Original Research Article

Safety and efficacy of intralesional MMR vaccine along with oral zinc in cutaneous warts

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Abstract

Background: Warts are one of the most common viral infections of humans in which the most frequently used modalities of treatment involve destruction of the affected area, which does not prevent recurrences and often results in scarring and not possible in multiple wart. Immune system plays an important role in the control of warts has led to the concept of immunotherapy for this condition. **Objective:** To evaluate efficacy and safety by combining two immunomodulator i.e. oral zinc and intralesional MMR vaccine for the treatment of cutaneous warts. **Material and Methods:** This double blind randomized controlled clinical trial was conducted in department of dermatology at saraswathi institute of medical college, Hapur on 50 patients with warts who were allocated to two groups including MMR group with oral zinc and normal saline group. MMR vaccine was injected intralesionally along with oral zinc in the first group, whereas normal saline was injected into the lesions in the second group. These injections were repeated every 2 weeks intervals for maximum 3 injections. All patients were followed up every 15day interval up to 45 days and then up to 6 months regarding relapses and finally, side effects, probable relapse, and therapeutic outcomes were evaluated and compared. **Result:** At the end of follow up period, therapeutic outcomes in the first group included complete cure in 80% cases, relative cure in 8% cases, and no cure in 12% cases. In normal saline group, these rates included complete cure in 4% cases, relative cure in 16% cases, and incomplete cure in 68% cases. No significant complication occurred in the two groups. **Conclusion:** On combining two immunomodulator for treatment of cutaneous wart is slightly better than used individually and is equally safe.

Key Words: MMR vaccine, Wart, Zinc.

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Received Date: 29/09/2017 Revised Date: 19/10/2017 Accepted Date: 28/11/2017
DOI: https://doi.org/10.26611/10214211

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 30 November 2017

INTRODUCTION

Verrucae (synonym: warts) are one of the most common viral infections of humans. These are caused by human papillomavirus (HPV). There are approximately 100 genotypes of these DNA viruses. Transmission of HPV occurs most commonly by direct contact with individuals who may be harbouring subclinical or manifesting clinical HPV-associated lesions, or by indirect means such as through contaminated surfaces and objects.[1] The overall incidence is approximately 150 per 100 000 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[2] 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[2,6] There is currently no specific antiviral therapy available to cure HPV infection. Existing modalities of treatment including electrocautery, cryotherapy which involve destruction or removal of visible lesions do not prevent recurrences and may even result in scarring.[1,8] The treatment of warts depends on two main therapeutic options: the first is the conventional destructive and aggressive method, which includes treatment with chemical cautery, cryotherapy, electrocauterization, surgical excision, and laser ablation, and the second is immunotherapy, which is based on the activation of the immune system to deal with the virus and suppress its activity. Such therapy may be applied either topically or through intralesional injection or through systemic administration[3,5] In some

How to cite this article: Sachin Agarwal, Prashant Kumar Yadav, Amarjeet Singh Verma, Harmeet Kaur. Safety and efficacy of intralesional MMR vaccine along with oral zinc in cutaneous warts. *MedPulse International Journal of Medicine.* November 2017; 4(2): 103-105. https://www.medpulse.in/Medicine/

of the previous studies, it has been shown that mumps measles rubella (MMR) vaccine results in regression of warts via immunomodulation and induction of immune system. This method can be used in larger populations because of vaccine availability and safety. Due to the high prevalence of warts in various populations, especially in children, as well as the necessity of treatment, we evaluated the efficacy of two immunomodulator, intralesional MMR vaccine and oral zinc acetate 10mg/body weight in the treatment of cutaneous warts. However, for obtaining more definite results, this study needs to be repeated in the Iranian population.[4,7]

MATERIAL AND METHODS

This double blind randomized controlled clinical trial was conducted in SIMS from march 2017 to august 2017.Our study population included patients with warts who were candidates for treatment. Inclusion criteria were men and women above 18 years of age and women who were not pregnant or breast feeding, not having received anti wart treatment within the past 4 weeks, lack of viral infections such as herpes and/or bacterial infections, lack of any infective febrile disease, and completing the treatment course in this study. In this study, all the patients satisfying the inclusion criteria were evaluated until the required sample size was obtained. Selecting the patients in the two therapeutic case and control groups was performed by simple randomized method. Full information on the investigation objectives and methods was given to the patients, and consent was taken from the participants. At first, all patients underwent clinical examination by a dermatologist in the dermatology clinics to confirm the diagnosis of wart. Biopsy and histopathologic examination was done in the suspicious cases. Then, demographic information, clinical history, and present condition of their disease were demonstrated. The information included age, gender, disease duration, number of lesions, and involved sites. After selecting the patients who satisfied the inclusion criteria, the number of skin lesions was counted and recorded in the questionnaires, and then patients were allocated randomly to MMR with oral zinc as group 1 and normal saline as group 2.MMR vaccine 0.5 cc was injected intralesionally on single wart along with oral zinc of dose10mg/kg/day in group1, whereas normal saline was injected in the same volume into the lesions in the other group. These injections were repeated every 2 weeks for a maximum of three injections. Then all patients were followed up for 6 months and in 2 month intervals to evaluate and compare the side effects, probable relapse, and therapeutic outcomes. Lesions with size decrease of less than 50% were defined as no therapeutic response, size decrease between 50 and 99% as relative response, and complete removal of the lesions was considered as complete cure.

RESULTS

In this the study 25 patients were enrolled in each group and were evaluated. MMR group consisted of 14 males and 11females, whereas there were 17 males and 8 females in the control group. Frequency and therapeutic response rate in the two groups after treatment and according to the time elapsed after treatment are shown. The findings of this investigation show that there was no relapse in any of the treated cases in both groups. In addition, no important adverse effect was reported in any of the patients in both therapeutic groups. Pain at the time of injection was reported by 100% of patients in both groups; whereas influenza like syndrome was reported by 30% of the patients in the MMR group and no case in the normal saline group.

DISCUSSION

Various therapeutic options such as cryotherapy, 3cloroacetic acid, peudophylline, surgery by laser, topical cidofovir, electrocautery, retinoids, and salicylic acid have been recommended for treatment of wart. No specific treatment or therapeutic protocol is completely suitable for all of the patients. Although most of the therapeutic options result in clearing of virus within 16 months. There are clinical evidences that cellular immune responses play an important role in HPV infection and disease. T cell (CD4, CD8) infiltration, especially, has been found in the warts with spontaneous regression. In addition, prevalence of HPV related lesions increases in the HPV infected patients and transplant recipients. Both groups have a compromised cellular immune system. This finding indicates that if immunotherapy modalities are able to induce the immune system for destroying virus and the infected host cells, it could be considered as a therapeutic option for wart. Although the mechanism of effectiveness of intralesional injection of MMR vaccine and antigens has not yet been known, it seems that nonspecific inflammatory response to the antigens is the major mechanism of immunotherapy. Zinc is an important element that is found in every cell in the body. More than 300 enzymes in the body need zinc in order to function properly. It is also essential for the proper functioning of the immune system. In zinc deficiency, the function of the macrophages and T cells is impaired with fifty percent reduction in leucocytes and 40-70% reduction in antibody-mediated and cell-mediated immunity. The addition of zinc to a culture

system results in polyclonal stimulation of lymphocytes. Zinc has been previously used as an immunomodulator in a number of dermatological diseases such as erythema nodosum leprosum and dissecting cellulitis of scalp[1] The results of this study show that the sex ratio and age of the patients were nearly similar and there was no significant difference between the two groups. This finding indicates that underlying factors such as age and sex have not confounded the results of our study. In addition, the number of lesions at the beginning of study and therapeutic intervention had been somewhat similar. In the first post treatment visit, therapeutic response was seen in 60% of patients in the MMR group, whereas only 12% of the control group showed therapeutic response. This finding shows that the therapeutic effect of MMR was significantly more than that of normal saline. This effect had been observed early at the initiation of follow up period, while the therapeutic effect of MMR increased with passing time. This therapeutic effect of MMR was observed in both male and female patients. In this study, no important adverse effect occurred as a result of MMR injection, and the pain due to injection had been reported with normal saline injection too. On the other hand, influenza like syndrome was tolerable, and therefore, it is not considered as a contraindication for applying this therapeutic modality. And the documented side effect of zinc sulfate were nausea, vomiting and diarrhoea. Which did not require interruption of treatment. These adverse effects were attenuated by dividing the total dose into three daily doses and taking the medication together with meals. The results of our study are higher than previous studies using single immunomodulators. During the follow up period in the MMR group, no case of relapse was observed in the recovered lesions; and also, no adverse effect was reported.

Table 1:

Type of wart	Group A	Group B
Plane	18	17
Common	4	4
Plantar	3	4
Filiform	---	----

Table 2:

Site	Group A	Group B
Hand	16	14
Face	4	5
Feet	5	6

Table 3:

Age (years)	Treatment group	Placebo
18-30	14	15
31-42	8	5
>42	3	5

Table 4:

Time of Evaluation	Therapeutic Group	Therapeutic Response
1st visit	1	NR-10
		PR-10
		CR-5
	2	NR-20
		PR-2
		CR -1
2nd visit	1	NR-6
		PR-7
		CR-12
	2	NP-18
		PR-4
		CR-1
3rd visit	1	NR-3
		PR-2
		CR-20
	2	NR-17
		PR-5
		CR-1

CONCLUSION

Two immunomodulator with different mechanism of action can be combined for treatment of cutaneous wart and give synergistic effect and is slightly better than used individually and is equally safe.

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Source of Support: None Declared
Conflict of Interest: None Declared