1
5	Forearm	1
6	Face + Neck	6
7	Hand + Forearm	1
8	Hand + Face	2
9	Hand + Foot	1
10	Forearm + Foot	1

Table 4: Therapeutic response at the end of study. n- Total number of patients

Treatment response	First Visit		Second visit		Third visit	
	n	%	n	%	n	%
Grade I (no improvement)	10	22.73%	6	13.64%	5	11.36%
Grade 2 (<50% improvement)	21	47.73%	14	31.82%	13	29.54%
Grade 3 (>50% improvement)	8	18.18%	13	29.54%	9	20.46%
Grade 4 (100% improvement)	5	11.36%	11	25.00%	17	38.64%
Total	44	100.00%	44	100.00%	44	100.00%

Table 5: Patient satisfaction level at the end of the study

Patient satisfaction level	Score on the Likert scale	Number of patients who completed the study period (n=44)
Very much satisfied	5	23
Somewhat satisfied	4	9

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Undecided	3	4
Not satisfied	2	2
Not at all satisfied	1	6

Table 6: Descriptive study results table

	Percentiles			Mean Rank	Chi-square (P-value)
	25th	50th (Median)	75th		
First Visit	2.00	2.00	3.00	1.53	82.17 (0.001)
Second visit	2.00	3.00	4.00	2.09	
Third visit	2.00	3.00	4.00	2.38	

DISCUSSION

There are many treatments available for common warts, but none of them have been proven to be completely effective, and most of them are unsatisfactory. There is evidence that the immune system, specifically cell-mediated immunity, is involved in the development and persistence of warts. In HIV-infected patients, warts can spread rapidly, and spontaneously regressing warts show a significant influx of CD4+ lymphocytes in the epidermis and dermis.[12,13]

This proposed immunotherapy activates immunity, clearing treated and distant warts with varying efficacy.[12-15]

Our study found that the adult age group was most affected by common warts, particularly on the face, hands, and neck, likely due to increased exposure to trauma. There was a male predominance, with 77.28% of patients being male, possibly due to outdoor working conditions. Intralesional injection of MMR vaccine was effective in treating these warts.

The current study found that 17 out of 44 cases showed a complete response, whereas Agrawal et al.'s study reported a complete response in 18 (60%) out of 30 patients. The two studies had the same number of doses, three, but differed in sample size. (16) A study by Saini et al. found that 46.5% of the 86 patients had complete responses.[17] The studies by Nofal et al. and Chauhan et al. used five doses of MMR vaccine, resulting in a complete response rate of 81.4% and 82.4%, respectively.[8,18]

Thus the lower response in the present study correlates with the number of doses.

According to the current study, pain was a common issue but it was bearable and didn't last after the injection. Similarly, the pain was experienced by 85.7% and 60% of participants in studies conducted by Nofal et al. and Agrawal et al. respectively.[8,16]

During our study, we observed that 17 patients who had received MMR immunotherapy did not experience any recurrence during the three-month follow-up period. This finding is consistent with the results of studies conducted by Nofal et al,[8] and Zamanian et al,[14] in which no cases of relapse were reported.

CONCLUSION

Intralesional MMR vaccine therapy proved to be a simple and safe treatment option in cases having multiple warts. The generation of HPV-directed immunity via the induction of a delayed-type hypersensitivity reaction to an otherwise unrelated immunogen is one hypothesized mechanism of action of MMR vaccination and other lesional immunotherapeutic antigens. The response rate may increase if a higher concentration of vaccine (0.5ml) and a larger number of doses (maximum five doses) are given. Our findings imply that intralesional MMR might be used as a first-line therapy for numerous warts and as a second-line therapy for warts that are resistant to other treatments.

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