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Intralesional Injection of Measles, Mumps, and Rubella Vaccine in Molluscum Contagiosum Treatment: An Experimental Study

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Abstract

Molluscum contagiosum (MC) is a common viral infection that affects the skin and the mucous membranes. Several studies have shown that intralesional Measles, Mumps, and Rubella (MMR) immunotherapy is beneficial for treating warts. There is very little information about the effectiveness of this treatment method in patients with MC. The study's objective was to assess whether patients with MC benefit from intralesional MMR vaccination. This experimental study was carried out on 20 patients of MC (11 men and 9 women) who visited Sulaimani Dermatology Teaching Center, who received a maximum of six doses of intralesional MMR vaccine with an interval of two weeks between sessions. Three kinds of therapy responses were identified; complete, partial, and no response. A number of side effects were recorded. The mean ± SD of the age, duration of the disease, and the number of skin lesions were 17.9 ±17.1 years, 5.1 ±2.2 months, and 10.4 ±7.9 lesions, respectively. Sixty-five percent of patients had complete clearance, 25% with partial clearance and 10% experienced no clearance. According to the examined variables, no significant difference was present in the frequency of the various treatment responses ($p>0.05$). The noticed side effects were temporary mild redness, edema, and pain at the site of injection. Recurrence was not seen in any of the patients who responded completely to the treatment. Although it seems that intralesional MMR immunotherapy was effective and safe in the treatment of the skin lesions due to MC. To further support the results of the current study, larger prospective studies that are placebo-controlled and have longer follow-ups are required.

Introduction

Molluscum contagiosum (MC) is a viral infection affecting the skin and the mucous membranes. Young adults, children, and immunocompromised individuals are typically infected ***[1].*** Direct contact with skin or mucous membranes, including fomite dissemination, are the main routes of infection spreading. Untreated lesions can persist for up to two years before the spontaneous resolution occurs, with the time frame varying from a few months to years ***[2].*** A double-stranded DNA poxvirus called Molluscum contagiosum virus (MCV) causes Molluscum contagiosum. Four subtypes of the Molluscum contagiosum virus are known, and they are MCV-1 (98% of cases) is mostly seen in children, while MCV-2 is mainly responsible for skin lesions in people living with human immunodeficiency virus (HIV). Molluscum contagiosum virus 3 and 4 are present in Asia and Australia***[3, 4].***

MC lesions are typically found on exposed places in youngsters, however many cases in adults are confined to the genital region, suggesting sexual transmission, children can also develop genital and perianal lesions, but they are rarely connected to sexual transmission in this age group ***[5].*** Molluscum contagiosum is a common medical concern. In 2010, there were about 122 million cases. In people living with HIV, the clinical prevalence of Molluscum contagiosum may reach up to 18% ***[6].*** Worldwide, MC is more common

in children, while it can also affect adults and adolescents. It rarely occurs in infants under the age of one year and frequently affects kids between the ages of 2 and 5 ***[7].*** The incubation period ranges from two weeks to six months***[8].*** There is no evidence of gender domination ***[6].*** Lesions are firm, white to flesh-colored, dome-shaped, pearly papules, having a central umbilication from which one can express a cheesy material. Mollusca is usually one millimeter to one centimeter in diameter ***[9].***

Most of the time, the clinical features of *Molluscum contagiosum* can be used to make a diagnosis. Even though molluscum cannot be cultured in a laboratory, histological investigation of a lesion can nevertheless help in the diagnosis in cases when it is not clinically visible ***[10].*** The differential diagnosis of Molluscum contagiosum in children includes syringoma, closed comedones (whiteheads), and warts (including anogenital ones). In immunocompromised persons, molluscum contagiosum lesions may be atypical, have a greater size, and/or mimic malignancies, such as basal cell carcinoma or keratoacanthoma (for single lesions), or other infectious diseases, such as cryptococcosis and histoplasmosis (for extensive lesions)***[11].***

Patients and parents seek therapy for a variety of reasons, such as transmission to others, autoinoculation via scratching, and cosmetic value ***[12].*** The currently available treatment for MC lesions frequently necessitates numerous office visits. These methods consist of both physical removals of MC lesions using curettage, cryotherapy, or lasers as well as chemical removal of the infected skin using medications applied topically***[13].***

It is possible to utilize a variety of topical substances to cause mild to moderate inflammation and so maybe encourage the emergence of an immune response against the virus. Strong irritants like cantharidin, trichloroacetic acid, and diluted liquid phenol can hurt, blister, and leave scars, but with careful application and the right dilution, they can also speed up lesion elimination. Example of topical formulation is salicylic acid, adapalene, and nitric oxide cream and potassium hydroxide solution ***[14, 15].*** The immune system is used in immunotherapy to produce a focused immune response ***[12]***. Since the 1960s, measles, mumps, and rubella single component live attenuated vaccinations have been authorized in the USA ***[16].***

Immunotherapy is being used to treat troublesome skin conditions including MC, genital warts, alopecia areata, and common warts ***[4, 17].*** Warts are being treated using intralesional immunotherapy by the (measles, mumps, and rubella) MMR vaccination ***[18-20].*** Since cell-mediated immunity plays a role in the pathophysiology of MC, intralesional immunotherapy employing Candida and the MMR vaccine has been suggested ***[21]***.

Although many studies in the past have shown the significant superiority of intralesional MMR immunotherapy over placebo (normal saline) in removing warts, There aren't many studies on the efficacy of intralesional MMR immunotherapy for treating molluscum contagiosum ***[2, 22].*** Thus, we aimed to assess the efficacy of intralesional MMR vaccine in patients of molluscum contagiosum.

Materials and methods

A. Study approval and sample design

This study was accepted by the University of Sulaimani with the code 7-5-13527. Approval was taken from the Sulaimani Dermatology Teaching Center and consent was taken from the adult patients or parents of young patients. The current work is an experimental study conducted from the period of November 2021 to May 2022, in which twenty patients with MC were treated with the MMR vaccine. The mechanism of action, benefits, and advantages of the MMR vaccine was clarified to all patients.

B. Laboratory diagnosis and data collection

History was taken from all the patients regarding age, gender, residency, marital status, sexual contact, duration of the disease, history of chronic illness, history of hypersensitivity reaction to MMR vaccine, and family history of MC. The examination was done regarding the clinical characteristics (number, size, and

site) of the lesions. Each patient received up to a maximum of 6 doses of intralesional MMR vaccine. In each session, the patients received a dose of intralesional MMR vaccine, which was 0.5 ml for adults and 0.3 ml for pediatric age groups, with a 2-week interval between sessions (week zero, as well as 2^{nd}, 4^{th}, 6^{th}, $8^{th,}$ and 10^{th} weeks). Patients who had a complete response to treatment were followed up for 18 weeks to control recurrence. The response to the tested treatments was either complete (complete clearance of lesions), partial (decline in the size and/or the number of lesions), and no response (no change in the size and/or the number of the lesion). Slight side effects were seen among all tested patients. Pregnancy, immunosuppression, and history of hypersensitivity reaction to MMR vaccine were excluded.

C. *Statistical analysis*

Descriptive statistical tests including percentage, frequency, standard deviation, and the mean were used to describe the collected information. Also, Fisher's exact test was used to find the difference in the percentage of treatment response type (complete, partial, and no response) based on the demographic data, history, and the number of intralesional MMR dose and clinical variables. Data were analyzed using SPSS (version 25) software. The significance level was set at 0.05.

Results

The studied patients included 11 men (55%) and 9 women (45%). Their age ranged from 3 to 55 years with a mean ± SD of 17.9 ±17.1 years. Ninety-five of the samples were from the urban area, 70% were single, 85% did not have sexual relations, 85% did not have a previous history of MC, 85% did not have a history of previous treatment for MC, and 65% did not have a family history MC (Table 1).

Table- 1: Demographic characteristics of the studied patients.

Variable		**Frequency**	**Percentage**
Gender	Male	11	55
	Female	9	45
Age	<12	10	50
	12-40	6	30
	>40	4	20
Residency	Urban	19	95
	Rural	1	5
Marital Status	Single	14	70
	Married	6	30
History of Sexual Contact	Yes	3	15
	No	17	85
History of Molluscum contagiosum	Yes	3	15
	No	17	85
Previous treatment of Molluscum contagiosum	Yes	3	15
	No	17	85
Family history of Molluscum contagiosum	Yes	7	35
	No	13	65
Total		20	100

The most affected areas were the face (55%) followed by the genital tract (25%). The duration of getting the disease ranged from 3 to 12 months (mean ± SD of 5.1 ±2.2). The lesion numbers ranged in each patient between 1 and 30 lesions (mean ± SD of 10.4 ±7.9) (Table 2).

Table- 2: Clinical characteristics of the studied patients.

Variable		Frequency	Percentage
Site of the lesion	Face	11	55
	Neck	1	5
	Genital	5	25
	Other	3	15
Duration of the disease (month)	3-5	12	60
	6-8	6	30
	9-12	2	10
Number of lesions	<10	10	50
	10-20	8	40
	>20	2	10
Total		20	100

The dose numbers (treatment sessions) ranged between 2 to 6 with (mean ± SD of 4.4 ±1.6). In terms of response to treatment with MMR vaccine, 65% of patients experienced complete clearance, 25% with partial clearance, and 10% had no clearance. [The highlighted frame needs rewriting clearly] (Tables 3 and 4). (Table, 3). Of the thirteen patients who showed a complete response at 12 weeks, none had a recurrence and complete response was sustained in all the patients when followed up at 18 weeks.

Table- 3: Patient's response to the tested treatment.

Response to treatment	Number of patients	Percentage
Complete Response	13	65
Partial Response	5	25
No Response	2	10
Total	20	100

Regarding the response to the MMR vaccine doses, four patients have a complete response after two doses, two patients have a complete response after three doses, four patients have a complete response after four doses, two patients have a complete response after five doses, and only one patient has complete response after six doses (Figure 1).

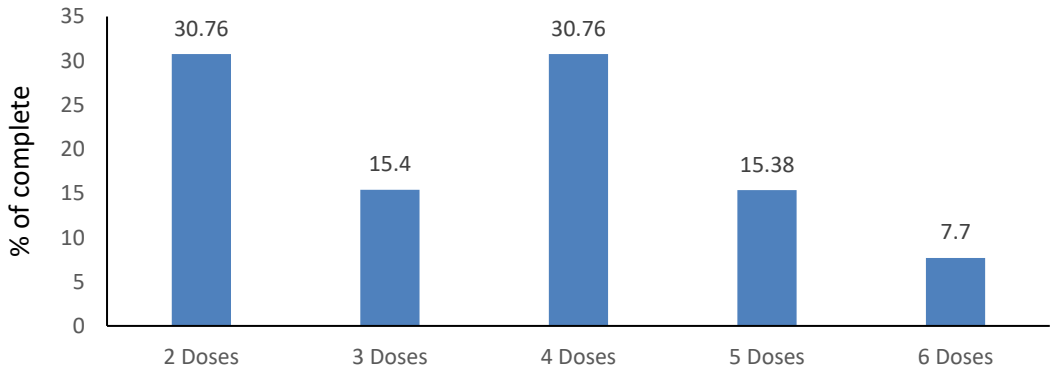

Figure -1: Relations between the numbers of tested doses with complete clearance.

According to the examined variables, there was no statistically significant difference in the percentages (Frequency) of the various treatment responses ($p>0.05$) (Table 4). All patients experienced temporary mild redness, edema, and tenderness at the site of injection.

Table- 4: Treatment responses based on the studied variables.

Variables		**Responses (no & %)**			**P-value**
		Complete	**Partial**	**No**	
Gender	Male	6 (54.5)	4 (36.4)	1(9.1)	0.642
	Female	7 (77.8)	1 (11.1)	1 (11.1)	
Age	<12	7 (70)	2 (20)	1(10)	0.847
	12-40	4 (66.7)	1 (16.7)	1 (16.7)	
	>40	2 (50)	2 (50)	0 (0.0)	
Chronic disease	Yes	0 (0.0)	1 (100)	0 (0.0)	0.353
	No	13 (68.4)	4 (21.1)	2 (10.5)	
Previous treatment of Molluscum contagiosum	Yes	2 (66.7)	1 (33.3)	0 (0.0)	0.798
	No	11 (64.7)	4 (23.5)	2 (11.8)	
Site of the lesion	Face	7 (63.6)	3 (27.3)	1 (9.1)	0.517
	Neck	0 (0.0)	0 (0.0)	1 (100)	
	Genital	4 (80.0)	1 (20.0)	0 (0.0)	
	Other	2 (66.7)	1 (33.3)	0 (0.0)	
Duration of the disease (month)	3-5	9 (75.0)	3 (25.0)	0 (0.0)	0.182
	6-8	4 (66.7)	1 (16.7)	1 (16.7)	
	9-12	0 (0.0)	1(50.0)	1 (50.0)	
Number of lesions	<10	7 (70.0)	2 (20.0)	1 (10.0)	0.913
	10-20	5 (62.5)	2 (25.0)	1 (12.5)	
	>20	1 (50.0)	1 (50.0)	0 (0.0)	
Total		13 (65.0)	5 (25.0)	2 (10.0)	-

Figures 2 shows a four years old child with MC in the face who completely recovered after receiving the 3rd dose of intralesional MMR vaccine.

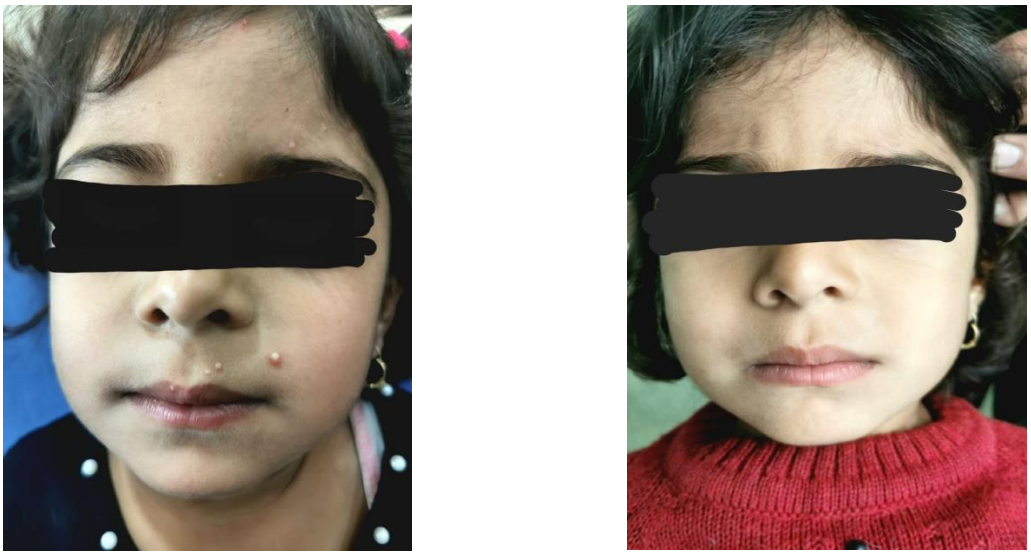

Figure- 2: (Left) Multiple *Molluscum contagiosum* on the face before treatment with MMR vaccine; (Right) complete clearance after 3rd dose of intralesional MMR vaccine.

Figure 3 shows a 46 years old man with MC in the genital who was partially recovered after receiving the 6th dose of intralesional MMR vaccine.

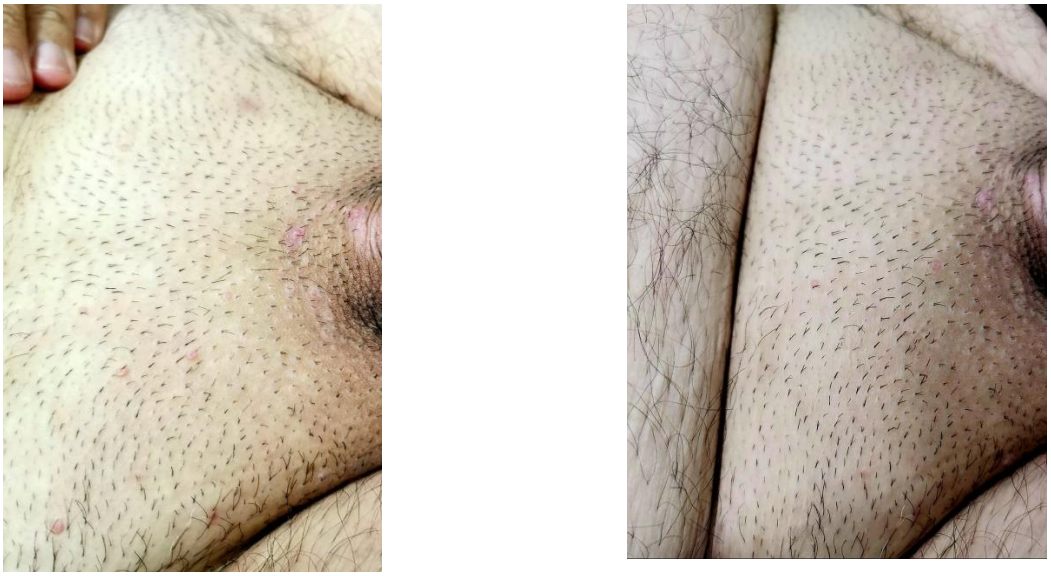

Figure- 3: (Left) Multiple *Molluscum contagiosum* on genital before treatment with MMR vaccine; (Right) partial clearance after 6th dose of intralesional MMR vaccine.

Discussion

In the current study, the most affected areas were the face, neck, and genital. This result is consistent with the study of Chauhan *et al.* who reported that 45% of the patients had facial skin involvement, although in our study, 50% of patients had more than 10 lesions which is parallel to their observations ***[19].***

All tested patients with MC infection received a maximum of six doses of intralesional MMR vaccine with an interval of two weeks between sessions. The study was stopped after 12 weeks. Out of the 20 examined patients, complete clearance was seen in 65% of patients. In our study, treatment response as early as four weeks was seen in one patient after second doses of intralesional MMR. The presence of viral antigens in the MMR vaccine reinforces each other and in turn cause more stimulation of the immune system. Our observations were in agreement with results recorded by other investigators who showed that MMR was effective in treating MC ***[2, 19].*** In a study conducted by Na et al. in South Korea, the success of intralesional MMR immunotherapy was observed in the treatment of four and one year-old children with MC and the lesions were resolved with no side effects, no scarring, and no signs of recurrence during a follow-up of three months ***[2].*** In another study that was conducted by Chauhan et al. on 22 patients with MC with a mean ± SD age of 19.7±10.9 years 18 patients (81.8%) had a complete clearance of lesions, with 4 patients (18.18%) having a partial response. No other adverse effects were seen in the patients except one patient who had post inflammatory hyperpigmentation ***[19].*** Based on the findings of our study and previous studies, MMR vaccine seems to be effective in the treatment of MC disease.

Advantages such as the availability of the vaccine, no long-term side effects such as scarring, no need to treat the entire lesion, no need for pre-treatment and time saving, cost-effectiveness and not having any recurrence have made MMR immunotherapy a feasible option in MC treatment compared to the old methods ***[12, 19, 23, 24].*** Although intralesional immunotherapy's exact method of action is still unknown, numerous studies have demonstrated the efficacy of intralesional MMR as an immunogen in the treatment of warts, making it a tried-and-true treatment option ***[19].*** In three studies, the rate of complete clearance of warts in patients treated with intralesional MMR immunotherapy was reported 81.4%, 82% and 86.7% ***[19, 25, 26].***
In the present study, complete response to treatment was seen at low doses. This finding is consistent with the findings of Chauhan et al and Na et al.'s studies ***[19].*** Based on the findings of our study and other similar studies, most complete responses appear to be achieved after the first few doses.

In the present study, no significant difference was observed between the percentages of the type of therapy response to the treatment according to the studied variables. Due to the lack of analytical findings in

similar studies, it was not possible to further compare and discuss the findings of the current study. All patients experienced temporary mild erythema, swelling, and tenderness at the site of injection and study among patients who respondent completely to the MMR vaccine none of the patients experiencing recurrence on follow-up done at week 18. In Chauhan et al and Na et al.'s studies no adverse effects such as pain, erythema, blistering, ulceration, pigmentary alteration was noted in any patient and also there was no signs of recurrence after 24 and 12 weeks follow-up, respectively ***[19].***

There were limitations to this study, the most important of which was the lack of a control group. We were unable to determine whether remission in patients with MC occurred spontaneously or as a result of therapeutic intervention. Lack of immunological evaluation and lack of follow-up of patients to identify cases of disease recurrence were other limitations of this study.

Conclusions

Intralesional MMR is safe, generally well-tolerated, and effective therapy for lesions of molluscum contagiosum. Although it seems that intralesional MMR immunotherapy was effective and safe in the treatment of the skin lesions of *Molluscum contagiosum*, to further support the results of the current study, larger prospective studies that are placebo-controlled and have longer follow-ups are required.

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