

## Review Article

# Effectiveness of measles, mumps and rubella vaccine as immunotherapeutic agent for cutaneous viral warts

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**Received:** 07 February 2020

**Accepted:** 17 March 2020

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### ABSTRACT

Immunotherapy for management of cutaneous wart with measles, mumps and rubella vaccine (MMR) is a promising new modality of management. Evaluation of the same has been done by various studies over the years reporting its effectiveness. A literature search was done using PubMed and google scholar. This short narrative review documents the response rates in various clinical studies done till 2019 which have reported the efficacy of MMR vaccine as an immunotherapeutic agent which ranged from 26-84% graded as complete response which is complete clearance of the treated warts. These studies were performed for evaluating MMR vaccine as single agent or done in comparison with other therapeutic agents. The broad range of responses points to a need of doing further clinical studies which will substantiate the effectiveness of MMR vaccine in the treatment of cutaneous warts.

**Keywords:** Cutaneous warts, Verruca, MMR vaccine, Immunotherapy

### INTRODUCTION

Human papilloma virus (HPV) infection can cause a frequent cutaneous condition of verrucae which is synonymous with warts. Although they are benign their treatment becomes essential as they may lead to disfigurement and may spread by pseudo koebnerization to other parts of the body causing physical and emotional distress to the patient and also because they can be transmissible to others.<sup>1-6</sup>

Despite knowing the causation, no specific antiviral treatment exists currently and the approach for managing warts still relies on conventional mode of treatment options which are destructive and aggressive mode of treatment, having the undesired disadvantage of causing scarring, high rates of recurrence and can be non-practical when it comes to treating multiple lesions or difficult to treat areas.<sup>7,8</sup>

To overcome these limitations, one emerging modality of treating warts is of immunotherapy. Mechanisms by which intralesional immunotherapy works are not yet fully elucidated but induction of a strong but non-specific inflammatory response has been suggested along with generation of lymphocytes and monocytes that boost Th1-subset cytokine responses. This will stimulate cytotoxic T cells and natural killer cells. This bolstered immune response destroys the injected locally treated lesion but has an additive effect on distant warts as well.<sup>9,10</sup> Frequently used immunotherapeutic agents are imiquimod, tuberculin, *Mycobacterium W* (Mw) vaccine, zinc, *Bacillus Calmette-Guerin* (BCG) vaccine, Human Papilloma virus (HPV), measles, mumps and rubella (MMR) vaccine, candida antigen and auto implantation therapy.<sup>11,12</sup> Amongst these agents, MMR vaccine is one such that has been reported to be effective and being part of immunization schedule is readily available in a hospital setting. This review aims to assimilate the response rates in various clinical studies which have

reported the efficacy of MMR vaccine as an immunotherapeutic agent.

**METHODS**

Literature search done in English language for this narrative review was collected in the month of September 2019. Potential articles related to the topic were retrieved from PubMed and google scholar until January 2019. Keywords used for search included cutaneous warts, verruca, MMR vaccine, immunotherapy, HPV. Seventeen articles were identified. One was excluded as it was a retracted article. Another excluded as it was a meta-analysis and also not accessible without subscription. Finally, fifteen articles were chosen and the relevant key information summarized. Six studies were randomised controlled trials, seven studies were prospective non randomised trials and two studies were retrospective case control studies.

**DISCUSSION**

One of the first study which reported MMR vaccine as a promising modality of treatment for cutaneous wart was

by Nofal et al in 2010 which had 135 patients in two groups, one received MMR vaccine and the other was saline as a control group.<sup>12</sup> Complete response was achieved in 80% and 84.6% in recalcitrant patients and multiple warts patients groups respectively. In 2013, another study conducted with 100 patients, half received MMR and the control group got normal saline. The MMR treated group showed high complete response 82% in comparison to the control group 0%.<sup>13</sup> Naseem et al found that in 150 patients out of 170 who completed their study, complete clearance was noted in 81.3% and partial response in 10%.<sup>3</sup>

Two studies were reported in 2014, one was a retrospective study by Na et al with 136 patients and 51.5% of patients showed greater than 50% decrease in the size and number of warts.<sup>14</sup> The second study was double-blind randomized controlled clinical trial (RCT) conducted on 24 patients with warts allocated to two groups of MMR and normal saline. The therapeutic response had increased when evaluated on the second to reach 87% and third after treatment visits in the MMR group to 92% in contrast to lower rates in the saline control group.<sup>15</sup>

**Table 1: Table depicting the various clinical studies done with MMR vaccine as immunotherapeutic agent.**

S. no.	Year	Study design	No. of patients enrolled	MMR single/comparative with another agent	Authors
1	2010	Randomised control trial	135	Single	Nofal et al <sup>12</sup>
2	2013	Randomised control trial	100	With saline control group	Mohamad et al <sup>13</sup>
3	2013	Prospective non randomised study	170	With saline control	Naseem et al <sup>3</sup>
4	2014	Retrospective study	136	Single	Na et al <sup>14</sup>
5	2014	Double blinded randomised control trial	24	With saline control group	Zamanian et al <sup>15</sup>
6	2015	Prospective non randomised study	70	Single	Nofal et al <sup>16</sup>
7	2015	Randomised control trial	30	With purified protein derivative (PPD), normal saline control group	Shaheen et al <sup>17</sup>
8	2015	Prospective non randomised study	30	Single	Raju et al <sup>18</sup>
9	2016	Prospective non randomised study	50	Single	Aarti et al <sup>19</sup>
10	2016	Randomised open label study	150	With trichloroacetic acid (TCA)	Saveta et al <sup>20</sup>
11	2016	Non randomised prospective study	100	Single	Saini et al <sup>21</sup>
12	2017	Retrospective case control study	40	With normal saline control group	Dhope et al <sup>22</sup>
13	2017	Double blinded randomised control clinical trial	50	MMR and oral zinc with normal saline control	Sachin et al <sup>23</sup>
14	2019	Prospective observational study	60	With cryotherapy	Vanarase <sup>24</sup>
15	2019	Prospective non randomised study	110	Single	Chauhan et al <sup>25</sup>

In 2015, Nofal et al did a study on 70 patients with multiple warts. 65 patients completed the study. Complete disappearance seen in 63%, partial resolution in 23% with no response in 14%.<sup>16</sup> Next study was an RCT conducted on 30 patients with multiple warts who were divided into 3 groups, 10 treated with PPD, 10 with MMR, and 10 with normal saline or control. A high rate of complete response was found with PPD 60% and MMR 80% compared with controls 0% for target warts.<sup>17</sup> The third study by Raju et al, in 27 out of 30 patients given MMR, complete clearance in 70.4% of patients, partial in 22.2% and 7.4% of patients had no clearance.<sup>18</sup>

50 patients were injected with MMR vaccine out of which complete clearance was seen in 72%, 16% reported partial clearing and 12% of patients showed nil response in a 2016 done prospective study.<sup>19</sup> A comparison study with MMR vaccine group and another receiving Trichloroacetic acid (TCA) application topically was by Saveta et al again in 2016. MMR group 49.3% had higher than 75% improvement with 26.44% demonstrating complete resolution but TCA only had 11.11% showing more than 75% improvement with complete resolution in 7.94%.<sup>20</sup>

Saini et al also conducted a prospective study with intralesional MMR in 2016 in which 86 patients out of 100 patients completed the study with complete resolution in 46.5% with partial response rates of 20.9%.<sup>21</sup>

Another retrospective case control study in 2017 by Dhope et al where 40 common wart cases were divided randomly into 2 groups had MMR vaccine group reporting complete response of 65% in comparison to normal saline control group reporting 5%.<sup>22</sup> On the other hand in the same year, a clinical trial of 50 patients with verrucae in two groups, one had MMR group with oral zinc and the other had normal saline. In the first group complete disappearance was seen in 80% cases, 8% noted relative clearing and nil response in 12% cases. In normal saline group complete cure was in 4% cases, relative response was in 16% cases and incomplete clearance in 68% cases.<sup>23</sup> A study was conducted in 60 patients by Varanase. Patients were kept into 3 groups, the first was treated with cryotherapy, second received MMR vaccine and third received a combined of two earlier groups therapy. Better response was noted in first group where MMR was given alone or the third with cryotherapy than first group with cryotherapy singly.<sup>24</sup>

51 patients out of 110 completed the prospective study and 82.4% of them attain full disappearance of warts by Chauhan et al in 2019.<sup>25</sup>

## CONCLUSION

This short narrative review encompasses different study designs including randomized control trials, prospective non randomized trials and retrospective case control

studies which evaluated the effectiveness of MMR vaccine in the management of cutaneous viral warts. Many have used MMR vaccine as single agent whilst others have done comparative studies with other therapeutic agents. The range of complete response was broad ranging from average of 26% to 84%. Hence it needs to be more extensively evaluated and supplemented by further clinical studies which will also help in making MMR vaccine conform to become a standard and effective modality of treatment.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

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**Cite this article as:** Wahengbam AD, Jeevan J, Dogiparthi S. Effectiveness of measles, mumps and rubella vaccine as immunotherapeutic agent for cutaneous viral warts. *Int J Res Dermatol* 2020;6:439-42.