Original Research Article

Study of Efficacy and Safety of Intralesional MMR in Treatment of Warts

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Article History
Received Oct 24, 2017
Received in revised form Nov 20, 2017
Accepted on Dec 6, 2017

Abstract:- Wart is a mucocutaneous disease developing as a result of proliferation of skin or mucosal cells infected with human papilloma virus (HPV). Management of periungual, palmer and plantar warts is quite difficult with traditional methods like TCA, electrosurgery & cryotherpy. Intralesional immunotherapy clears not only the local warts but also distant warts unlike traditional wart therapies. In our study to evaluate the efficacy and safety of intralesional MMR vaccine in treatment of warts, we included 50 patients with single or multiple reclcirant or non reclcirant periungual, palmar and plantar warts with 20 patients as controls who were injected with normal saline. MMR vaccine was injected in a single lesion or largest wart in case of multiple warts at 2 weekly intervals until complete clearance. Complete response was achieved in 86.6% of patients with periungual, palmer and plantar warts and 20% in control group. Pain during injection was found in 85.7% patients. Intralesional immunotherapy by MMR vaccine in a promising effective and safe treatment modality for warts.

Key Words:- Warts, Mucocutaneous, Human Papilloma Virus, Recalcitrant, Immunotherapy

Introduction

Wart is a mucocutaneous disease that develops as a result of proliferation of skin or mucosal cells infected with human papilloma virus (HPV) with obliteration of normal skin markings over the cutaneous lesions. [1,2]Management of verrucae, particularly over the periungual area and over the soles, is often frustrating to the patient and the physician alike. Currently available treatment modalities include topical keratolytic applications, cryosurgery, laser surgery, electrosurgery, bleomycin, curettage, many of them likely to be very painful, unsightly and prone for recurrences. [3]Intralesional immunotherapy utilizes the ability of the immune system to mount a delayed hypersensitivity response to various antigens and also the wart tissue. Immunotherapy is associated with the production of Th1 cytokines which activate cytotoxic and natural killer cells to eradicate HPV infection, clearing not only the local warts but also distant warts unlike traditional wart therapies. [4]This method is useful in larger populations because of vaccine availability and safety.[5] Due to the high prevalence of warts in various populations and the necessity of treatment, we evaluated the efficacy of MMR vaccine injection in the treatment of cutaneous warts.

Material And Methods

This was interventional study was conducted in department of dermatology, Government Medical College and Rajindra Hospital, Patiala in 2015-2016.Fifty patients with single or multiple recalcitrant or non-recalcitrant periungal, palmar and plantar warts were included in the study. Only patients having single or multiple palmar and plantar warts (from 2 up to 7 warts) with age more than 12 years, receiving no concurrent systemic or topical treatment of warts were included. Patients with fever or signs of any inflammation or infection , children less than 12 years of age,pregnant and lactating women, patients with immunosuppression,

patients who received any other treatments for their warts in the last month before enrolment or having past history of asthma, allergic skin disorders, meningitis or convulsions were excluded from the study. Subjects were randomly assigned to two groups; the first group (30 patients) received intralesional MMR vaccine0.5cc, and the second group (20 patients) received intralesional saline in same volume as thestudy group. Pre-treatment photographs were taken. Single lesion or largest wart in case of multiple lesions was selected for injection at 2-week intervals until complete clearance or for a maximum of four treatments. Response to treatment was evaluated by decrease in size of warts and photographic comparison. The response was considered complete if there was disappearance of wart(s) and return of normal skin marking, partial if the wart(s) had regressed in size by 50-99% and no response if there was 0-49% decrease in wart size. Follow-up was done every 2 months for 6 months for detecting recurrence. Data were entered, checked and analyzed using the SPSS 20 version. Data were expressed as mean ± SD for quantitative variables, and number and percentage for qualitative ones. Chi-square test and t-test were used as appropriate. P-values <0.05 were considered significant.

Results

Out of the 30 patients in study group (33.33%) were in the age group of (21-30) years while 26.67% of patients belonged to the age group (11-20) years. In control group, out of 20, 45% of subjects belonged to the age group (21-30) years while 30% of subjects were in age group (11-20) years.[Table 1] Mean age of study groups' patients was 42.23±10.24 years and in control group was 39.25±12.26 years. Both the groups ($X^2 \geq 10.00$, $p>0.05$) were age matched and thus they were comparable. Study group comprised of 60% males and 40% females while the control group comprised of 55% males and 45% females[Table 2].There was no statistically significant difference among both groups on gender ($X^2 \geq 2.44$, $p>0.05$).On both study and control group maximum of four treatment was given.

Table 1: Showing Age Range of Both Groups

Age Range	Study Group (N=30)		Control Group (N=20)	
	No.	Percentage	No.	Percentage
11-20	08	26.67	06	30
21-30	10	33.33	09	45
31-40	06	20	02	10
41-50	04	13.33	02	10
51-60	02	6.67	01	5
Total	30	100	30	100
Mean±SD	42.233 ±10.24		39.25±12.26	
p-value	0.219 (No-Sig.)			

Table 2: Showing Sex Information of Both Groups

Sex	Study Group (N=30)		Control Group (N=20)		Total		p value
	No.	Percentage	No.	Percentage	No.	Percentage	
Female	12	40	9	45	21	42	0.118 (No-Sig.)
Male	18	60	11	55	29	58	
Total	30	100	20	100	60	100	

Table 3: Showing Clinical Responses among the Studies Patients

Clinical Response	Study Group (N=30)		Control Group (N=20)	
	No.	Percentage	No.	Percentage
Complete Response	26	86.67	04	20
Partial Response	3	10	02	10
No Response	1	3.33	14	70
X^2	73.89			
p value	0.001 (Sig.)			

Patients showing complete response were 86.6% in study group (Fig. 1 & 2) while 20% in control group (P value .001, statistically significant)

Discussion

Treatment of common warts is frustrating for both physician and patient because optimal treatment having high efficacy and lowrecurrence has not been explored till date.[6]Currently available destructive modalities are painful, ineffective, costly and may be associated with disfiguring, scarring and high recurrence rates.[3] Several immunotherapeutic agents with variable efficacy have been used for the treatment of different types of warts, including common warts.[7]Intralesional immunotherapy has the potential advantage of clearance of both treated and untreated distant warts without scarring, a presumed lower rate of recurrence and a high safety profile.

We evaluated the role of MMR vaccine in the treatment of warts in our study on 50 patients. Out of 30 in the, 86.6% of the patient in the study group showed complete clearance of the warts.

Mean age group of study group was 32.4 in a study by Nofal (2010) [4]. In our study the mean age was 42.3.Our results with MMR-treated group showed a closely similar response rate to those previously reported by Nofal (2010) [4] and Gamil et al. (2010) [5] in their study on MMR vaccine in treatment of plantar warts with 87% complete clearance.

The exact mechanism of action of intralesional immunotherapy is still obscure. Intralesional antigen injection probably induces strong non-specí c iń ammatory response against theHPV-infected cells.[9,10]It has also been suggested that the trauma of injection itself,or the bystander effect, may cause wart clearance in previously sensitized individuals.[11]Intralesional immunotherapy causes release of different cytokines such asIL-2, IL-4, IL-5, IL-8, INF-gamma TNF-alpha which stimulate a strong immune response against HPV.[10,12]Proliferation of peripheral blood mononuclear cells following immunotherapy promotes Th1 cytokine responseswhich further activate cytotoxic T cells and natural killer cells toeradicate HPV-infected cells.[12]

There are a few side effects reported by most of the studies. The most common include injection site reactions and flu like symptoms Flu-like symptoms that resolved rapidly within 24 h by non-steroidal anti-inflammatory drugs has been reported in six patients in a study by Nofal (2010) [4]. Side effects are probably due to injection of the antigen into the circulation with subsequent immunological response and elaboration of cytokines. [13] The only side effect observed in our study was Pain during in 85.7% patients and none of our patient complained of Flu like symptoms . Most of these reactions last up to 24 hours and resolve with the use of nonsteroidal anti-inflammatory drugs.

Fig 1 Multiple Palmar Warts

Before Treatment **After Treatment**

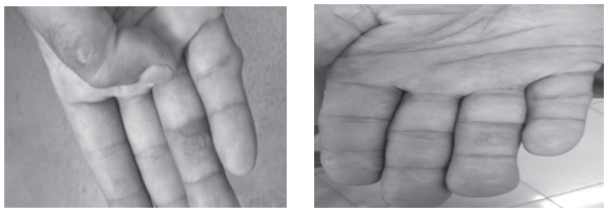
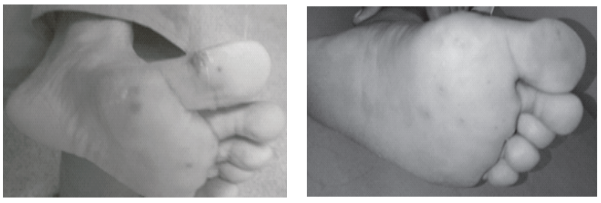


Fig 2 Multiple Hyperkeratotic Plantar Warts

Before Treatment **After Treatment**



Conclusion:

Intralesional immunotherapy is a safe and effective treatment modality for treatment of otherwise treatment- resistant periungual, palmar and plantar warts.

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