

# The Efficacy of Intralesional Measles, Mumps, Rubella (MMR) Antigen in Treatment of Common Warts

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## ABSTRACT

**Aim:** To evaluate the efficacy of a new antigen combination measles, mumps, and rubella (MMR) antigen in the treatment of common warts.

**Methods:** The study included 170 patients with single or multiple, recalcitrant or non-recalcitrant common warts both less and more than 6 months duration in all age groups. MMR antigen was injected into single lesions or largest wart in case of multiple lesions at 2-week intervals until complete clearance or for a maximum of 3 treatments. Follow-up was done every 2 weeks for one and half month to detect any recurrence.

**Results:** There were total 170 patients on which 20 were lost or left the study in a period of 6 months. Multiple warts were observed in majority of patients 95(63.3%) irrespective of gender and age. As long as the response is considered regarding the injection therapy, most of the patients received 2 injections. There were some patients who showed just partial response up to 3 injections, those were of total 15(10%). Majority of the patients had warts on upper limb 65(43.3%). The final efficacy came as 81.3% which shows that a large number of (122) patients show complete response to the MMR vaccination.

**Conclusion:** Intralesional immunotherapy by MMR vaccine came to be as simple, effective, and safe treatment for common warts. This study proved cost effective because in the previous studies patient is treated for long time but our result showed that same patient can be treated in 1 to 2 month with MMR vaccination with 3 injections. It is also evaluated that this treatment is also effective in local population and can be implemented.

**Keywords:** Intralesional, measles, mumps and rubella antigen, common warts

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## INTRODUCTION

Warts are benign epidermal tumors caused by human papilloma virus (HPV), a ds-DNA virus. Warts appear in various forms including verruca vulgaris, plane, plantar, myrmecia, coalesced mosaic, filiform or digitate and periungual. The overall incidence is approximately 150 per 100 000<sup>1,2</sup> population. They show the increasing trends during school years to reach a peak in early adulthood. Common warts are usually situated on dorsum of hands and fingers but may occur anywhere on the skin and mucous membrane. They are usually asymptomatic but there may be tenderness when fissured or growing beneath the nail plate and warts on eyelids may be associated with conjunctivitis or keratitis.

They are contagious in nature, however commonly considered harmless and typically disappear spontaneously after a few months but can last for years and can recur. The malignant change in warts is extremely rare. Despite numerous therapeutic modalities, treatment of common warts remains a continuing challenge and there is no universal consensus about optimal treatment. The commonly used treatment options are electrocautery,

cryotherapy, lasers, topical chemotherapeutic agents, zinc sulfate and surgical curettage<sup>3,4</sup>. On the other hand, several immunotherapeutic agents with variable efficacy have been used for treatment of warts<sup>5</sup>. Other than MMR vaccine, the commonly used intralesional antigens are candida and tuberculin<sup>6</sup>. In one study intralesional immunotherapy by measles, mumps and rubella (MMR) vaccine showed promising effects for common multiple warts in which efficacy in terms of complete and partial response was seen in 64 patients out of 70 i-e 91.4% with 5 doses at 2week interval for 2 and half month follow up<sup>7</sup>. But since we were interested to give three doses at 2 weeks interval for 1and half month follow up, so we assumed that efficacy will be achieved in in 70% of patients with common warts. Similarly, in another study intralesional immunotherapy by MMR vaccine showed almost same response ( 87%) when used in planter warts<sup>8</sup>. In one of the local study, treatment was effective upto 67% in patients receiving intralesional (candida) antigen therapy<sup>9</sup>. On contrary, the therapeutic response reported with different intralesional antigens are King et al. (50%)<sup>10</sup> and Horn et al (53%).<sup>11</sup> Many studies have been conducted in this aspect in developed countries but

published data in developing countries like Pakistan is limited. Small sample size taken in different comparative studies of intralesional MMR done abroad ranging from 70(in each group) to 140 total. We wanted to generate local data with large sample size of 170 cases so that proper management could be done to prevent this undesirable morbidity.

**MATERIALS AND METHODS**

A prospective study was done including patients with common warts who attended the Dermatology outpatient department of Sheikh Zayed Hospital, FPGMI, Lahore, from 21th February, 2012 to 21th August, 2012. All clinically diagnosed cases of either gender and age as having 1 or multiple common warts of size ≤ 5mm on any body part without prior treatment were included in the study after informed consent.

**Exclusion criteria:** Patient with prior known allergic response to MMR vaccine and atopic patients, pregnant or lactating mothers, patient with acute febrile illness and patients with immunosuppression/ HIV Infection were excluded.

Information was collected in the form of questionnaire that included age and sex, baseline characteristics of the warts including number (single/multiple), site (upperlimb/lowerlimb/body), size (≤5mm), duration(<12months ) and presence or absence of distant warts were evaluated at the start of study. All patients received a dose of 0.5ml intralesional MMR vaccine into a single wart or largest wart in case of multiple lesion. Intralesional vaccine was given after every 2 weeks into same wart till the disappearance of wart(s) or maximum of 3 doses. The study population was followed up at 2 week interval for a total period of one and half month from start of treatment. The response of treatment was evaluated by decrease in size of wart (s) at each follow up visit. Since the intralesional MMR vaccine had no harmful effect on human body, therefore no ethical issues were relevant.

The data was analyzed by using SPSS 15.0. Sample size of 170 cases was calculated with 95% confidence level, 7% margin of error and taking assumed percentage of efficacy i.e., 70% of intralesional MMR vaccine in the treatment of common warts. Quantitative variables like age of patient was presented as mean and standard deviation. Qualitative variables like sex of patient and efficacy was expressed in terms of frequency, percentage and proportions. Effect modifiers like number (single/multiple), site (upperlimb/lowerlimb/body), size (≤5mm), duration (<12months) were addressed through stratification.

**RESULTS**

There were total 170 patients on which 20 were lost or left the study. So the total sample size for statistical analysis comes to be as 150. There were 72 males and 78 females with a mean age of 28.34±10.59. The duration of the medication was one and half month in most of the patients. Multiple warts were observed in majority of patients 95(63.3%) irrespective of gender and age. Most of the patients 87(58.0%) did not have warts at different anatomic site. As long as the response is considered regarding the injection therapy, most of the patients received 2 injections in less than one and half month and 121(81%) cured from disease by showing a complete response. There were some patients who showed just partial response to the 3 injections in one and half month duration, those were total 15(10%). Majority of the patients had warts on upper limb 65(43.3%). The mean value for injections came as 2.50±0.57. The final efficacy came as 121(81%) which shows that a large number of patients show complete response to less than 3 injection. Male and females almost show almost equal response to the therapy.

Table 1: Age of patient

	N	Mean	Std. Deviation
Age of patient	150	28.3400	10.59747

Table 2: Gender of patient

Gender	Frequency	%age
Male	72	48
Female	78	52

The mean age of the patients who were enrolled in this study was 28.34 with a standard deviation of 10.59.

Out of total 150 patients there were 72(48.0%) were male while 78(52.0%) were female patients who were taken as sampling units in this study. When the mean frequency of site of warts was calculated, it comes out to be as 2.14 that means most of the patients have upper limb site of wart but there was 1.3 standard deviation was also calculated showing that site of wart can be lower limb or body. Majority of the patient required mean 2.5 injections to cure the warts with a standard deviation of 0.57.

Majority of patients 95(63.3%) had multiple warts while 55(36.7%) had single warts.

87(58%) patients had distant warts while 63(42%) did not had distant warts.

Table 3: Site of Warts

	N	Mean	Std. Deviation
Site of warts	150	2.1400	1.30065
	150		

Table 4: Number of Injections Received

	n	Mean	Std. Deviation
Number of injections required/received	150	2.5000	.57638
N	150		

Table 5: Number of warts

Warts	Frequency	%age
Single	55	36.7
Multiple	95	63.3

Table 6: Distant warts

Warts	Frequency	%age
Present	63	42.0
Absent	87	58.0

Table 7: Response to Treatment

	Frequency	%age
Complete response	121	81
Partial Response	15	10
No Response	14	9

Table 8: Efficacy

	Frequency	%age
Yes	121	81
No/partial	29	19

Out of total 150 patients majority of patients 121(81%) showed complete response to the treatment while 15(10%) patient showed Partial response and 14(09%) did not show any response to the treatment. Efficacy of the treatment was 81% as out of total 150(100%) patients 121(81%) showed effect of treatment while 28(18.7%) did not responded to the treatment. Out of total 72 male patients 25 had single wart while 47 had multiple warts. On the other hand out of 78 females 30 had single wart while 48 had multiple warts.

Table 9: Gender of patient \*No of warts Crosstabulation

	Number of warts		
	Single	Multiple	Total
Male	25	47	72
Female	30	48	78

Table-10: Gender of patient\* Efficacy Cross tabulation

	Efficacy		Total
	Yes	No	
Male	61	11	72
Female	60	18	78

## DISCUSSION

Treatment of warts is difficult for both patients and physician as well. Currently Available destructive treatment options include cryosurgery, laser surgery,

electrosurgery, bleomycin, curettage, and topical keratolytic applications; many of them are likely to be very painful, ineffective, costly and prone for recurrences. Recurrence rates of warts up to 30% have been reported with destructive treatment probably due to lack of immune response.

Immunotherapy for warts has been performed with different immunotherapeutic agents e.g diphenylcyclopropanone (DCP), imiquimod, tuberculin, and autologous vaccines. The use of DCP is limited by allergic contact dermatitis, urticarial reactions and pigmentary disturbances.

Autologous vaccine therapy is limited by the oncogenic potential of the virus. Therefore, a safe, inexpensive, effective and simple immunotherapeutic agent is needed for the management of warts.<sup>12</sup> Among these agent Intralesional immunotherapy is effective and safe. It has advantage of clearance of both treated and untreated distant warts. The exact mechanism of action of intralesional treated immunotherapy is still obscure. Intralesional antigen injection probably induces strong non specific inflammatory response against the HPV-infected cells<sup>13</sup>. Intralesional immunotherapy has been shown to be associated with release of different cytokines. Several immunotherapeutic agents with variable efficacy have been used for the treatment of different types of warts, including common warts<sup>11</sup>. Intralesional injection of mumps antigen has been used in a similar way for treating recalcitrant warts with comparable efficacy<sup>7,8</sup> which paved the way for the use of the measles, mumps and rubella (mmR) vaccine to treat resistant warts<sup>14</sup>.

In our study no statistically significant association was found between the therapeutic response to MMR antigen and different clinical variables, including age, gender, number, site and duration of warts. The results of the present study demonstrated a high frequency of that patients whose show complete response to the injection (81%). Similar findings have also been reported by other studies Wiley-Blackwell found Intralesional immunotherapy by MMR vaccine is a promising effective and safe treatment modality for common warts, particularly the multiple ones (84.6%).

The rubella vaccine was effective in reducing cases from 57,600 in 1969 to 213 cases in 1996. In another study by Nofal A showed Intralesional immunotherapy by MMR vaccine is a promising effective and safe treatment modality for common warts, particularly the multiple ones: Clifton et al used intralesional mumps and Candida antigen for the treatment of recalcitrant warts in children. They reported a 47% clearance of warts injected directly and 0 a 34% clearance for distant warts. The efficacy of the therapeutic response to intralesional MMR

antigen compare to other intralesional agent was much higher e.g., reported by Kus et al (29.4%), Clifton et al<sup>15</sup> (47%), King et al<sup>10</sup> (50%) response. While in another study Signore<sup>107</sup> showed (51%) therapeutic response to candida antigen and Horn et al<sup>11</sup> found (53%) therapeutic response to mumps, candida and trichophyton skin test antigen, Johnson and Horn showed (70.9%) response using a combination of skin test antigen. Another studies Phillips et al 10(72%) and Johnson et al 11(74%), Brunk 9 (85%), Gupta et al<sup>16</sup> 18(88.9%) and Maronn et al 8(87%) shows higher response than that of other.

Intralesional immunotherapy by MMR vaccine is associated with mild side effect such as erythema, edema, itching and pain at injection site. Those symptoms resolved rapidly within 24 hrs without any treatment in most of the patient. Only 2 patients have taken NSAID for symptomatic relief. No swelling or purities at injection site was noted. More aggressive side effect such as wound or scarring was not observed.

## CONCLUSION

Intralesional immunotherapy by MMR vaccine came to be as simple, effective, and safe treatment for common warts. This study proved cost effective because in the previous studies patient is treated for long time but our result shows that same patient can be treated in 1 to 2 month with MMR vaccination with 3 injections. It is also evaluated that this treatment is also effective in local population and can be implemented.

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