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Research Article

Efficacy and Safety of Intralesional Injection of Mumps measles-Rubella (Mmr) Vaccine in the Treatment of Multiple Cutaneous Warts: A Clinical Trial.

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ABSTRACT

Introduction: Cutaneous warts are common benign skin lesions caused by human papillomavirus (HPV). Conventional treatments such as cryotherapy, salicylic acid, and electrosurgery are often associated with recurrence, pain, and variable efficacy. Intralesional immunotherapy using vaccines such as measles-mumps-rubella (MMR) has emerged as a promising alternative by stimulating host immune responses against HPV.

Aims: To evaluate the efficacy and safety of intralesional MMR vaccine in the treatment of multiple cutaneous warts.

Materials and Methods: This was an open-label, uncontrolled clinical trial conducted in the Department of Dermatology, Venereology and Leprosy at Rajendra Institute of Medical Sciences (RIMS), Ranchi. The study was carried out over a period of one year and seven months, from 01 March 2017 to 30 September 2018. A total of 81 patients with multiple cutaneous warts attending the outpatient department were initially recruited based on eligibility criteria, of whom 81 patients completed the study and were included in the final analysis. The study evaluated the efficacy and safety of intralesional MMR vaccine in the treatment of cutaneous warts.

Results: In patients with verruca vulgaris (n = 42), the mean number of warts decreased from 8.43 at baseline to 1.60 at the final follow-up, showing a statistically significant reduction ($p < 0.0001$). In the verruca plana group (n = 12), the mean number of lesions showed a marked decline from 52.42 at baseline to 7.42 at final follow-up, also demonstrating highly significant improvement ($p < 0.0001$). Similarly, in patients with palmoplantar warts (n = 27), the mean lesion count reduced from 9.37 to 1.04, with a highly significant response ($p < 0.0001$).

Conclusion: Intralesional MMR vaccine is an effective and safe immunotherapeutic modality for the treatment of multiple cutaneous warts. It offers the advantage of treating both local and distant lesions with minimal adverse effects, making it a promising alternative to conventional destructive therapies.

Keywords: Cutaneous Warts; Human Papillomavirus; Intralesional Immunotherapy; MMR Vaccine; Measles-Mumps-Rubella; Dermatology; Wart Treatment; Immunomodulation; Clinical Trial.

INTRODUCTION

Cutaneous warts are common benign epidermal proliferations caused by infection with the human papillomavirus (HPV), a double-stranded DNA virus with tropism for keratinized epithelium. They are frequently encountered in dermatological practice and can affect individuals of all age groups, with higher prevalence in children, adolescents, and immunocompromised patients. Although many warts undergo spontaneous regression due to host immune response, a substantial proportion persist, spread to adjacent sites, or recur after treatment, leading to physical discomfort, psychological distress, and cosmetic concern [1].

Multiple clinical variants of warts exist, including common warts (verruca vulgaris), plantar warts, flat warts, and periungual warts. Among these, multiple cutaneous warts are particularly challenging to treat due to their widespread distribution and tendency for recurrence. The management of cutaneous warts remains difficult despite the availability of various destructive and non-destructive modalities. Conventional therapies such as cryotherapy, electrocautery, surgical excision, salicylic acid application, and laser ablation aim to physically destroy the lesion but are often associated with pain, scarring, incomplete clearance, and high recurrence rates [2,3]. Additionally, these modalities typically target individual lesions rather than addressing the underlying viral infection or inducing systemic immunity.

The limitations of conventional therapies have led to increasing interest in immunotherapeutic approaches, which aim to stimulate the host immune system to recognize and eliminate HPV-infected cells. Intralesional immunotherapy has emerged as a promising strategy in this context. Various antigens and vaccines, including Candida albicans antigen, purified protein derivative (PPD), and Bacillus Calmette–Guérin (BCG), have been investigated with encouraging results [4]. Among these, the measles-mumps-rubella (MMR) vaccine has gained attention due to its established safety profile, widespread availability, and ability to induce a strong cell-mediated immune response.

The mechanism of action of MMR vaccine in wart therapy is believed to involve nonspecific immune activation. Intralesional injection of the vaccine triggers a delayed-type hypersensitivity reaction, leading to the activation of antigen-presenting cells, T-helper lymphocytes, and cytotoxic T cells. This immune cascade not only targets the injected wart but may also result in regression of distant untreated lesions, suggesting a systemic immunological effect [5]. This feature makes MMR vaccine particularly useful in patients with multiple or recalcitrant warts, where localized destructive therapies may be insufficient.

Several clinical studies have reported promising outcomes with intralesional MMR immunotherapy. Nofal et al. demonstrated significant clearance rates in patients with multiple warts, with minimal adverse effects and low recurrence [6]. Similarly, studies by Hussein et al. and El-Zawahry et al. have shown comparable efficacy, reinforcing the potential role of MMR vaccine as an alternative treatment modality [7,8]. However, variations in study design, dosing protocols, and patient populations necessitate further evaluation to establish standardized treatment guidelines.

Safety is a critical consideration in any therapeutic intervention. The MMR vaccine is generally well tolerated, with most adverse effects being mild and transient, such as pain at the injection site, erythema, swelling, and occasional low-grade fever. Serious adverse reactions are rare, making it a relatively safe option compared to more invasive procedures [9]. Importantly, its use in immunotherapy for warts does not carry the same risks of scarring or pigmentary changes associated with destructive techniques.

Despite growing evidence supporting intralesional MMR immunotherapy, there remains a need for further well-designed clinical trials to evaluate its efficacy, safety profile, and long-term outcomes across diverse populations. Standardization of dosage, injection intervals, and treatment duration is also required to optimize clinical outcomes and facilitate broader adoption in dermatological practice.

The present clinical trial aims to evaluate the efficacy and safety of intralesional MMR vaccine in the treatment of multiple cutaneous warts, with a focus on clinical response, resolution of distant lesions, recurrence rates, and adverse effects.

MATERIALS AND METHODS

Study Design: The study was designed as an Open Uncontrolled Clinical Trial of MMR Vaccine and was carried out at a single centre**.**

Study Place: Department of Dermatology, Venereology & Leprosy, Rajendra Institute of Medical Sciences (Rims), Ranchi

Period of Study: 1 Year 7 Months (01-03-2017 to 30-09-2018)

Study Population: A total of 100 patients attending the OPD of Department of Dermatology, Venereology & Leprosy, were recruited in the Study after satisfying the subject selection criteria.

Sample Size: 81 patients

Study Variables:

- Type of Wart
- Gender
- Occupation
- Treatment Outcome – Reduction in Number of Warts
- Treatment Response and Adverse Effects

Inclusion Criteria:

i. Male or female patients with multiple cutaneous warts ((≥ 2) who were candidate

for treatment between 18 and 65 years of age (both inclusive).

ii. Patients who gave their informed consent**.**

Exclusion Criteria:

- Any previous wart therapy in last 1 month before enrolment.
- Pregnant and lactating women.
- Any evidence of immunosuppression (eg. HIV infection, organ transplantation, long term steroid use etc.).
- Any other systemic disease (eg. liver or kidney disorder).
- Presence of genital warts Presence of mucosal warts. Presence of ulcerated or inflamed warts

Statistical Analysis:

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate.

Explicit expressions that can be used to carry out various t-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a t-distribution under the null hypothesis is given. Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test.

Once a t value is determined, a p-value can be found using a table of values from Student's t-distribution .If the calculated p-value is below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favour of the alternative hypothesis.

P-value ≤ 0.05 was considered for statistically significant.

Image Gallery

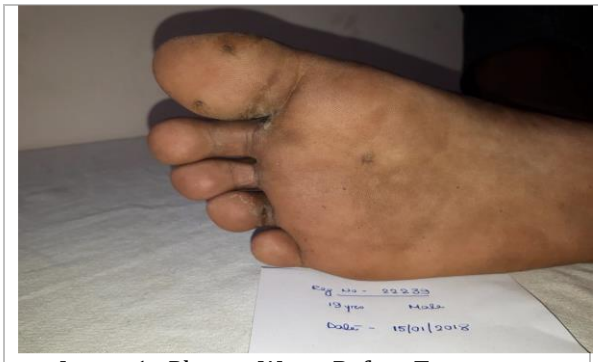


Image 1: Plantar Warts Before Treatment Sessions

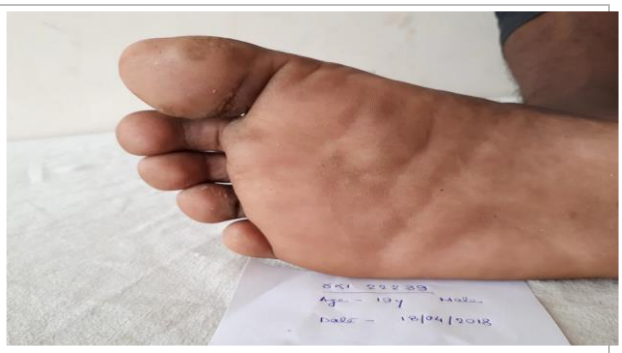


Image 2: Complete Clearance Of Plantar Warts After Treatment With Mmr

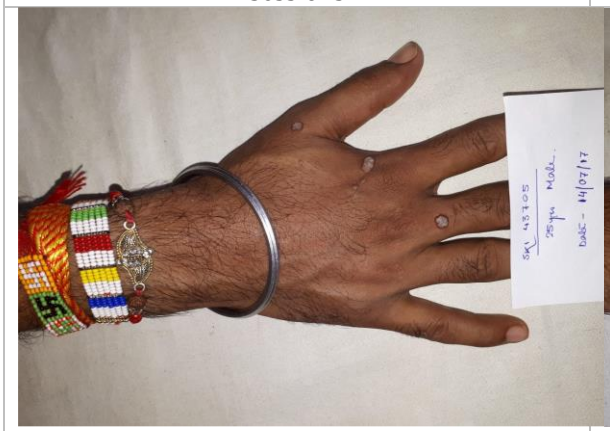


Image 3: Verruca Vulgaris Before Treatment Sessions

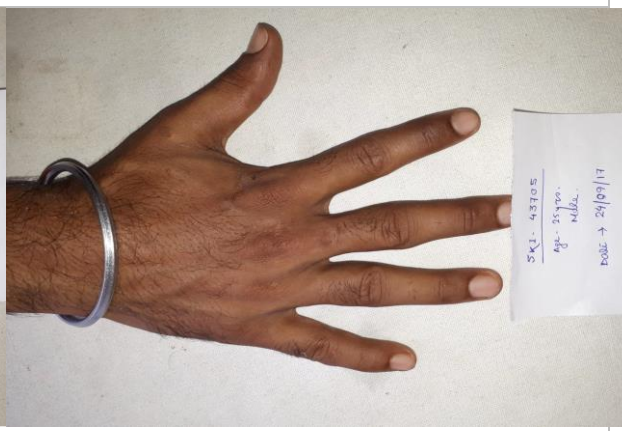


Image 4: Complete Clearance Of Verruca Vulgaris After Treatment With Mmr.

RESULT

Table 1: Distribution of Clinical Types of Warts (n = 81)

Type Of Wart	Number Of Patients	Percentage (%)
Verruca Vulgaris	42	51.9
Verruca Plana	12	14.8
Palmoplantar Wart	27	33.3
Total	81	100

Table 2: Gender-wise Distribution of Patients (n = 81)

Gender	Number Of Patients	Percentage (%)
Male	42	51.9
Female	39	48.1
Total	81	100

Table 3: Occupational Distribution of Patients (n = 81)

Occupation	Number Of Patients	Percentage (%)
Students	25	30.9
Non-Agricultural Indoor Workers	24	29.6
Homemakers	22	27.2
Agricultural Workers	5	6.2
Non-Agricultural Outdoor Workers	5	6.2
Total	81	100

Table 4: Treatment Outcome – Reduction in Number of Warts

Type Of Wart	Baseline Mean	Final Mean	Reduction (%)	P-Value
Verruca Vulgaris	8.43	1.6	81.08%	<0.0001
Verruca Plana	52.42	7.42	85.85%	<0.0001
Palmoplantar Wart	9.37	1.04	88.93%	<0.0001

Table 5: Treatment Response and Adverse Effects

A. Complete Clearance Rate

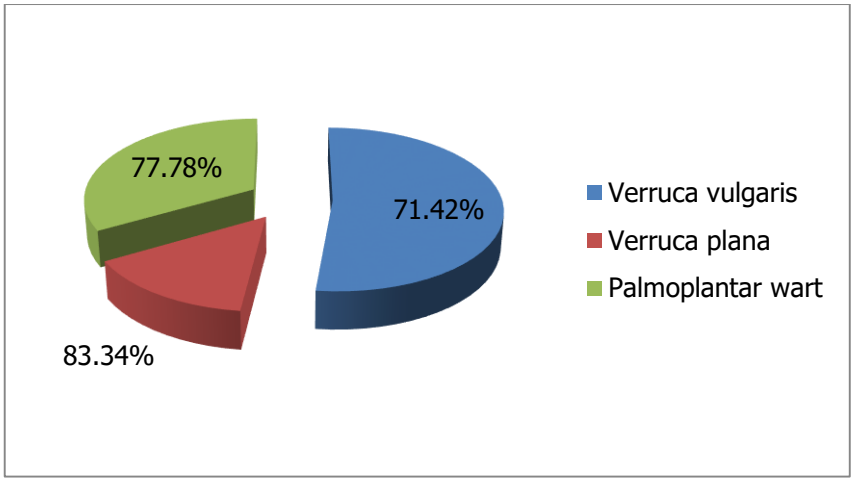
Type Of Wart	Patients (N)	Complete Clearance	Percentage (%)
Verruca Vulgaris	42	30	71.42
Verruca Plana	12	10	83.34
Palmoplantar Wart	27	21	77.78
Overall	81	61	75.3

B. Adverse Effects

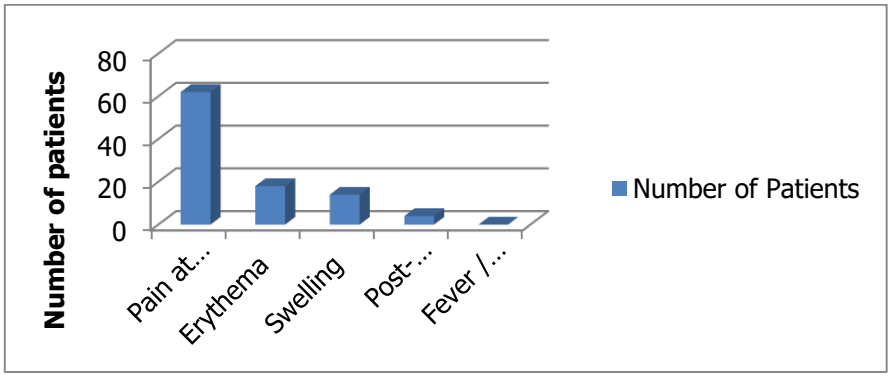
Adverse Effect	Number Of Patients	Percentage (%)
Pain At Injection Site	62	76.54
Erythema	18	22.22
Swelling	14	17.28
Post-Inflammatory Hyperpigmentation	4	4.9
Fever / Systemic Symptoms	0	0

Treatment Response and Adverse Effects

A. Complete Clearance Rate



B.Adverse Effects



A total of 81 patients who completed the study were included in the final analysis. Among them, 42 patients (51.9%) presented with verruca vulgaris, 12 patients (14.8%) had verruca plana, and 27 patients (33.3%) were diagnosed with palmoplantar warts.

In terms of demographic distribution, the study population showed a slight male predominance with 42 males (51.9%) and 39 females (48.1%).

Out of the total 81 patients included in the study, the majority were students, accounting for 25 patients (30.9%). This was followed by non-agricultural indoor workers, who comprised 24 patients (29.6%), and homemakers, who included 22 patients (27.2%). A smaller proportion of patients were involved in outdoor occupations, with 5 patients (6.2%) being agricultural workers and another 5 patients (6.2%) being non-agricultural outdoor workers.

In patients with verruca vulgaris (n = 42), the mean number of warts decreased from 8.43 at baseline to 1.60 at the final follow-up, showing a statistically significant reduction ($p < 0.0001$). In the verruca plana group (n = 12), the mean number of lesions showed a marked decline from 52.42 at baseline to 7.42 at final follow-up, also demonstrating highly significant improvement ($p < 0.0001$). Similarly, in patients with palmoplantar warts (n = 27), the mean lesion count reduced from 9.37 to 1.04, with a highly significant response ($p < 0.0001$). Out of the 81 patients who completed the study, a high rate of complete clearance was observed following intralesional MMR vaccine therapy. In the verruca vulgaris group (n = 42), 30 patients achieved complete clearance, accounting for 71.42% of cases. In the verruca plana group (n = 12), 10 patients showed complete clearance, representing 83.34% of patients. In the palmoplantar wart group (n = 27), 21 patients achieved complete clearance, corresponding to 77.78% of cases. Out of the 81 patients who completed the study, adverse effects following intralesional MMR vaccine injection were generally mild and self-limiting. The most common side effect was pain at the injection site, reported by 62 patients (76.54%). Erythema was observed in 18 patients (22.22%), while swelling at the injection site occurred in 14 patients (17.28%). Post-inflammatory hyperpigmentation was noted in 4 patients (4.9%).

DISCUSSION

Cutaneous warts are benign proliferations of the skin caused by human papillomavirus (HPV) and are commonly encountered in dermatological practice. They remain difficult to treat due to their persistence, recurrence, and variable response to therapy. In the present study, 81 patients completed the trial, among whom verruca vulgaris was the most common type (51.9%), followed by palmoplantar warts (33.3%) and verruca plana (14.8%). A similar pattern has been reported by Bunney MH et al. [11], who observed verruca vulgaris as the predominant clinical subtype in their epidemiological study of warts. Likewise, Rock B et al. [12] noted that common warts constitute the majority of HPV-related cutaneous lesions in clinical practice.

A slight male predominance was observed in the present study (51.9% males vs. 48.1% females), which is comparable to findings reported by Massing AM and Epstein WL [13], who documented a marginal male predominance in their population-based study of cutaneous warts. The occupational distribution showed that students formed the largest group (30.9%), followed by indoor workers and homemakers. This observation is consistent with Johnson SM et al. [14], who reported a higher prevalence of warts among younger individuals, especially students, due to increased contact exposure and minor skin trauma facilitating viral entry.

Intralesional MMR immunotherapy demonstrated significant efficacy in all wart types in the present study. Verruca vulgaris showed an 81.08% reduction in lesion count, verruca plana 85.85%, and palmoplantar warts 88.93% ($p < 0.0001$). Similar findings were reported by Horn TD et al. [15], who demonstrated that intralesional antigen-based immunotherapy produces significant regression of both treated and untreated warts through immune activation. Additionally, Micali G et al. [16] explained that MMR vaccine stimulates a strong Th1-mediated immune response leading to clearance of HPV-infected keratinocytes.

The overall complete clearance rate in this study was 75.30%, with the highest response observed in verruca plana (83.34%). Comparable results were reported by Vandana R et al. [17], who observed significant clearance rates using intralesional immunotherapy in multiple cutaneous warts. Similarly, Johnson SM et al. [18] reported 60–80% response rates with antigen-based immunotherapy in recalcitrant warts. However, Shenefelt PD et al. [19] reported comparatively lower response rates, attributing this to variability in host immune response and shorter treatment duration.

Adverse effects in the present study were mild and self-limiting. Pain at the injection site was the most common (76.54%), followed by erythema (22.22%) and swelling (17.28%). Post-inflammatory hyperpigmentation was rare (4.9%), and no systemic adverse effects were observed. These findings are consistent with Cunningham AL et al. [20], who reported only minor local reactions following intralesional immunotherapy without any serious systemic complications.

CONCLUSION

Intralesional MMR vaccine immunotherapy is an effective and safe treatment modality for multiple cutaneous warts. Verruca vulgaris was the most frequently encountered clinical type, followed by palmoplantar warts and verruca plane. The study population predominantly consisted of young adults with a slight male preponderance and a higher representation of students and indoor workers. A significant clinical improvement was observed across all types of warts following treatment, with marked reduction in lesion burden and statistically highly significant response. A substantial proportion of patients achieved complete clearance, including those with multiple and recalcitrant lesions, indicating strong therapeutic efficacy of the intervention. The treatment was well tolerated, with adverse effects being mild, transient, and predominantly limited to local injection site reactions. No serious systemic complications were observed, confirming a favorable safety profile.

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