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**Research Article**

# Measles, mumps and rubella vaccine as an intralesional immunotherapy in treatment of warts

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## ABSTRACT

**Background:** To observe the efficacy and safety of intralesional Measles Mumps and Rubella (MMR) vaccine in the treatment of warts.
**Methods:** 50 patients with single or multiple warts more than 06 months duration in all age groups were included in the study. The patients received intralesional MMR vaccine 0.5ml into a single wart or the largest wart in case of multiple lesions at interval of two weeks for three treatments. The response was evaluated as 0-49% as no response, 50-99% as partial response and 100% as complete response. Follow up was made every 02 weeks for 06 weeks and then monthly for 06 months to detect any recurrence.
**Results:** Complete response was seen in 36 (72%), partial response in 08 (16%) and no response in 06 (12%) patients. No recurrence was observed. Pain at the site of injection in 18 (36%) and flu like symptoms in 02 (04%) patients were observed.
**Conclusions:** Intralesional immunotherapy with MMR vaccine was found to be a simple, effective, and safe treatment for warts. This study proved to be cost effective as patients can be treated with just 03 doses of MMR vaccine given at the interval of two weeks.

**Keywords:** Warts, Measles, Mumps and Rubella vaccine, Intralesional immunotherapy, MMR

## INTRODUCTION

Warts or verruca vulgaris are hyperkeratotic papillomas caused by infection with Human Papilloma Virus (HPV). They are more frequently seen on the hands of children and young adults, but may be located on any cutaneous or mucosal surface. Although there are many destructive and immunotherapeutic options available for the treatment of warts, no single treatment has yet proven 100% effective.[1]

Destructive therapies include either topical agents such as salicylic acid, podophyllotoxin, trichloroacetic acid, formaldehyde, 5-flurouracil and photodynamic therapy or surgical methods such as cryosurgery, laser ablation, electrocautery and surgical excision. Immunotherapeutic agents include contact sensitizers, imiquimod, intralesional interferons and oral drugs such as levamisole, cimetidine and zinc sulphate.[1-4] Previous mentioned methods are not always successful and may be associated with adverse events. Even when existing warts are successfully eradicated, patients may develop new warts in other areas.[5,6]

There are new trends towards the use of immunotherapy in treatment of warts, as the immune system seems to play an important role in the control of warts infection. Although the exact mechanisms are unclear but most evidences suggest that cell mediated immunity plays an important role in control of HPV infection as the incidence of warts increases in subjects with cell mediated immune defects (Human immunodeficiency virus (HIV) infection patients, malignant diseases etc).[6-8] In some of the previous studies, it has been shown that

intralesional measles-mumps-rubella (MMR) vaccine results in regression of warts via immunomodulation and induction of immune system. This method can be used in larger populations because of vaccine availability and safety.[9] 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 MMR vaccine injection in the treatment of warts.

## METHODS

This was a prospective study conducted in the Dermatology outpatient department of V.S Hospital, Ahmedabad over a period of one year from July, 2014 to June, 2015. A total of 50 patients who gave informed consent prior to the treatment were included in the study. The study was started after taking due permission from Institutional Review Board (IRB), NHL Medical College, Ahmedabad.

### *Inclusion criteria*

- Clinically diagnosed patients having single or multiple warts with more than 6 months duration
- Patients of both genders of all age groups
- Patients not taking any systemic or topical treatment of warts for the last 04 weeks

### *Exclusion criteria*

- Patients with past history of allergic response to MMR or any other vaccine
- Patients with acute febrile illness or any bacterial infection
- Patients with immunosuppression / HIV Infection
- Pregnant or lactating women
- Patients having past history of asthma, allergic skin disorders or convulsions.

Detailed information of all the patients satisfying inclusion criteria was recorded in preformed questionnaires. This included,

- Personal data: name, age, sex, occupation
- Past history: previous treatments, recurrence and duration of the warts
- Medical history: systemic diseases as HIV, diabetes, asthma, allergic skin disorders or convulsions
- Drug history: corticosteroids or other immunosuppressive drugs
- Clinical data: site, size, number, distribution, presence or absence of distant warts
- Photography of the lesions: Before the first treatment session, two weeks after the last dose and six months after the last dose.

All patients received a dose of 0.5 ml intralesional MMR vaccine into a single wart or the largest wart in case of multiple lesions. Intralesional vaccine was given every 02 weeks into the same wart for 03 doses. The response of treatment was evaluated by decrease in size of wart(s), decrease in number of warts and photographic comparison. The response was considered complete if there was complete clearance of the wart(s), partial if the wart(s) had regressed in size by 50–99% and no response if there was 0–49% decrease in wart(s). Immediate and late adverse effects of MMR vaccine were evaluated after each treatment session. Follow up was made every 02 weeks for 06 weeks and then monthly for 06 months to detect any recurrence.

Data was analysed using Microsoft Excel for Age and Gender distribution, Number of warts, Distribution of warts, and response to treatment.

## RESULTS

A total of 50 patients were included in the study which was conducted over a period of one year.

**Table 1: Age and Gender distribution.**

| Age group (years) | Males | Females | Total |
|---|---|---|---|
| < 18 | 08(16%) | 05(10%) | 13(26%) |
| 18-45 | 17(34%) | 11(22%) | 28(56%) |
| > 45 | 07(14%) | 02(04%) | 09(18%) |
| Total | 32(64%) | 18(36%) | 50(100%) |

Table 1 shows that out of 50 patients, 32 (64%) were male and 18 (36%) were female patients. Maximum 28 (56%) patients belonged to 18-45 years age group while there were 13 (26%) patients in <18 years age group and 09 (18%) patients belonged to >45 years age group.

**Table 2: Number of warts.**

| Warts | Frequency |
|---|---|
| Single | 15 (30%) |
| Multiple | 35 (70%) |
| Total | 50 (100%) |

Table 2 shows that 35(70%) patients were having multiple warts and 15(30%) patients were having single wart.

**Table 3: Distribution of warts.**

| Site | Frequency |
|---|---|
| Face & Neck | 09 (18%) |
| Upper Limb | 20 (40%) |
| Lower Limb | 07 (14%) |
| Genitals | 10 (20%) |
| Plantar | 04 (08%) |
| Total | 50 (100%) |

Table 3 demonstrates that Upper limb particularly the dorsa of hands was the most common site affected in 20(40%) followed by genitals in 10(20%), face and neck in 09(18%), lower limb in 07(14%) and plantar surface in 04 (08%) patients. 26(52%) patients were having distant warts at different anatomic sites.

**Table 4: Response to treatment.**

| Response | Multiple warts | Single wart | Overall response |
|---|---|---|---|
| Complete (100%) | 29 (58%) | 07 (14%) | 36 (72%) |
| Partial (50-99%) | 04 (08%) | 04 (08%) | 08 (16%) |
| No (0-49%) | 02 (04%) | 04 (08%) | 06 (12%) |
| Total | 35 (70%) | 15 (30%) | 50 (100%) |

Table 4 shows that out of 50 patients included in study, 36 (72%) showed complete response i.e. 100% clearance of warts, 08 (16%) showed partial response i.e. 50-99% clearance of warts and 06 (12%) showed no response i.e. 0-49% clearance of warts. Results demonstrated that patients having multiple warts showed better response as compared to response in patients having a single wart.

**Table 5: Response to treatment in male and female patients.**

| Response | Male | Female | Overall |
|---|---|---|---|
| Complete (100%) | 24 (48%) | 12 (24%) | 36 (72%) |
| Partial (50-99%) | 04 (08%) | 04 (08%) | 08 (16%) |
| No (0-49%) | 04 (08%) | 02 (04%) | 06 (12%) |
| Total | 32 (64%) | 18 (36%) | 50 (100%) |

Table 5 shows that out of 36 patients who showed complete clearance of warts, 24 patients were male and 12 patients were female. Side effects observed during the study were pain at the site of injection in 18 (36%) patients and flu like symptoms in 02 (04%) patients. No recurrence was observed in any patient during six months follow up period post treatment.

**Figure 1: Pre-treatment clinical photo before first dose.**

**Figure 2: Post treatment clinical photo-six months after the last dose.**

## DISCUSSION

Warts are a mucocutaneous disease that develops as a result of proliferation of infected skin or mucosal cells with human papilloma virus (HPV). There are over 100 types of this virus and some of them have contributed in the pathophysiology of warts.[10,11] Although these viruses create no acute signs or symptoms, they induce slow growth of lesions that can remain for a long time.[12] Infections due to these viruses may result in a wide spectrum of clinical manifestations in the skin and mucosa. Primary manifestations of HPV infection include common warts, genital warts, flat warts, and deep palmoplantar warts.[13,14]

Treatment of warts is often frustrating for both the physician and patient because optimal treatment with high efficacy and low recurrence has not been explored to date. Various therapeutic options such as cryotherapy, tricloroacetic acid, podophylline, surgery by laser, topical cidofovir, electrocautery, retinoids, and salicylic acid have been recommended for treatment of warts.[15] No specific treatment or therapeutic protocol is completely suitable for all of the patients. Although most of the therapeutic options result in clearing of the virus within 1-6 months, in 20-30% of the patients, relapses and new lesions will appear as a result of failure of the cellular immune system to detect and remove the lesions.[7]

Currently available destructive modalities may be painful, ineffective, costly, and may be associated with disfiguring scarring and high recurrence rates.[1,2] On the other hand, several immunotherapeutic agents with variable efficacy have been used for the treatment of different types of warts, including common warts.[4,16] Among these agents is the recently used intralesional immunotherapy which has been shown to be an effective and safe modality. It has the potential advantages of clearance of both treated and untreated distant warts without scarring, a presumed lower rate of recurrence and a high safety profile.[3,4] Hence, it was considered

worthwhile to generate more data regarding this promising modality using a new antigen combination: MMR vaccine in the treatment of warts.

The results of present study demonstrated high therapeutic response (72%) to intralesional MMR vaccine in treatment of warts. The therapeutic response to intralesional MMR vaccine in our study was much higher than that reported by Kus et al.[17] (29.4%), Clifton et al.[18] (47%), King et al.[19] (50%), Signore[20] (51%) and Horn et al.[21] (53%), slightly higher than that reported by Johnson and Horn[22] (70.9%), similar to that reported by Phillips et al.[23] (72%) and slightly lower than that reported by Johnson et al.[24] (74%) , Brunk[25] (85%), Gupta et al.[26] (88.9%) and Maronn et al.[27] (87%). The presence of three synergistic viral antigens in MMR vaccine that could be associated with higher stimulation of the immune system may explain the relatively higher response in our study as compared to most of the related studies which utilize either a single antigen[17-24] or a combination of antigens.[19,22]

The exact mechanism of action of intralesional immunotherapy is still obscure. Intralesional antigen injection probably induces strong non-specific inflammatory response against the HPV infected cells.[24,26] It has also been suggested that the trauma itself, or the bystander effect, may cause wart clearance in previously sensitized individuals.[17] Intralesional immunotherapy has been shown to be associated with release of different cytokines such as IL-2, IL-4, IL-5, IL-8, INF-c and TNF-a that stimulate a strong immune response against HPV.[21,26]

Intralesional immunotherapy is usually associated with mild insignificant side effects such as flu like symptoms, edema, erythema, itching and pain at the site of injection.[3] In the case of MMR vaccine, tolerable pain at the injection site was the main side effect observed in 18 (36%) patients. Flu-like symptoms within 12 hours of injection, that resolved rapidly within 24 hours by non-steroidal anti-inflammatory drugs has been reported in 02 (04%) patients in the present study. No swelling, redness, or pruritus at the site of the injection was observed in the present study as compared to some other related studies.[21,22,24] No serious side effects were reported in patients included in this study. Regarding the number of warts, we found a significant better response in multiple lesions than in single ones. In the present study, we have not demonstrated any recurrence in six months follow up after treatment by intralesional MMR vaccine. A similar observation of absent or low rates of recurrence have also been reported by similar related studies.[23-26]

Intralesional MMR vaccine has shown significant advantages over other treatments. Most of the recently available treatments are painful and need multiple visits. Intralesional immunotherapy with MMR vaccine leads to clearance of distant non injected warts too with just three injections. Patients could appreciate that they were free of residual scars and could go about their daily routine activities with ease. This study proved to be cost effective as patient can be treated in one to two month with MMR vaccination. It seems to be effective, with good cure rates and excellent safety profile, but how exactly it works to stimulate immunity to cause wart clearance still need to be studied further. We recommend the use of intralesional MMR vaccine in larger well controlled studies and in comparison with other therapeutic modalities.

## CONCLUSIONS

Intralesional immunotherapy with MMR vaccine was found to be a simple, effective, and safe treatment for warts. This study proved to be cost effective as patients can be treated with just 03 doses of MMR vaccine given at the interval of two weeks.

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