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Research Article

A prospective randomized open label comparative study of efficacy and safety of intralesional measles, mumps, rubella vaccine versus 100% trichloroacetic acid application in the treatment of common warts

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ABSTRACT

Background: Treatment of warts represents a continuing challenge for dermatologists as many of the available therapeutic modalities are associated with unsatisfactory results and high recurrence rates. Several clinical trials have proved the efficacy of intralesional immunotherapy by different antigens including MMR vaccine in the treatment of different types of warts.
Methods: Total 150 patients having common warts over hands and feet including palmar and plantar warts were included in the study and were randomly divided into two groups. Group 1 consisted of 87 patients in whom MMR vaccine was given intralesionally in the largest wart whereas in Group 2, 63 patients were applied 100% trichloroacetic acid locally to the warts. These treatments were repeated 2 weekly for total three treatments. Patients were assessed for treatment response monthly for 3 months.
Results: A highly significant difference was found in the response rates between the two groups ($p<0.001$). In the MMR group, 49.43% patients had >75% improvement and 26.44% patients had complete resolution whereas in TCA group, 11.11 % had >75% improvement and 7.94% patients had complete resolution. In the MMR group, side effects included pain at the injection site 100%, flu like symptoms 1.15 %, post-inflammatory hyperpigmentation 1.15% and tenderness 1.15% whereas in the TCA group all patients experienced burning sensation and 2 (3.17%) patients had post-inflammatory hyperpigmentation.
Conclusion: Intralesional MMR vaccine is an effective treatment for warts without any significant side effects.

Keywords: Immunotherapy, MMR vaccine, Warts

INTRODUCTION

Warts or verrucae are benign proliferation of the skin or mucosa that is caused by infection with human papillomavirus (HPV).[1] HPV is a double stranded DNA virus and over 118 types of HPV have been identified.[2] Common warts are mainly caused by HPV-2, but can also be caused by HPV-27, 57, 1 and 4. They are most commonly situated on back of the hands and fingers, but may occur anywhere on the skin.[3] Currently available treatment modalities for warts include topical agents such as salicylic acid 12-26% with lactic acid, podophyllotoxin, trichloroacetic acid, formaldehyde, 5-fluorouracil, photodynamic therapy, surgical methods like cryosurgery, electro surgery, laser ablation, surgical excision. Oral drugs like levamisole, cimetidine, zinc sulphate and immunotherapeutic agents including imiquimod, contact sensitizers, intralesional interferons have been used.[4] Intralesional immunotherapy uses the immune system's capacity to mount a type 1 helper T cell (TH 1) mediated delayed-type hypersensitivity response to various antigens, including HPV.[5] Treatment of warts is often difficult and most of the available treatments are

destructive leading to trauma and scarring and are also associated with recurrences. Destructive modalities like electro cautery and chemical cautery are painful procedures difficult to use in children. Lesions on periungual area and palmo plantar warts are difficult to treat. Intralesional immunotherapy with measles, mumps, rubella (MMR) vaccine has been reported as an effective treatment for warts, as indicated by higher response rates and distant response rates in subjects receiving these antigens. It is also effective in recalcitrant warts.[6]

METHODS

This open label, randomized, comparative study was conducted in the Out Patient Department of Dermatology, Venereology and Leprology of SMGS Hospital, Government Medical College, Jammu from November 2013 to October 2014. The study was approved by Institutional Ethics Committee, Government Medical College Jammu.

150 patients of common warts who fulfilled the inclusion and exclusion criteria were included in the study. Inclusion criteria were patients in the age group of 10 to 60 years having common warts over hands and feet including palmar and plantar warts and duration of warts 3 months or more. Exclusion criteria were children less than 10 years of age, elderly patients more than 60 years of age, pregnant women, lactating women, immunosuppressed individuals, diabetic patients, patients who received any other treatment for warts in last one month, acute febrile illness, patients with history of bleeding diathesis or coagulopathies, past history of asthma, allergic skin disorders, meningitis or convulsions.

A detailed history regarding the age, sex, duration of disease was noted. Baseline characteristics of the wart including site, size and number were evaluated at the start of the study and subsequently at 2 weekly intervals during the treatment and then monthly for 3 months during post treatment follow up period. Any side effects of the treatment were recorded at each visit. A written informed consent was obtained from all the patients and each procedure was carried out under all aseptic precautions.

Patients were randomly divided into two groups. In the first group (group 1), intralesional MMR vaccine 0.3 ml was given in the largest wart and in the second group (group 2), paring of the wart was done followed by 100% trichloroacetic acid application. Maximum five warts were pared in one session. Treatment was given at 2 weekly interval for total three treatments. All the patients were followed up monthly for a period of 3 months. Response to treatment was evaluated by decrease in size and number of the lesions locally as well as at distant sites and photographic record was maintained.

Response to treatment was graded as

Grade 0 - No response or aggravation

Grade I - ≤ 25% reduction in size

Grade II- 26- 50% reduction in size

Grade III- 51-75% reduction in size

Grade IV- >75% reduction in size

Data was analyzed using chi-square test, t-test, Fisher exact test wherever applicable; p value<0.05 was considered significant.

RESULTS

In the present study, 150 patients with a mean age of 21.52±9.39 (range: 10-55) years of either sex clinically diagnosed as cases of common warts were enrolled. There were 87 patients in the intralesional MMR group and 63 patients in 100% trichloroacetic Acid group. Mean age was 22.39±9.35 years in MMR group and 20.31±9.38 years in TCA group, which showed no statistical significant difference (p = 0.18). MMR group consisted of 51 (58.62%) males and 36 (41.38%) females, whereas there were 37 (58.73%) males and 26 (41.27%) females in TCA group. Comparison of these showed no statistical significant difference (p = 0.98).

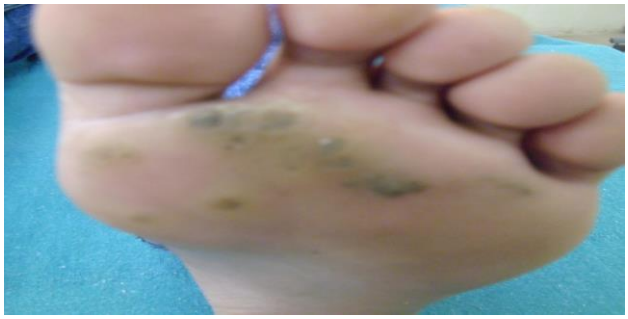

Figure 1: Plantar warts in a patient before treatment.

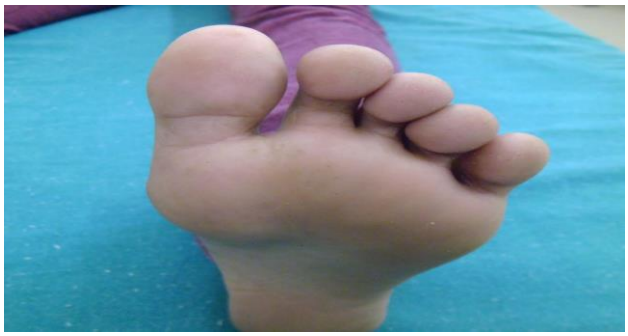

Figure 2: Post treatment clinical photo at 3 months after the last dose of intalesional MMR vaccine.

Distant warts were present in 24 out of 87 (27.59%) patients in MMR group and 8 out of 63 (12.70%) patients in TCA group.

At 2 and 4 weeks no significant difference was seen in the response rates between the two groups (Table 1). At 1 month post treatment follow up, statistically significant difference was seen in the response rates between the two groups (p=0.03). In MMR group, 10 (11.49%) patients had no response, 9 (10.34%), 28 (32.18%), 7 (8.05 %) and 24 (27.59%) patients had grade I, II, III and IV response respectively. In TCA group, 17 (26.98%) patients had no response, 11 (17.46%), 15 (23.81%), 7 (11.11%) and 8 (12.70%) patients had grade I, II, III and IV response respectively (Table 2).

At 2 months follow up period, comparison between the two groups showed statistically highly significant difference in the response rates (p<0.001). In MMR group, 7 (8.05%) patients had no response, 3 (3.45%), 21 (24.14%), 9 (10.34%) and 37 (42.53 %) patients had grade I, II, III and IV response respectively. In TCA group, 22 (34.92%) patients had no response, 6 (9.52%), 14 (22.22%), 7 (11.11%) and 8 (12.70%) patients had grade I, II, III and IV response respectively (Table 2).

At 3 months follow up period also, statistically highly significant difference was seen in the response rates between the two groups (p<0.001). In MMR group, 6 (6.90 %) patients had no response, 4 (4.60%), 15 (17.24%), 9 (10.34%) and 43 (49.43%) patients had grade I, II, III and IV response respectively. In TCA group, 23 (36.51%) patients had no response, 5 (7.94%), 14 (22.22%), 7 (11.11%) and 7 (11.11%) patients had grade I, II, III and IV response respectively (Table 2). 23 (26.44 %) patients in MMR group showed complete (100 %) resolution of the lesions as compared to 5 (7.94%) patients in TCA group.

No significant difference was seen in the response rates in distant warts between the two groups. In MMR group, out of 20 patients with distant warts, 14 showed no response, 1 had grade I response, 4 had grade II and 1 had grade III response in distant warts. In TCA group, distant warts showed no response.

No significant side effects were seen in both the groups. In MMR group, all patients complained of pain during injection, 1 patient had flu-like symptoms which resolved in 1-2 days, 1 patient had post-inflammatory hyperpigmentation and 1 had tenderness at the injection site. In TCA group, all patients experienced burning sensation during TCA application and 2 patients had post-inflammatory hyperpigmentation.

Table 1: Comparison of response during treatment at 2 and 4 weeks in two groups.

Response	2 weeks		4 weeks	
	Group1 (MMR) (n=87) no (%)	Group2 (TCA) (n=63) no (%)	Group 1(MMR) (n=87) no. (%)	Group2 (TCA) (n=63) no (%)
Grade 0	49 (56.32)	42 (66.67)	19 (21.84)	16 (25.39)
Grade I	25 (28.74)	14 (22.22)	27 (31.03)	23 (36.51)
Grade II	7 (8.04)	3 (4.76)	26 (29.88)	19 (30.16)
Grade III	0	0	3 (3.45)	0
Grade IV	1 (1.15)	0	4 (4.60)	1 (1.59)
Lost to follow-up	5 (5.75)	4 (6.35)	8 (9.20)	4 (6.35)

Table 2: Comparison of response during follow-up period in two groups.

Response	1 month		2 months		3 months	
	Group1 (MMR) (n=87) no.(%)	Group2 (TCA) (n=63) no.(%)	Group 1	Group 2	Group 1	Group 2
Grade 0	10 (11.49)	17 (26.98)	7 (8.05)	22(34.92)	6 (6.90)	23 (36.51)
Grade I	9 (10.34)	11 (17.46)	3 (3.45)	6 (9.52)	4 (4.60)	5 (7.94)
Grade II	28 (32.18)	15 (23.81)	21(24.14)	14(22.22)	15(17.24)	14(22.22)
Grade III	7 (8.05)	7 (11.11)	9 (10.34)	7 (11.11)	9 (10.34)	7 (11.11)
Grade IV	24 (27.59)	8 (12.70)	37(42.53)	8 (12.70)	43 (49.43)	7 (11.11)
Lost to follow-up	9 (10.34)	5 (7.94)	10(11.49)	6 (9.52)	10 (11.49)	7 (11.11)

DISCUSSION

Immune mechanisms have been suggested to explain the spontaneous resolution of warts. If this immunity could be enhanced, wart resolution could be long lasting. The stimulated immune system would destroy all warts in the body, sparing patients from local treatment for each individual wart.[7] It has been reported that untreated warts resolve after injection of only one wart with intralesional immunotherapy that induces HPV-directed immunity.[8] Antigens used for intralesional immunotherapy include tuberculin, BCG, mumps, candida and trichophyton and MMR.[9-12]

The results of this study showed that at the end of the study, in the MMR group 43 (49.43%) patients had >75 % improvement out of which 23 (26.44%) patients had complete resolution of the lesions. Nofal and Nofal in 2010 observed complete response with intralesional MMR vaccine in 80% of patients of common warts.[12] Gamil et al in 2010 reported complete clearance in 87% patients, partial response in 4.3% and no response in 8.7 % of the patients of plantar warts with intralesional MMR vaccine.[6] Mohamad et al in 2013 found complete response in 82% patients, partial response in 6% and no response in 12 % patients of plantar warts with intralesional MMR vaccine.[13] Zamanian and Mobasher in 2014 observed complete cure in 75% patients, relative cure in 16.66 % and no cure in 8.33 % patients of warts with intralesional MMR vaccine.[14] Na et al in 2014 in their study with intralesional MMR vaccine in warts, found that 51.5% patients experienced > 50% reduction in size and number of warts.[15] Nofal et al in 2014 observed complete clearance of warts in 63% patients, partial response in 23% and no response in 14% patients with MMR vaccine.[16] There were higher response rates in these studies as compared to our study because these studies used either more doses of intralesional MMR vaccine or their follow up period was longer. The number of patients with grade IV response or complete clearance of the warts progressively increased in our study when assessed at 2 weeks and then subsequently at post treatment monthly follow up visits.

In the TCA group, only 7 (11.11%) patients had >75% improvement and total 5 patients showed complete resolution of the warts. Nath et al in 1990 used 50% trichloroacetic acid (TCA) in genital warts and observed that warts cleared in 81% patients in 3 months.[17] Pezeshkpoor et al in 2012 observed that 33.3% patients had mild response, 20% had moderate response and 46.7 % had good response in common warts with 80% TCA solution.[18] These studies showed higher response rates as weekly applications were done and also number of applications were more.

On comparison between the two groups, statistically highly significant difference was seen in the response rates at the end of the study.

In the present study no significant difference was seen in the response rates in distant warts between the two groups. Gamil et al in 2010 reported complete response in 83.3 % of patients with distant warts,[6] Mohamad et al in 2013 observed complete response in 88.9% and partial response in 11.1% patients with distant warts.[13] Na et al in 2014 reported good response in 46.7% patients who had distant warts.[15] Nofal et al in 2014 found complete response in 74.5% of patients presenting with distant warts.[16] Higher response rates in distant warts in these studies may be due to either more number of treatments or longer follow up period.

CONCLUSION

In conclusion it may be said that intralesional MMR vaccine is an effective treatment for warts as compared to 100% TCA application without any significant side effects. It is a promising modality for the treatment of multiple and recalcitrant warts. Other modalities commonly used in our set up like electro cautery are associated with pain, scarring and chances of recurrence. Intralesional immunotherapy uses immune system's capacity to mount a type 1 helper T cell mediated delayed type hypersensitivity response to the antigen which accelerates destruction of virus and infected host cells. It can eradicate not only the treated wart but also the distant warts and therefore the antigen is usually injected in the largest wart. So it seems to be effective with good response rates and without any significant side effects, as seen in our study.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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