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Original Research Paper

Dermatology

MEASLES-RUBELLA VACCINE WITH ORAL ZINC VERSUS MEASLES-RUBELLA VACCINE MONOTHERAPY FOR PALMOPLANTAR WARTS

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ABSTRACT

Introduction Immunotherapy works by increasing cell mediated immunity against HPV. Some studies have shown that combining immunomodulators with different MOA can result in a synergistic effect that is slightly better than single therapy. **Aim & Objectives:** To compare the efficacy of Intralesional measles-rubella (MR) vaccine with oral zinc VS IL MR vaccine monotherapy in treatment of palmoplantar warts **Materials and methods:** In this hospital based, interventional study, 20 clinically diagnosed cases of palmoplantar warts were enrolled and randomly divided into 2 groups of 10 patients each. Group A received 0.5 ml/2 units of MR vaccine, injected into the largest wart. The dose was repeated at 2-week intervals until complete clearance or maximum of 3 doses with oral zinc for one month. Group B received only 0.5ml/2 units of MR vaccine for the same period. Follow up was every 2 weeks for 3 months after last injection. Clinical improvement assessed by physician's global assessment using visual analogue scale score. Statistical analysis done using SPSSversion21. **Results:** In group A complete clearance in 60%, excellent response in 30%and good response in 10% , while in group B complete clearance in 50%,excellent response in 30% and good response in 20%.The mean number of injection for complete clearance 3.6 in group A & 3.8 in group B. No recurrence in either group. Clinical improvement slightly better in group A than in group B. **Conclusion:** In our study we found combination of two immunomodulators for the treatment of warts is slightly better than when used individually.

KEYWORDS : MR Vaccine, Wart, Zinc

INTRODUCTION:

One of the most prevalent viral illnesses brought on by the human papillomavirus is warts (HPV). [1] HPVs are common, non-enveloped, tiny double-stranded DNA viruses with epitheliotropy. [2] Based on DNA analyses and serological identification of type-specific antibodies against HPV capsid antigens, over 150 different papillomavirus types have been identified. [3,4] Common warts, also known as verruca vulgaris, are typically brought on by Human Papillomavirus (HPV) types 1, 2, 4, 27, or 57, while plane warts are brought on by HPV types 3 or 10.[5]

Warts are horny or papillomatous-surfaced papulonodular epidermal lesions. Between the ages of 12 and 16, the incidence of cutaneous warts peaks at 7% to 10% of the overall population. [5] Warts can stay present for years before unexpectedly disappearing at any moment between a few months and a few years later. Children can experience clearance even after just a few months, with 50% clearing by one year and roughly 65%-78% clearing by two years. [5, 6] Factors including viral strain, host immunological state, extent, and duration of warts affect the rate of elimination.[7]

Warts on the skin can vary in kind and morphology. Common warts (Verruca vulgaris), plane warts, plantar warts (Superficial and Deep), Filiform warts, Digitate warts, anogenital warts, Butcher's warts, etc. are among the different forms of cutaneous warts.

Warts can spread directly through contact or indirectly through fomites. Warts are common in restrooms and swimming pools because macerated skin is more susceptible to minor abrasions and infections and thus acts as a conduit for HPV to the basal keratinocytes, the primary targets for HPV infection.[4,5] They go through a latent period of slow replication there, and as the epidermis thickens, they cause epidermal hyperplasia and hyperkeratosis.[8]

Destructive therapies are frequently connected to variable success, high recurrence, and substantial adverse effects like scarring. They are typically unpleasant, call for numerous sessions and individual treatment of each wart. [9] As a result, immunotherapy is growing in acceptance, particularly for the treatment of recalcitrant cutaneous and genital warts. Various topical, intralesional (IL), and systemic medications are among them.[10]

According to certain research, combining immunomodulators with various MOA can have a synergistic effect that is marginally superior to solo therapy. [11] It has been demonstrated that the MR vaccine's immunomodulation and immune system stimulation cause warts to disappear. As a result of the accessibility and safety of vaccines, this strategy can be applied to bigger populations. We examined the effectiveness of two immunomodulators, the intralesional MR vaccine and oral zinc acetate 10 mg/body weight, in the management of cutaneous warts due to the high frequency of warts in various groups, particularly in children, as well as the requirement for treatment. This study needs to be conducted again in the Indian population, nevertheless, in order to get more definitive results.[12,13]

AIM & OBJECTIVES:

- To compare the efficacy of Intralesional measles-rubella (MR) vaccine with oral zinc VS Intralesional measles-rubella vaccine monotherapy in treatment of palmoplantar warts.

METHODOLOGY

After receiving approval from the institutional ethical committee, a hospital-based interventional investigation was carried out. The study was carried out in the dermatology department at Kurunji Venkataramana Gowda Medical College and Hospital (KVG), Sullia, India. The study was conducted for 6 months. Twenty clinically diagnosed cases of palmoplantar warts were enrolled and randomly divided into 2 groups of 10 patients each. The trial included all individuals with warts who had not received any prior therapy with either topical or destructive methods for at least one month and were between the ages of 10 and 70. We disqualified patients with warts that had secondary infections, women who were pregnant or nursing, people with keloidal tendencies, people who had HIV and other signs of immunosuppression, and people who had a history of hypersensitivity to intralesional

injection. Patients having a history of asthma, allergic skin conditions, meningitis, or convulsions were also disqualified.

A consistent protocol was applied to all of the patients, which included taking a consent from every patient, thorough medical history and performing systemic and cutaneous examinations. Complete history comprised complete history as well as demographic information (name, age, gender, address, and occupation) (disease duration, presence or absence of distant warts, drug intake, or systemic illness).

Group A received **0.5 ml/2 units of Measles rubella vaccine (MR VACCINE)** using insulin syringe 30G (, injected into the largest wart. The dose was repeated at 2-week intervals until complete clearance or maximum of 3 doses along with **10 mg/Kg/day of oral zinc sulphate** (maximum 600 mg/day) for one month.

Group B received only measles rubella vaccine **0.5ml/2 units of MR vaccine** for the same period.

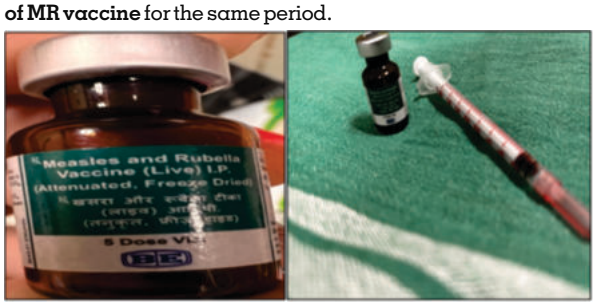

Figure 1: Measles And Rubella Vaccine Injection Vial; Insulin Syrine(30g) For Administration

Follow up was done two both group patients every 2 weeks for 3 months after last injection.

The clinical improvement was evaluated as follows:

- **Complete clearance:** All treated warts have completely vanished, and the skin's texture at the area has returned to normal.
- **Excellent response:** Fewer treated warts are still visible, and the size and number of warts have decreased.
- **Good response:** Warts have shrunk slightly in size but not in number.
- **Poor response:** Wart size and number have not changed significantly.
- **Recurrence:** Recurred during the research period

The Statistical Package for Social Sciences (SPSS), 21 version, was used to analyse the collected data. Student's t-tests for quantitative variables and χ^2 test for categorical variables were used to assess the associations. All significance tests used a 5% level of significance.

RESULTS

In this the study 10 patients were enrolled in each group and were evaluated. The mean age of group A was comparable to group B ($p>0.05$). There was no statistically significant difference between the group A and group B in terms of age, gender, and occupation. (Table 1). Table 2 shows the comparison of wart characteristics in study groups. The two groups were comparable in terms distribution and number of warts ($p>0.05$).

Table 1: Demographic and baseline parameters of study groups

Parameters		Group A	Group B	p-value
Mean age (SD)		33.5±12.9	36.83±14.5	0.594
Gender (Female/male) [n%]		4/6 0%,60%]	3/7 [30%,70%]	0.639
Occupation	Student	3 (30%)	2 (20%)	0.986
	Medical professional	3 (30%)	4 (40%)	
	Manual labor	1 (10%)	1 (10%)	
	Sedentary worker	1 (10%)	1 (10%)	
	Housewives	2 (20%)	2 (20%)	

Table 2: Comparison of characteristics of warts in study groups.

Characteristics of warts		Group A	Group B	p-value
Distribution	Palmar wart	7 (70%)	6 (60%)	0.639
	Plantar wart	3 (30%)	4 (40%)	
Number of warts	1	2 (20%)	2 (20%)	0.935
	2	6 (60%)	5 (50%)	
	3	1 (10%)	2 (20%)	
	4	1 (10%)	1 (10%)	

Clinical response was evaluated during follow-up at 1st and 3rd months. We found no statistical significance between two groups though clinically, we found group A had better response than group B. (Table 3, Figure 1 and 2).

Table 3: Clinical response in study groups

Follow-up	Response	Group A	Group B	p-value
1 month	Complete clearance	0	0	0.648
	Excellent response	1 (10%)	2 (20%)	
	Good response	7 (70%)	5 (50%)	
	No response	2 (20%)	3 (30%)	
3 months	Complete clearance	6 (60%)	5 (50%)	0.808
	Excellent response	3 (30%)	3 (30%)	
	Good response	1 (10%)	2 (20%)	
	No response	0	0	
Mean number of injections		3.6±0.9	3.8±1.2	0.678

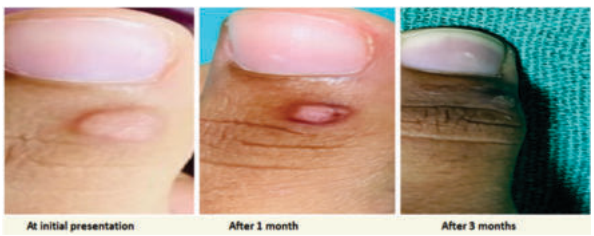

Figure 2: Clinical response in group A

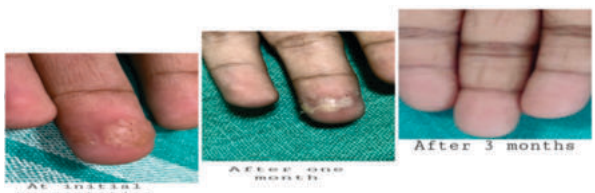

Figure 3: Clinical response in group B

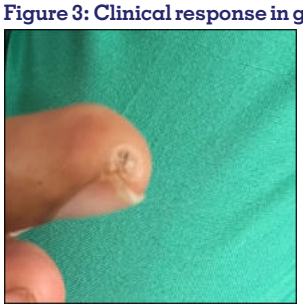

Figure 4: At initial presentation

Figure 5: After 2 months treatment with MR with Zinc

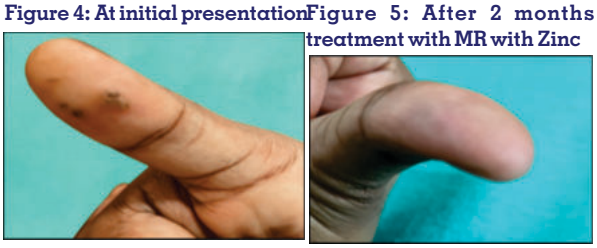

Figure 6: Clinical response in group B

No major adverse effect was noted during our study period apart from flu like symptoms pain at the site of injection and nausea , which was almost same in both the groups. No recurrence in either group during our study period time.

Figure 7: Post MR injection erythema over lesion

DISCUSSION

Destructive therapies are frequently linked to severe pain, tissue damage, and subsequent scarring, particularly over the fingers and toes. This is challenging because patients cannot completely rest these sites and are likely to be exposed to various physical and chemical agents with ongoing microtrauma. As a result, injectable therapy is a good choice for treating digital warts.[12]

Every cell in the body contains zinc, a vital element. Additionally, it is crucial for the immune system to work properly. In the past, dermatological conditions that involved immunomodulation have been treated with zinc. [14] For the treatment of resistant warts, a placebo-controlled (PC) experiment utilising oral zinc sulphate 10 mg/kg (2.5 mg/kg/d elemental zinc) once daily was attempted. [15] Compared to 0% of the placebo group, complete clearance was observed in 87% of the therapy group. Patients with resistant warts received oral zinc sulphate 10 mg/kg/d for up to 2 months in another randomised double-blind placebo-controlled (DB PC) experiment.[16]

Complete clearance rates were 76.9% (10/13) in the therapy group and 7.8% (1/13) in the placebo group after two months. Warts did not disappear asymptomatically as they would have in the course of the disease's normal progression. Instead, it was accompanied with itchiness, an initial rise in the size and number of lesions, and then a decline after two weeks. A DB PC study, however, was carried out by Lopez-Garcia et al. in 50 patients with fewer than five resistant warts. [17] They noted that neither of the patients in either group had low baseline zinc levels and showed comparable clearance rates with zinc sulphate and placebo (28% vs. 24%).

For a period of three months, Stefani et al randomized.'s double-blind experiment evaluated zinc sulphate (10 mg/kg/d) with cimetidine (35 mg/kg/d) for the treatment of resistant warts in 18 patients. They discovered that zinc was more efficient than cimetidine.[18]

This study by Abdel Aal et al. revealed that although oral zinc sulphate could have the advantages of being non-invasive, non-scarring, and having few side effects, it was not particularly effective and should not be used as a stand-alone treatment for warts.[19]

Combining two immunomodulators has not been the subject of many research for warts. In our investigation, we discovered that two immunomodulators with distinct modes of action can be used in combination to treat cutaneous warts and may produce a synergistic effect that speeds up wart clearance.

Limitations:

- A larger sample size would have yielded results with more validity.
- The study has been done in a single centre.

CONCLUSION

In our study we found combination of two immunomodulators for the treatment of warts is slightly better than when used individually. Not many studies have been done combining two immunomodulators for warts. In our study we found Two immunomodulator with different mechanism of action can be combined for treatment of cutaneous wart and may give synergistic effect leading to faster clearance of warts.

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Conflict Of Interest-None

Source Of Funding- None

Ethical Approval-Approved

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