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Original Research Article

Therapeutic evaluation of intralesional measles, mumps and rubella vaccine in palmoplantar warts

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ABSTRACT

Background: Warts are common viral infections of the skin caused by human papilloma virus. Most of the treatment modalities for common warts remain unsatisfactory. Immunotherapy has become one of the important therapeutic modality. This study was conducted to evaluate the efficacy of intralesional measles, mumps and rubella (MMR) vaccine immunotherapy in palmoplantar warts.
Methods: 60 patients of various age groups and both sexes who have single or multiple palmoplantar warts not on any other concurrent systemic or topical therapy were randomly included for the study. Patients with other types of warts, signs of other infection, pregnancy, lactation and immunosuppression were excluded from the study. MMR Vaccine was injected intralesionally at 2 week intervals until complete clearance or for a maximum of 3 treatments. The outcome in terms of treatment relapse, recurrences and adverse effects were evaluated.
Results: Only 54 patients completed the study and 41 (75.9%) of them showed complete response and 13 (24%) of them showed partial or no response.
Conclusions: Intralesional MMR vaccine therapy appears to be a safe and effective treatment option with no significant adverse effects and low recurrence.

Keywords: Warts, Immunotherapy, MMR vaccine

INTRODUCTION

Warts are benign epidermal tumours caused by HPV, a ds-DNA virus. They show tropism for epithelial cells, causing mucocutaneous manifestations.[1] Cutaneous warts manifests as verruca vulgaris, plane, plantar, myrmecia, mosaic, filiform or digitate and periungual. The incidence of cutaneous warts is around 150 per 100000 population.[2] Warts are more common in children and young adults. Common warts occur mostly over the dorsum of hands and fingers. They are asymptomatic usually except plantar and periungual warts which may produce pain. Warts are contagious in nature. The spontaneous resolution rate for warts is 65-78%. The associated cosmetic disfigurement, tendency to spread and the associated poor quality of life makes it necessary to intervene faster. Management of palmoplantar and periungual warts are usually painful, unsightly and prone for recurrences. There are various destructive and immunotherapeutic treatment modalities for cutaneous warts, but no single treatment has yet proven to be 100% effective.[3]

Treatment of warts includes topical drugs like salicylic acid, trichloroacetic acid, podophyllotoxin and 5 flurouracil. The other surgical modalities which pose a risk of scarring includes radiocautery, cryotherapy, surgical excision and carbon dioxide laser. Systemic drugs like levamisole and zinc sulphate have also been

tried.[4] Immunotherapy is one of the recent modality of treatment for cutaneous warts.

The basis of immunotherapy is the manipulation of the immune system to achieve a human papilloma virus targeted immune reaction.[5] Injection of viral antigen results in peripheral blood mononuclear cell proliferation, promoting Th1 cytokine responses, particularly interferon gamma and interleukin 2,4. This causes activation of cytotoxic T cells and natural killer cells that eradicates the human papilloma viral infected cells. Immunotherapy also stimulates tumour necrosis factor α and interleukin 1 release, downregulating gene transcription of HPV virus.[6] Immunotherapy can be tried in patients with recalcitrant, recurrent, extensive or difficult to treat areas like periungual and palmoplantar warts. The various agents used in immunotherapy of warts include topical agents like imiquimod, sinecatechins, BCG and intralesional agents like Mw vaccine, BCG vaccine, PPD, MMR vaccine, candida extract, trichophyton antigen, tuberculin, vitamin D_3 and interferon alpha 2B. Systemic immunotherapy agents are zinc, cimetidine, levamisole, echinacea, propalis and HPV vaccines.[7]

Objective

The objective of the present study was to evaluate the therapeutic efficacy and safety profile of intralesional measles, mumps and rubella (MMR) vaccine in the treatment of recalcitrant palmoplantar warts.

METHODS

This randomized interventional study, after proper approval included 60 patients collected over a period of one year from December 2017 to November 2018, who attended dermatology outpatient department in ESI Medical College Hospital. The study inclusion criteria are patients of any age group, both sexes having single or multiple palmoplantar warts not on any other concurrent systemic or topical therapy. Exclusion criteria included patients with other types of warts, signs of any other infection, pregnancy, lactation and immune suppression. Detailed history was taken to note the duration, number of warts, and the sites involved. Demographic details including age and sex were noted. Photographic documentation was done. Written consent was obtained from all of the patients. The MMR vaccine was reconstituted and a volume of 0.3 ml was injected with insulin syringe into the wart or into the largest wart in patients with multiple warts. This intralesionally in one of the largest wart or in multiple wart lesions. This was repeated every 2 weeks until complete clearance of all the warts or for a maximum of 3 treatment sessions. Patients were assessed at the beginning of the study and during each treatment session to record the reduction in the size and number of warts, side effects like pain, hypopigmentation or flu like symptoms.

The clinical response was graded into complete (complete cure), partial (if there was decrease in the size or decrease in the number of warts) and no response (no change in size and number of warts). The patients were followed up every 2 months for a period of 6 months to detect any recurrence. Data were entered and analysed using the SPSS software. Data were expressed as mean±SD for quantitative variables and number and percentage for qualitative variables.

RESULTS

A total of 60 patients were included in the study, of which 6 patients lost follow up during the study. There were 33 males and 21 females with M: F ratio of 1.57:1. The patients were aged between 19 and 55 years with a mean age of 26.4. Majority of the patients (36 patients) had multiple warts. Only 18 patients had single wart. The duration of warts ranged from 20 days to 9 months, with a mean of 3 months 20 days. Baseline characteristics of the patients as shown in table 1.

Table 1: Baseline characteristics of the patients.

Age in years	19-55	Mean: 26.4
Male/female ratio	33:21	1.57:1
Number of warts (%)		
Single	18	33.3
Multiple	36	66.6
Duration of warts		
Less than 1 month	15	27.7
3-6 months	29	53.7
6-9 months	10	18.5

Out of the total 54 patients, 41 (75.9%) showed complete response and 7 (12.9%) showed partial response while 6 patients (11.1%) showed no response [Figure 1 and 2]. Response to treatment was shown in Table 2.

Table 2: Clinical response to treatment.

	Complete response	Partial response	No response
No. of patients	41	7	6
Group (%)	75.9	12.9	11.1

Figure 1: Before and after intralesional injection MMR.

Most of the patients reported mild to moderate injection site pain at the time of intralesional injection. No other local or systemic side effects were noted. There was no recurrence of warts at the end of the study.

Figure 2: Before and after intralesional injection MMR.

DISCUSSION

Palmoplantar warts are resistant to most of the topical modalities of treatment and recurrence is common with the surgical modalities. Immunotherapy has become one of the important therapeutic tool.[8] Intralesional immunotherapy has been shown to be associated with release of different cytokines. Several immunotherapeutic agents with variable efficacy have been used for the treatment of warts.[9]

In our study no statistically significant association was found between the therapeutic response to MMR antigen and different clinical variables like age, gender, number and duration of warts. Our study showed a high rate of complete clearance in 75.9% of patients. Study by Nofel et al reported complete clearance of warts in 81.4% of patients in the MMR group compared with 27.5% of patients in the placebo group.[10] Wiley- Blackwell found intralesional immunotherapy by MMR vaccine is an effective and safe therapeutic modality for common warts in around 84.6% of patients. Gamil et al showed a complete response of 87% in 40 patients with intralesional MMR vaccine.[11] A study by Na et al, involving 136 patients with cutaneous warts showed only 5.6% complete resolution and 51% partial resolution. Many authors have used different immunotherapeutic agents for intralesional injection. Kus et al using tuberculin antigen showed a 29.4% clearance.[12] Clifton et al using intralesional mumps or candida antigen showed 47% clearance.[13] Horn et al showed 53% clearance by using intralesional immunotherapy with mumps, candida and trichophytin skin test antigens. The findings in various studies indicate that a higher clearance response is noted in studies using a combination of antigens than using a single antigen.

In our study, apart from injection site pain, no other side effects were noted. The side effects reported by most of the studies include injection site reactions and flu like symptoms. Most of these resolve within 24 hours. Rare adverse events include painful purple digit and post-immunotherapy revealed cicatrix.[14] In a study by Dhope et al, erythema, swelling and flu like symptoms were seen after MMR injection in 25%, 20% and 10% respectively.[15] In Kenawi et al study with BCG antigen, flu like symptoms were noted in all patients with lesional ulceration in 26.7% and necrosis in 16.7%.[16] A study by Munnagi et al also showed that intralesional MMR is safer, better and effective treatment modality of multiple warts compared to BCG.[17]

CONCLUSION

Immunotherapy for warts with various agents has shown significant results in terms of safety and efficacy. Intralesional MMR vaccine is an important modality for the treatment of palmoplantar warts, with good cure rates and excellent safety profile. It is a simple, cost-effective, and non-destructive treatment option with good tolerability. Combination of immunotherapy with other destructive modalities has shown an increased therapeutic response in recalcitrant and recurrent cases.

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