MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.7.218.220

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Key Words
Extensive warts, recalcitrant warts, MMR

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Received: 2 May 2024
Accepted: 12 June 2024
Published: 13 June 2024

Citation: K. Vivekanandh, S. Shakthi Juwala, Anandan Govindaraj Vimal Kumar, R. Agnes Varshini, P.A. Sree Parvathi, J.A. Reshma, A.J.S. Pravin and J. Nivinsimon, 2024. Efficacy of Intralesional MMR in Extensive and Recalcitrant Warts: An Open Uncontrolled Study. Res. J. Med. Sci., 18: 218-220, doi: 10.36478/makrjms.2024.7.218.220

Efficacy of Intralesional MMR in Extensive and Recalcitrant Warts: An Open Uncontrolled Study

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Abstract
Extensive warts is a challenging condition to treat. Intralesional MMR is a new modality which acts by enhancing cell-mediated immunity against the warts. To evaluate the efficacy and safety of intralesional MMR in extensive and recalcitrant warts. Open uncontrolled study. 60 patients with multiple warts of varying sizes and duration were included in the study. 0.2-0.5-mL MMR solution was injected at the base of the wart. A maximum of 5 warts were injected per session at 3-week intervals until resolution or for a maximum of 4 treatments. Patients were followed up for 6 months to detect any recurrence. Data were compiled in MS Excel and analyzed with the SPSS statistical software version 20. Complete response was seen in 41/60 (68.3%), partial response in 11/60 (18.3%) and no response in 8/60 (13.3%). Average sittings required to achieve complete resolution was 3.54. Side effects like erythema, oedema, pain and flu like symptoms were seen in 10% which were either self limiting or managed with analgesics. Recurrence was seen in 8%. Intralesional MMR is effective, safer and an inexpensive treatment option for extensive and recalcitrant warts.

INTRODUCTION

Warts are benign epidermal proliferations of the skin and mucosa caused by human papilloma virus (HPV). Although spontaneous resolution occurs in most cases, patients seek treatment as they are cosmetically disfiguring and sometimes painful[1]. Conventional methods include topical keratolytics, electro coagulation, cryotherapy or laser therapy. These are associated with scarring, frequent recurrences and not suitable for the treatment of extensive and recalcitrant warts[2]. Recently immunotherapy is being tried widely for the above cases. These include measles, mumps, rubella (MMR), tuberculin purified protein derivative (PPD) and Mycobacterium vaccine[3]. MMR vaccine clears the virus and infected keratinocytes by stimulating humeral and cellmediated immunity. The use of three antigens together helps to incite a stronger immune response against HPV with the production of IL 1, IL 2, IL 4, IL 5 and TNF a. IL 1 and TNF a have been shown to have antiviral effects on HPV, through the down regulation of its gene transcription. There are hardly any studies in the literature supporting the use of intralesional MMR in multiple and recalcitrant warts[4].

Settings and Design: This is an open uncontrolled study conducted on patients attending dermatology OPD in a tertiary care centre. Period of study was 1 year (March 2022-March 2023). Sixty consecutive patients, who were newly diagnosed clinically and old patients who were advised to stop any treatment for 8 weeks, having 2 or more recalcitrant warts (persistent for a period of more than 6 months, resistant to at least 2 conventional treatment modalities) were included in the study. Exclusion criteria were age <12 years, mucosal and genital warts, pregnancy, lactation and immuno suppressive patients. Formal consent was taken from each patient, before starting therapy, after full explanation regarding the nature of disease, course and method of treatment, duration and follow up. Ethical clearance from scientific group for this study had been taken. The characteristics of the warts such as type, size, number were noted and clinical photographs were recorded at the baseline and during each follow-up visit. Using a insulin syringe with the bevel facing upward, 0.2-0.5 mL MMR vaccine (0.5 ml) was slowly injected into the base of each wart. A maximum of 5 warts were injected per session. The injections were performed at 3 weekly intervals until complete resolution or for a total of 4 sessions. Depending on the decrease in wart size, response rate was classified as complete, if they showed a complete disappearance, partial if some remained unchanged or regressed in size but not 100% and no response if there was no improvement at all. Patients were followed up for further 6 months to detect any recurrence.

Data were compiled in MS Excel and analyzed with the SPSS statistical software version 20.

RESULTS AND DISCUSSIONS

Among the 60 patients, 38 were males and 22 were females. Age of the patients ranged from 12 to 65 years, with a mean of 24 years. The duration of warts ranged from 1 month to 76 months, with a mean of 6 months. The number of warts ranged from 3 to <46. Of these, 25 (42%) patients had palmoplantar warts, 29 (48%) had common warts, 3 (5%) had periungual warts, 1 (2%) had filiform warts and 2 (3%) had plane warts. The dimensions of the lesions ranged from 1×2mm to 3.5 × 3.0 mm. Multiple non-contiguous sites were involved in 18 patients (36%). (Table 1) Complete response was seen in 41/60 (68.3%), partial response in 11/60 (18.3%) and no response in 8/60 (13.3%). Average sittings required to achieve complete resolution was 3.54 (Figures 1A-3B). Side effects like erythema, oedema, pain and induration were seen in 10% which were either self limiting or managed with analgesics. Recurrence was seen in 3 patients (8%).

Viral warts are benign proliferations of the epithelium caused by human papilloma virus (HPV) infection. Various therapeutic modalities are available for viral warts, depending on extension and severity of the disease. Treatment of viral warts can be especially difficult in extensive and recalcitrant warts and it needs multiple sittings by destructive methods such as electro cautery, which are associated with scarring and recurrences[2]. Immunotherapy induces cell mediated immunity against HPV virus leading to complete regression of both treated and distant warts with low recurrence[5].

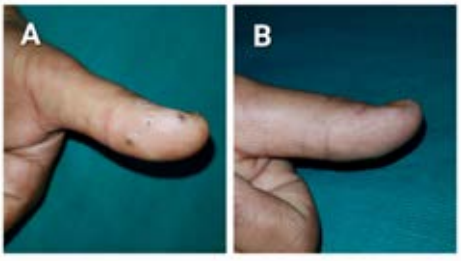

Fig. 1:A. Warts over left thumb before treatment. B. Complete clearance after 2 sitting

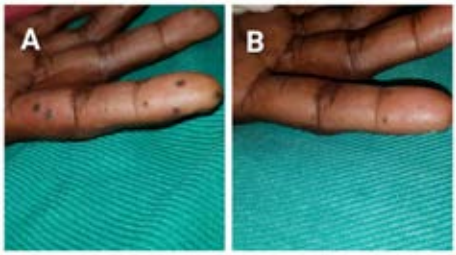

Fig. 2:A. warts over right index finger before treatment. B. Near complete clearance after 2 sittings

Table 1: Epidemiological Data

Total Patients	n = 60
Age (years): Mean±SD	24
range	12-65
Sex: Males	38 (63%)
Females	22 (36%)
Duration (months): Mean	6 months
Types: Palmoplantar	25
Common	29
Periungual	3
Filiform	1
Plane	2

Immunotherapy has been tried with BCG vaccine, MMR vaccine, purified protein derivative, bleomycin, Mycobacterium vaccine, vitamin D and Candidaantigen[6]. Several studies have been published showing the efficacy of Intralesional Injection of the Measles-Mumps-Rubella Vaccine into Resistant PalmoplantarWarts.

Mohammad Sadegh Rezaiet[7] reported successful treatment of resistant palmoplantarwartspatient withMMR vaccine.The effect of MMR on warts was thought to be due to its HPV targeted immune reaction.

Zamanian[8] used intralesional injection of MMR vaccine in patients with wart which showed mean age was20.1±10 years in thenormal saline group and 18.9±12 years in the MMR group

Nofal[9] carried out study to assess theefficacy of intralesional injection of mumps measles rubellavaccine in patients with single or multiple recalcitrant or nonrecalcitrant common warts in 135 patients. This study showedcomplete response in 57 patients (81.4%), partial response inseven patients (10%) and no response in six patients (8.6%)of the MMR group.

In a study by Mohamad[10] 100 patients with plantar warts were given MMR vaccine.

The results revealed that out of 100 patients 82% had complete clearance compared with Partialresponse was 6% and the rate of no response was12% which was significantly higher than that of control group.

Na[11] in a 2-year retrospective study of using MMR vaccinefor warts, among 136patients, 26.5% showed complete response. Adverse effects noted were pruritus, burning and pain, response was better in common warts when compared to plane warts and They opined that a better response was noted with more sessions.

CONCLUSIONS

To conclude, intralesional MMR injection is an inexpensive, cost-effective and safe option among the available treatments for multiple and recalcitrant warts. The main limitation of our study was that there was no control group. More randomized clinical trials with greater sample size and longer follow-up are required.

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