Effect of Measles Mumps Rubella Vaccine in Treatment of Common Warts

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Abstract

Background: There are many destructive and immunotherapeutic options available for the treatment of common warts, but no treatment is 100% effective and usually cause pain and scarring. Recently, intralesional immunotherapy with skin test antigens and vaccines has been shown to be effective in the management of warts. We evaluated the efficacy of Measles Mumps Rubella (MMR) vaccine injection in the treatment of cutaneous warts. Aim: To study the efficacy of intralesional MMR vaccine in the treatment of common warts. Materials and Methods: A case–control study was conducted in AVBR Hospital, Sawangi (Meghe), Wardha, in 2015–2016. Forty clinically diagnosed cases of cutaneous common wart were selected in the study and were put randomly into two groups (20 in each group). Group 1: included twenty patients subjected to intralesional injection of 0.5 ml MMR vaccine. Group 2: included twenty patients as a control group and subjected to intralesional injection of 0.5 ml saline. These injections were repeated every 3 weeks intervals for maximum three injections. Follow-up of patients was done every 6 months for clinical assessment of results and to study recurrence. Results: A significant difference was found between the therapeutic responses of common warts to MMR. Vaccine and normal saline (control) group. At the end of 9 weeks (third visit), about 65% patients treated with MMR vaccine showed complete clearance compared with 5% of the control group. Grade 3 response was 20% versus 10% respectively; whereas Grade 2 response was observed in 10% versus 25%, respectively, and as regards no response, it was 5% versus 60% in MMR vaccine and control group, respectively. Conclusion: We found that the treatment of common warts by MMR vaccine is effective, with good cure rates, and excellent safety profile.

Keywords: Common warts, efficacy, immunotherapy, measles mumps rubella vaccine, therapeutic, vaccine

Introduction

Common warts or verruca vulgaris are hyperkeratotic papillomas caused by multiple strains of human papillomavirus (HPV). Papillomaviruses are ubiquitous, epitheliotropic nonenveloped small double-stranded DNA viruses. Primary manifestations of HPV infection include common warts, genital warts, flat warts, and deep palmpoantar warts (myrmecia).

Although warts may resolve spontaneously in 65%–78% of the patients within 2 years,[1,2] many patient seek treatment because warts can be unsightly, tender, or painful. There are many destructive and immunotherapeutic options for common warts such as topical salicylic acid, cantharidin, bleomycin sulfate, cryotherapy, laser ablation, trichloroacetic acid, formaldehyde, 5-fluorouracil, photodynamic therapy and surgery, contact sensitizers, imiquimod, intralesional interferon, electrocautery, and oral drugs, such as levamisole, cimetidine, and zinc sulfate.[3,6]

Many observations have suggested that wart proliferation is inhibited by the immune system, particularly the cell-mediated immunity.[2,7] If this local cellular immune response could be enhanced, wart resolution could be long lasting. Due to the high prevalence of warts in various populations, especially in children, as well as the necessity of treatment, we evaluated the efficacy of intralesional measles mumps rubella (MMR) vaccine in the treatment of cutaneous warts.

Materials and Methods

The study was done after obtaining the Institutional Ethics Committee approval and in accordance with good...
clinical practice guidelines. Clinically diagnosed cases of cutaneous common wart that fulfilled the inclusion criteria (patients having single or multiple common warts and palmoilplantar warts, age more than 12 years and with no concurrent systemic, or topical treatment of warts within the past 4 weeks) coming to dermatology OPD of AVBR Hospital, Sawangi, Wardha, were selected to participate in the study. Patients with fever or signs of any inflammation or infection, children <12 years, pregnant and lactating female, immunocompromised patients, patients having anogenital warts and verruca plana and history of asthma, allergic skin disorders, meningitis, or convulsions were excluded from the study. Patients were clearly explained the nature of the study, and written informed consent was taken for the participation in the study. Detailed demographic data of each participant were collected. The detailed cutaneous examination was conducted in bright light, and appropriate digital photographs were taken. Patients were divided randomly (alternately) into two groups (Group A and Group B). Group A had received 0.5 ml of MMR vaccine in the base of target wart, and Group B had received 0.5 ml intraleisional normal saline (0.9%) in the target wart (usually the largest wart) at 3 weeks interval for a maximum of three treatments.[8] MMR vaccine was available in the form of single-dose vial of freeze-dried vaccine. It was reconstituted with 0.5 ml of diluent (water for injections). After completion of treatment schedule, the patients were followed every month for 6 months for clinical assessment of results and recurrence. Data obtained was analyzed with following statistical tools.

- Fisher’s exact test
- Chi-square with Yates’ correction
- Chi-square without Yates’ correction.

Assessment of efficacy

Photographic evaluation: At the end of the study period, pre- and post-intervention photographs were assessed to compare the degree of reduction wart.

The response was evaluated as follows:

- Grade 1 - No response
- Grade 2 - 0%–49% reduction in size Partial response
- Grade 3 - 50%–99% reduction in size Complete response
- Grade 4 - Complete disappearance of the lesion.

Resolution of distant untreated warts was also assessed.

Observations and Results

Totally 50 patients, 23 patients in MMR Group and 27 patients in control group of common wart who attended outpatient department AVBR, Sawangi, were enrolled for this study; however, three patients of MMR group and seven patients of control group were lost for follow-ups. Therefore, the sample size was of forty patients with twenty patients in MMR group and control group each.

At the end of 3rd week (first follow up visit), grade of response in MMR group compared with control group was Grade 1 response in 25% versus 75%, respectively, Grade 2 response in 60% versus 25%, and Grade 3 response in 15% versus 0%, respectively [Graph 1]. None of the group showed Grade 4 response at the end of 3rd week.

After the end of 6 weeks (second visit), grade of response in MMR group compared with control group was Grade 1 response in 10% versus 70%, respectively, Grade 2 response was almost similar, i.e., 30% versus 25% and Grade 3 response seen in 40% versus 5%, respectively, whereas Grade 4 response was observed in 20% of MMR-treated group compared with 0% of control group [Graph 2].

At the end of 9 weeks (third visit) Grade 1 response found in 5% versus 60%, Grade 2 response in 10% versus 25% and Grade 3 response seen in almost similar number of patients, i.e., 20% versus 10%, whereas Grade 4 response was observed in 65% versus 5% patients of MMR and control group, respectively [Graph 3 and Figures 1-4]. Table 1 summarizes the therapeutic response in the two groups at the end of treatment.

As regards the response of the wart to the treatment, MMR-treated group gave better results compared with the normal saline group, higher rates of complete response (65%
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Table 1: Therapeutic response in patients at the end of 4th visit

| Grade of response | Number of patients (%) | MMR group (n=20) | Placebo group (n=20) |
|-------------------|------------------------|------------------|---------------------|
| Grade 1 (no response) | 1 (5) | 12 (60) |
| Grade 2 (0%-49% reduction in size) | 2 (10) | 5 (25) |
| Grade 3 (50%-99% reduction in size) | 4 (20) | 2 (10) |
| Grade 4 (complete disappearance of lesion) | 13 (65) | 1 (5) |

χ², P = 21.55, 0.0001 (S)

S: Significant, MMR: Measles, mumps, rubella

Table 2: Frequency and therapeutic response rate in measles mumps rubella, and placebo group

| Number of visit | Therapeutic groups | Therapeutic response | Number of patients (%) | χ², P |
|-----------------|--------------------|----------------------|------------------------|-------|
| First visit (at 3rd week) | MMR group (n=20) | Grade 1 | 5 (25) | 10.88, 0.0043 (S) |
| | | Grade 2 | 12 (60) | |
| | | Grade 3 | 3 (15) | |
| | | Grade 4 | 0 | |
| | Placebo group (n=20) | Grade 1 | 15 (75) | |
| | | Grade 2 | 5 (25) | |
| | | Grade 3 | 0 | |
| | | Grade 4 | 0 | |
| Second visit (at 6th week) | MMR group (n=20) | Grade 1 | 2 (10) | 18.54, 0.0001 (S) |
| | | Grade 2 | 6 (30) | |
| | | Grade 3 | 8 (40) | |
| | | Grade 4 | 4 (20) | |
| | Placebo group (n=20) | Grade 1 | 14 (70) | |
| | | Grade 2 | 5 (25) | |
| | | Grade 3 | 1 (5) | |
| | | Grade 4 | 0 | |
| Third visit (at 9th week) | MMR group (n=20) | Grade 1 | 1 (5) | 21.55, 0.0001 (S) |
| | | Grade 2 | 2 (10) | |
| | | Grade 3 | 4 (20) | |
| | | Grade 4 | 13 (65) | |
| | Placebo group (n=20) | Grade 1 | 12 (60) | |
| | | Grade 2 | 5 (25) | |
| | | Grade 3 | 2 (10) | |
| | | Grade 4 | 1 (5) | |

S: Significant, MMR: Measles, mumps, rubella

Local tissue destruction is a commonly employed method in the treatment of warts. However, it is not practical for multiple lesions, palmoplantar and facial lesions because of associated scarring or pigmentation. Most of the current therapeutic options results in the clearing of wart within 1–6 months, but in 20%-30% of the patient do relapse, and new lesions may appear as a result of failure of the cellular immune system to detect and remove the lesions completely. Immunotherapy aims to achieve an HPV-targeted immune reaction and offers a theoretical advantage in the effective control of viral proliferation. Hence, to stimulate cell-mediated immunity, various antigens of fungal, mycobacterial, and bacterial origins have been used. Specific factors accounting for the variability of innate responsiveness to HPV are incompletely understood.

Discussion

Local tissue destruction is a commonly employed method in the treatment of warts. However, it is not practical for multiple lesions, palmoplantar and facial lesions because of associated scarring or pigmentation. Most of the current therapeutic options results in the clearing of wart within 1–6 months, but in 20%-30% of the patient do relapse, and new lesions may appear as a result of failure of the cellular immune system to detect and remove the lesions completely. Immunotherapy aims to achieve an HPV-targeted immune reaction and offers a theoretical advantage in the effective control of viral proliferation. Hence, to stimulate cell-mediated immunity, various antigens of fungal, mycobacterial, and bacterial origins have been used. Specific factors accounting for the variability of innate responsiveness to HPV are incompletely understood.

Graph 3: Response rate at third visit

Table 3 shows pain was observed in maximum patients, i.e., 85% of MMR-treated patients whereas erythema, swelling, and flu-like symptoms were seen in almost some numbers of patients, i.e., 25%, 20%, and 10%, respectively.
In our short study, most of the patients belonged to adult age group. Hands, feet, and face involvement was commonly seen in our study group might be because of more exposure and susceptible for trauma, pricks, and inoculation. Most of the patients were students, with few doctors, butchers, farmer, and one anatomist by profession. In our study, there were 18 (90%) male and 2 (10%) female in MMR group while control group included 19 (95%) males and 1 (5%) females, with a male predominance. Males were more affected than females may be due to outdoor working condition. We document the effectiveness of intralesional injection of MMR vaccine in common warts. In this study, we found as regards the response of the wart, MMR-treated group gave significantly better results compared with the control group, Comparison of these rates showed statistically significant difference between the two groups ($P < 0.001$).

In the first posttreatment visit, therapeutic response was seen in 75% of patients in the MMR group, including 15% Grade 3 cure and 60% Grade 2 cure, whereas only 25% of the control group showed therapeutic response. In the second and third posttreatment visits, the proportion of therapeutic response had increased in the MMR group and reached 90% and 95%, respectively, whereas these rates in the control group were significantly lower. As regards the response of the wart at the end of the fourth visit, MMR-treated group gave higher rates of complete response (65% versus 0%, respectively); but as regards partial response, it was 10% versus 25%, respectively, and as regards no response, it was 5% versus 60%.

| Side effects         | Number of patients (%) |
|----------------------|------------------------|
| Pain                 | 17 (85)                |
| Erythema             | 5 (25)                 |
| Swelling             | 4 (20)                 |
| Flu-like symptoms    | 2 (10)                 |
respective. When we compared number of warts reduction at the end of treatment (fourth visit) between MMR group and placebo group, the difference was significant ($P = 0.0010$). There was $69.52\%$ reduction in the number of warts in MMR group at the end of the fourth visit as compared with only $23.46\%$ reduction in placebo group. In our study, side effects includes pain, which was seen in almost all the patients ($85\%$) and few patients experience erythema ($25\%$), swelling ($20\%$), and flu-like symptoms ($10\%$) in MMR-treated group whereas side effects such as pain, swelling, and erythema was seen in control group. Recurrence of warts was observed in our study. In MMR-treated group, 9 warts recurred out of total 82 warts during 6 months follow-up period whereas, in placebo group, 45 warts recurred out of total 80 warts. In this study, we found MMR-treated group gave significantly better results compared with the control group, higher rates of complete response.

Zamanian, et al.\cite{21} (MAR 2014) carried out study to assess the efficacy of intralesional injection of mumps-measles-rubella vaccine in patients with wart which showed mean age was $18.9 \pm 12$ years in the MMR group and $20.1 \pm 10$ years in the normal saline group.

In a study by Meena et al.\cite{22} using MWV for the treatment of multiple warts, a sensitization dose of 0.1 ml was given in each deltoid region at the baseline. After 2 weeks, subsequent injections were given at an interval of 1 week intralesionally into three to five lesions at a time. Complete clearance of warts at the site of injection was seen in $33 (83\%)$ patients with $23 (70\%)$ of the 33 patients showing resolution of the distant untreated warts.

In a study by Mohamad et al.,\cite{23} MMR vaccine was given in the treatment of plantar warts in 100 patients. This study showed a significantly higher rate of complete clearance compared with the control group ($82\%$ vs. $0\%$, respectively). The rate of partial response was $6\%$ versus $30\%$, and the rate of no response was $12\%$ versus $70\%$, respectively.

In a study by Nimbalkar, et al.,\cite{24} each patient of viral wart was injected with $10 \text{ TU}$ of tuberculin purified protein derivative (PPD) (0.1 ml) intralesionally in the largest wart at 2 weekly intervals. Clinical assessment was done 3 weeks after the completion of treatment. The study showed that out of 45 patients, $62.2\%$ showed complete clearance, eight patients $17.8\%$ showed partial clearance, and $20\%$ patients showed no improvement.

In another study by Gupta et al.,\cite{25} in which killed MWV was used for the treatment of anogenital warts, a sensitization dose of 0.1 ml was given in each deltoid, and intralesional injections were given in $\leq 3$ warts at a time, which were repeated at weekly intervals. There was complete clearance of warts in eight out of the nine patients ($88.9\%$) who were treated.

Saoji et al.,\cite{26} carried out the study with 61 patients of difficult-to-treat warts who were treated with 2.5 TU of PPD intralesionally in a few warts. A total of four sessions were given at 2 weekly intervals, and patients were followed up for 6 months after the last dose. Forty-two ($76\%$) patients showed complete clearance after four sessions while the remaining 13 ($24\%$) patients were nonresponders.

In study by Nofal et al.,\cite{27} study included 135 patients with single or multiple recalcitrant or nonrecalcitrant common warts received intralesional MMR vaccine. The results revealed complete response in 57 patients ($81.4\%$), partial response in seven patients ($10\%$), and no response in six patients ($8.6\%$) of the MMR group.

**Conclusion**

From our study, it can be inferred that intralesional MMR vaccine promises as an effective therapeutic modality in common warts, particularly multiple warts as it has advantage of injecting single wart. It seems to be effective, with good cure rates, excellent safety profile and cost-effective. It is effective equally at injected and warts at distant site, and prevent reoccurrence of wart with complete clearance.

**Recommendation**

We recommend the use of intralesional MMR vaccine in larger well-controlled studies and in comparison with other therapeutic modalities, particularly the traditional ones.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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