

The Effect of Intralesional Injection of MMR in Treatment of Viral Warts

S.M.Rezk, O.H.Alkady and R.T.Farag

Dermatology, Venereology and Andrology Dept., Faculty of Medicine, Benha Univ., Benha, Egypt
E-Mail: R.Farag@gmail.com

Abstract

Warts are common viral infections of the skin and mucous membranes that are caused by the human papilloma virus (HPV). Warts are prevalent worldwide. Recently, immunotherapy with intralesional antigens or vaccines has been tried for the treatment of common warts with encouraging results. It could lead to resolution without any physical changes or scarring and in addition would augment the host response against the causative agent. The aim of this study is to evaluate the effect of intralesional injection of MMR vaccine with intralesional injection of saline in patients with viral warts. This study was carried out in Dermatology, Venereology and Andrology Department Outpatients Clinics, Benha University Hospitals. This study included 38 patients with viral warts. 18 patients were injected with MMR vaccine while 20 patients were injected with saline as control. Approval of Dermatology, Venereology and Andrology Department and Ethics Committee in the Faculty of Medicine, Benha University was taken before preceding the study. Written consent was taken from all participants involved in this study. Comparing between response obtained after MMR injection and saline injection in control group revealed significantly better response in MMR group when compared to control groups ($p < 0.001$ for each). 14 patients (77.8%) reached complete response after MMR injection while no patient responded to saline injection. No significant association was found regarding response of mother warts to recurrence in all studied cases' groups. MMR injection showed significantly better response of mother wart when compared to control group. MMR injection showed significantly better response of other warts when compared to control group.

Keywords: Warts, MMR, Intralesional, Human Papilloma Virus, Viral Infections.

1. Introduction

Warts are common viral infections of the skin and mucous membranes that are caused by the human papilloma virus (HPV). Warts are prevalent worldwide [1]. There are over 100 different types of HPV. The appearance of warts is determined by the type of virus and the location of the infection. Common warts are most often seen on the hands and present as skin coloured papules with a rough verrucous surface. Flat warts are most often seen on the backs of the hands and on the legs [2].

Recently, immunotherapy with intralesional antigens or vaccines has been tried for the treatment of common warts with encouraging results. It could lead to resolution without any physical changes or scarring and in addition would augment the host response against the causative agent [3].

Human papilloma virus (HPV) vaccines have led to a significant reduction in the incidence of genital warts and cervical neoplasias, however; they do not target genotypes specific to other cutaneous sites [4].

Intralesional mumps, measles and rubella vaccine (MMR) immunotherapy perhaps employs the ability of the immune system to recognize viral antigens that induces a delayed-type hypersensitivity reaction not only to the antigen but also against the HPV, thereby increasing the ability of the immune system to recognize and clear HPV. Consequent to this, the stimulated immune response can clear all lesions on other body sites along with locally treated lesions [5].

2. Patients and methods

This study was carried out in Dermatology, Venereology and Andrology Department Outpatients Clinics, Benha University Hospitals from June 2019 till January 2020. Approval of Dermatology, Venereology and Andrology Department and Ethics Committee in the

Faculty of Medicine, Benha University was taken before preceding the study. Written consent was taken from all participants involved in this study.

Type of Study: A case control study.

Patients: This study included 38 patients complaining from viral warts. Patients were divided into 2 groups.

Control: 18 patients were injected with MMR vaccine and 20 patients were injected with normal saline as control group. This control group was be age and sex matched with the other group.

Exclusions criteria: The following exclusion criterion was used for all subjects: renal diseases, liver diseases, any other dermatological diseases and those who are on systemic or topical therapy for more than one month before the start of the study.

Method: All individuals were being subjected to the following:

1. History taking: including age, sex, duration, course, family history, previous treatments, response to previous treatments, and associated autoimmune or allergic diseases.
2. Complete general examination
3. Complete dermatological examination of viral warts to determine the severity of warts using cutaneous warts as baseline and follow up scoring system.
4. The individuals will be classified in to 2 groups:
 - a) Group (A): will be formed of 18 patients injected intralesionally by MMR vaccine; 9 patients injected with 0.2ml in mother wart (largest lesion) only while 9 patients injected in all warts with maximum 0.5 ml of MMR in each session for maximum 4 sessions (one session every 2 weeks).
 - b) Group (B): Control group will be formed of 20 patients injected intralesionally by normal saline (0.2 ml) at base of wart.

All patients were followed every session for size of wart up to 2 months after last session and CWARTS was used in last visit to record the effect of the therapy[6].

Statistical analysis: Key results were being tabulated and analysed by suitable statistical methods using the computer

program Statistical Package for the Social Sciences (SPSS).

3. Results

Table (1) Comparison of response of mother wart at the last follow up to various treatment modalities.

		Complete response		Partial response		No response		P1
		N	%	N	%	N	%	
Control	N=20	0	0%	0	0%	20	100%	-
MMR	N=18	14	77.8%	3	16.70%	1	5.60%	<0.001

p1, comparison versus control groups.

The study was conducted on 38 patients with warts. Their mean age was 19 years , with 12 males and 26 females .All studied cases presented by pain and skin lesions, with gradual onset and progressive course. The median disease duration was about one year .The most common wart type was the common warts, located mostly on hands and feet. Comparing response obtained after

MMR injection and that obtained after saline injection in control group. There was significantly better response in MMR group when compared to control groups (p<0.001) Table (1).

Most of MMR group patients 77.8% reached complete response after 4 sessions, while 3 patients had partial response and only one patient showed no response.

Table (2) Comparison of response of mother wart between those injected with MMR to all or mother wart.

		Complete response		Partial response		No response		p
		N	%	N	%	N	%	
MMR (All)	N=10	7	70%	2	20%	1	10%	0.570
MMR (Mother)	N=8	7	87.5%	1	12.5%	0	0%	

No significant difference was found regarding response of mother wart between those injected with MMR to all or mother wart.

No significant differences were found regarding response of the mother wart between those injected with MMR to all the warts or to only the mother wart Table (2).

Table (3) Association of response of mother warts to duration, type, site and size in MMR group (n=18).

		MMR injection (n=18)						p
		Complete response		Partial response		No response		
		N=14		N=3		N=1		
Duration (years)	Median (range)	0.9	0.3-3	0.7	0.5-2	0.2	0.2-0.2	0.255
Type	common	4	28.6%	1	33.3%	0	0%	0.804
	palmar	1	7.1%	0	0%	0	0%	0.860
	plantar	4	28.6%	1	33.3%	0	0%	0.804
	periungual	1	7.1%	0	0%	0	0%	0.860
	verruca	3	21.4%	1	33.3%	1	100%	0.415
Site of mother wart	condyloma	1	7.1%	0	0%	0	0%	0.860
	hand	3	21.4%	0	0%	0	0%	0.598
	Foot	7	50.0%	1	33.3%	0	0%	0.570
	Face and scalp	3	21.4%	2	66.7%	1	100%	0.084
	Genital	1	7.1%	0	0%	0	0%	0.860
Baseline size (mm)	Median (range)	5	2-20	12	3-15	3	3-3	0.473

No significant association was found regarding response of mother wart to duration, type, site and size in MMR group Table (3).

Table (4) Association of response of mother warts to features of mother wart in MMR group (n=18).

		MMR injection (n=18)						p
		Complete response		Partial response		No response		
		N=14		N=3		N=1		
Number of lesions	Mean (range)	5	2-10	20	5-25	20	20-20	0.041
	≤5	8	57.1%	1	33.3%	0	0%	0.571
	>5	6	42.9%	2	66.7%	1	100%	
Arrangement	Solitary	8	57.1%	1	33.3%	0	0%	0.571
	confluent	6	42.9%	2	66.7%	1	100%	
Level	elevated	9	64.3%	3	100%	1	100%	0.649
	skin level	5	35.7%	0	0%	0	0%	
Aspect	rough	10	71.4%	2	66.7%	1	100%	0.804
	not lobed	4	28.6%	1	33.3%	0	0%	
Border	sharp	10	71.4%	3	100%	0	0%	0.159
	not sharp	4	28.6%	0	0%	1	100%	
White skin flakes		0	0.0%	0	0%	0	0%	-
Black dots		1	7.1%	0	0%	0	0%	0.860
Color	skin color	11	78.6%	3	100%	1	100%	0.598
	red	3	21.4%	0	0%	0	0%	
Border erythema		2	14.3%	0	0%	0	0%	0.725
Callus		2	14.3%	1	33.3%	0	0%	0.547

Lower number of lesions was significantly associated with better response to MMR injection. Otherwise, no significant association was found regarding response to features of mother wart in MMR group.

Lower number of lesions was significantly associated with better response to MMR injection (P=0.041). Otherwise, no other significant association was found regarding response to features of mother wart in MMR group Table (4).

4. Discussion

Cutaneous warts are treated primarily with destructive methods such as cryotherapy or electrocautery. These modalities of treatment are time-consuming and may be associated with scarring in multiple warts. Immunotherapy is emerging as a new modality of treatment which acts on enhancing cell-mediated immunity against human papillomavirus for clearance of both treated and distant warts [7].

Use of the three antigens—measles, mumps, and rubella—together help in eliciting a stronger immune response against HPV through the production of various cytokines like interleukin (IL)-2, IL-4, IL-5, and tumor necrosis factor- α [8].

Our present finding were in agreement with a previous study p^[9] that found highly significant difference with the therapeutic response of common warts to MMR vaccine with complete response in about 80% of cases. Also^[8] reported similar finding, they reported relative complete response on 2nd visit in about 87.5% of patients injected by MMR vaccine compared with 68% of control patients injected by normal saline.

In another study [10] observed complete and partial clearance of wart lesion (67.4%) with MMR injection into mother warts, that come also in line with current findings.

Also in agreement with our results, another study^[7] revealed a statistically significant difference between the two groups: 68 percent of patients in the MMR group showed complete response compared to 10 percent in the

control group. A clinical response on the basis of type of warts was also observed in the MMR injection group: palmoplantar warts showed the best response, followed by common warts. Complete clearance was seen in 70 percent of palmoplantar warts and 68 percent of common warts after five injections. The authors explained that better response was observed in this particular types due to more number of cases complaining of planter warts in their study [11].

The present study demonstrated that comparing response of mother wart at the last follow up. Regarding comparison between response obtained after MMR injection and response obtained after saline injection in control group revealed significantly better response in MMR group when compared to control groups (p<0.001 for each). While as regard comparing response of other warts, the response obtained after MMR injection revealed significantly better response when compared to control groups (p<0.001 for each).

5. Conclusion

MMR injection showed significantly better response of mother wart when compared to control group. MMR injection showed significantly better response of other warts when compared to control group. The lowest number of lesions was significantly associated with better response to MMR injection. MMR is shown to be an effective intralesional therapy to treat common cutaneous warts.

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