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War on warts: Unveiling intralesional Marvels Vitamin D vs MMR Vaccine showdown

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Abstract:

Background: Cutaneous warts caused by human papillomavirus (HPV) are often resistant to conventional destructive therapies. Intralesional immunotherapy has emerged as a novel treatment modality that stimulates the host immune system to clear both local and distant lesions.

Objective: To compare the efficacy and safety of intralesional Vitamin D3 and MMR vaccine in the treatment of cutaneous warts.

Methods: This prospective interventional study was conducted at SS hospital, SSIMS, Davangere from January 2022 to July 2023. This study enrolled 50 patients with cutaneous warts, of whom 40 completed the treatment protocol. Patients were randomly divided into two groups: Group 1 received intralesional Vitamin D3 (0.2 mL), and Group 2 received intralesional MMR vaccine (0.5 mL). Injections were repeated at regular intervals.

Results: In the MMR vaccine group, 60% of patients achieved complete response, 20% showed partial response, and 20% had no response. In the Vitamin D3 group, complete response was observed in 8.33% of patients after one or two doses, and in 41.67% of patients after three to four doses. Both groups showed resolution of distant, non-injected warts. No significant adverse effects were reported in either group.

Conclusion: It is concluded that both the intralesional MMR vaccine and Vitamin D3 are effective and safe options for the treatment of cutaneous warts. MMR vaccine produced a faster and higher clearance rate, while Vitamin D3 showed a slower, dose-dependent response. Both agents induced systemic immunity capable of clearing distant lesions, making them valuable immunotherapeutic alternatives to destructive treatments.

Keywords: Warts, Intralesional, Vitamin D3, MMR vaccine

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Introduction

Warts, also known as verrucae, are harmless growths of skin caused by human papillomavirus (HPV). Warts may look ugly, sometimes hurt, and seem never to go away. Usually, cryotherapy, electrocautery, slathering the lesion with salicylic acid, or using a laser are done to remove the skin growth [1]. On the other hand, these methods can also result in recurrences, harm to nearby tissues, scarring, and

pain. Because therapies are not working as intended, immunotherapy is gaining popularity as a way to marshal the patient's immune system against SARS-CoV-2 virus-infected cells [2]. Intralesional immunotherapy is helping to improve the treatment of warts, especially when there are several difficult-to-treat lesions. By delivering the treatment, the therapies try to boost the body's immune system, causing it to

clear both the wart that is treated and any others around the body. Recently, vitamin D3 and the MMR vaccine have shown quite promising results when treated intralesionally [3].

In recent years, interest has grown regarding the connection between vitamin D3 and immunodermatology [4]. In immune cells such as T lymphocytes, dendritic cells, and macrophages, this protein is activated by its receptor (VDR). It is expected that under the influence of Vitamin D3, monocytes will become efficient macrophages, promote phagocytosis, and reduce the levels of critical pro-inflammatory cytokines such as IL-6 and TNF- α [5]. It is thought that when Vitamin D is injected into the type of tumor, it may allow the body to recognize and clear HPV-infected cells at the site of the injection. Besides, it usually causes little to no harm, except for some pain or swelling [7].

Across from MRNA is a vaccine also known as the MMR, a live vaccine intended to immunize kids against various viruses. The use of intralesional treatment relies on a mechanism called molecular mimicry and bystander activation [7]. The injection activates Th1 and Th2 types of immune response, which help promote the killing of HPV-infected cells by T-cells [8]. Some clinical studies indicate that this treatment often results in healing warts both where injected and at other untreated areas. Even so, fever, flu-like symptoms, or allergic reactions are possible and may affect each patient differently [9]. HPV can lead to warts on both the skin and mucous membranes such as the genitals, mouth, or throat. Most cases of HPV come about due to flaws in the skin's protective layer. Trauma and maceration are common causes leading to the condition. People continue to get infected, due to the presence of the remaining virus. According to some evidence, intralesional immunotherapy is significant because it has an influence on both treated and untreated sites [10].

Objective

- We sought to study and compare the efficacy, safety profile, and recurrence rates of intralesional immunotherapy modalities (vitamin D3; measles, mumps, and rubella [MMR] vaccine).
- An open-label interventional study was carried out at a dermatology outpatient department (OPD)

in a tertiary care center attached to a medical college. After receiving approval from the institutional ethics committee

Methodology

A total of 50 patients clinically diagnosed with cutaneous warts were enrolled in the study. Out of these, 40 participants completed the full treatment course and follow-up evaluations. The study was conducted following informed consent from all participants and approval from the institutional ethical review board.

Inclusion Criteria

- Patients aged between 5 and 70 years with clinically diagnosed cutaneous warts.
- Patients who had not received any treatment for warts in the preceding four weeks.
- Patients without secondary bacterial or fungal infection at the site of warts.

Exclusion Criteria

- Patients with oral or anogenital warts.
- Patients younger than 2 years or older than 70 years of age.
- Immunocompromised individuals, pregnant or lactating women.
- Patients with active bacterial or viral infections.
- Individuals with a known hypersensitivity to the intralesional agents used in the study.
- Patients unwilling to provide informed consent or to participate in the study.

Study Design and Intervention

Following enrollment and written informed consent, the participants were randomly divided into two groups. Group 1 received intralesional vitamin D3 therapy, while Group 2 received the intralesional MMR vaccine. In Group 1, the selected wart(s) were first injected with 0.2 mL of lignocaine for local anesthesia. After ensuring adequate numbness, 0.2 mL of vitamin D3 was slowly injected at the base of each wart. In Group 2, the MMR vaccine was reconstituted with sterile water, and 0.5 mL of the solution was similarly injected into the base of the wart(s). The injections were administered under sterile conditions by trained clinicians. The treatments were repeated at

regular intervals as per the study protocol until complete clearance or until the maximum number of sessions was reached.

Evaluation of Response

Clinical response to treatment was documented using standardized digital photographs taken at baseline and each subsequent follow-up visit. The final response was recorded at the end of the study period based on the visual and clinical assessment of the lesions. The outcomes were categorized as complete response, partial response, or no response. A complete response was defined as total clearance of all warts, including both the treated lesions and any distant, untreated ones. A partial response referred to a noticeable reduction in the number or size of the warts without complete resolution. No response indicated that there was no significant change in the existing lesions or the development of new warts during immunotherapy.

Adverse events and any signs of recurrence were also noted during the follow-up period.

Statistical Analysis

Data were analyzed using SPSS v21. Continuous variables, such as age, were expressed as mean $\pm$ standard deviation (SD), while categorical variables, including treatment response rates and gender distribution, were presented as frequencies and percentages. A p-value of less than 0.05 was considered statistically significant.

Results

The demographic profile of the study participants indicated that the mean age across both treatment groups Vitamin D3 and MMR vaccine was comparable, with the majority of patients falling within the 21 to 30 years age bracket.

Table 1: Age Distribution of Participants in Group-A and Group-B

Age Group (years)	Group-A (n = 20) n	%	Group-B (n = 20) n	%
≤ 20	5	25%	4	20%
21–30	7	35%	8	40%
31–40	4	20%	3	15%
41–50	3	15%	2	10%
> 50	1	5%	3	15%
Total	20	100%	20	100%

Table 2: Gender Distribution of Participants in Group-A and Group-B

Gender	Group-A (n = 20) n	%	Group-B (n = 20) n	%
Male	13	65%	12	60%
Female	7	35%	8	40%
Total	20	100%	20	100%

Among the 20 patients treated with the MMR vaccine, a complete response was observed in 12 patients, accounting for 60% of the group. Four patients (20%) demonstrated a partial response, characterized by reduction in size or number of lesions but not complete clearance. The remaining four patients (20%) exhibited no response to the intralesional therapy. These findings highlight the MMR vaccine as a moderately effective immunotherapeutic agent for wart resolution in a majority of treated individuals. In the Vitamin D3 group, a dose-dependent response

trend was observed. Complete response was noted in one patient (8.33%) after a single dose, and in another patient (8.33%) after two doses. A higher number of patients—five in total (41.67%)—required three to four doses to achieve complete clearance of both treated and distant lesions. This suggests that while Vitamin D3 may require more sessions to reach optimal efficacy, it holds potential as a robust immune-stimulating agent when administered appropriately over time.

THERAPUTIC RESPONSE (N-40)

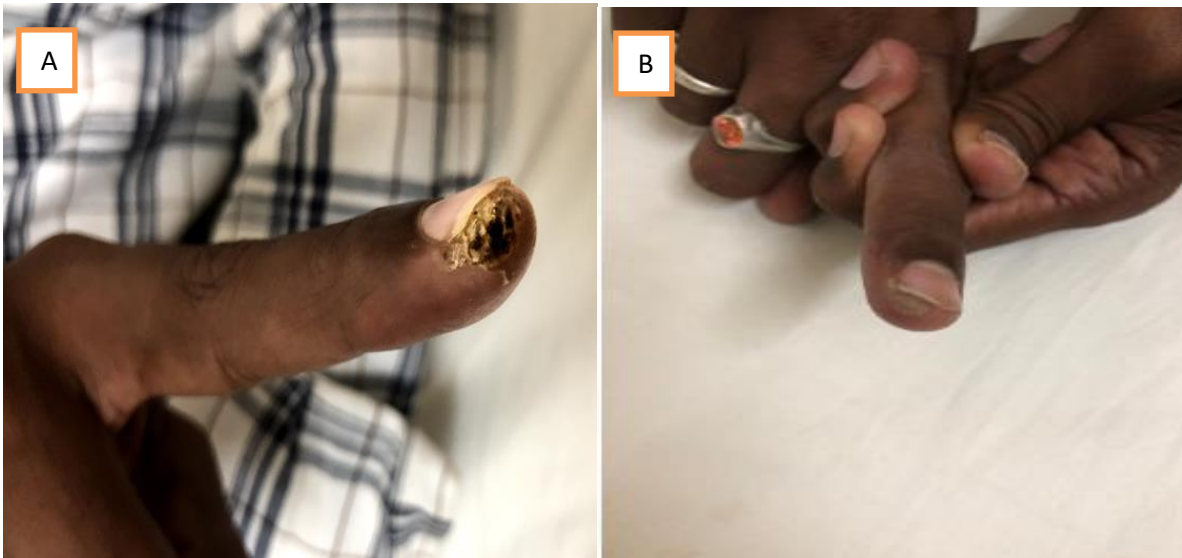
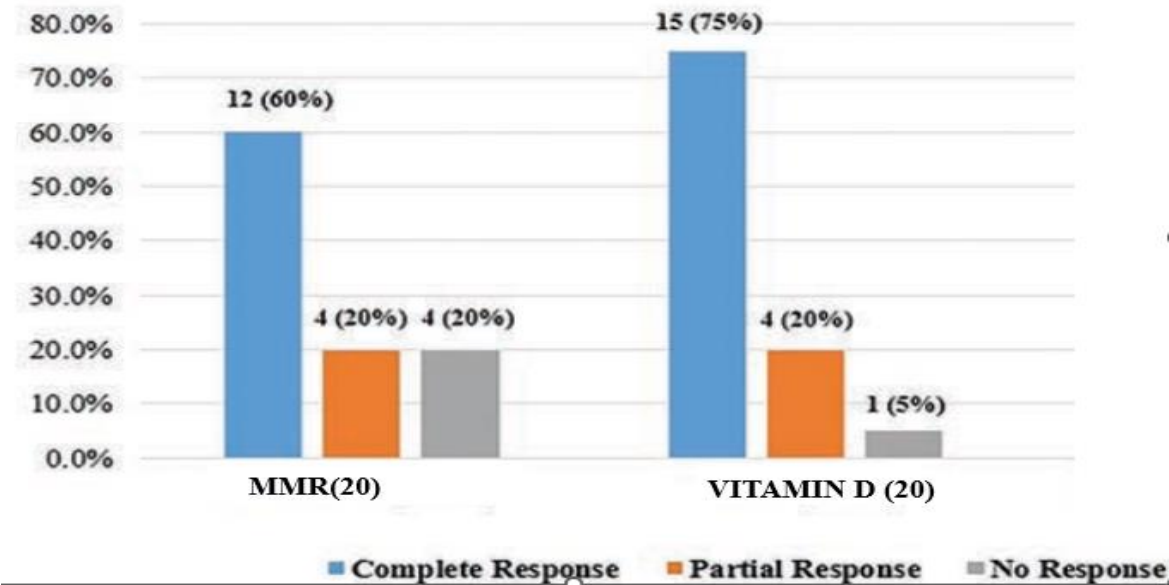


Figure 1: Clinical images showing treatment response in a patient with periungual wart.
(A) Pre-treatment photograph of the right index finger displaying a thickened, necrotic nail plate with yellow-brown discoloration and crusting, consistent with a periungual wart.
(B) Post-treatment photograph showing significant clinical improvement, with resolution of the lesion, normalization of the nail bed, and absence of crusting or active inflammation following intralesional immunotherapy.



Figure 2: Clinical response of a plantar wart to intralesional immunotherapy.

- (A) Pre-treatment image of the plantar surface of the foot showing a hyperkeratotic lesion with central black dots and surrounding callus, consistent with a classical plantar wart.**
- (B) Post-treatment image showing complete resolution of the wart, with restoration of normal skin texture and pigmentation, and no residual lesion or inflammation noted.**



Figure 3: Intralesional therapy outcome in a patient with periungual wart involving the little finger. (A)

- Pre-treatment image showing a large, thickened, verrucous lesion encircling the nail of the right fifth finger, characteristic of an extensive periungual wart.**
- (B) Post-treatment image demonstrating complete clinical resolution of the wart with re-epithelialization of the affected area, minimal residual pigmentation, and preserved nail integrity.**



Figure 4: Bilateral plantar wart clearance following intralesional immunotherapy.

- (A) Pre-treatment image showing multiple well-defined, hyperkeratotic verrucous lesions on the pressure points of both soles, consistent with bilateral plantar warts.**
- (B) Post-treatment image demonstrating complete clinical resolution with reconstitution of normal plantar skin architecture and absence of wart recurrence or residual scarring.**

Discussion

It is difficult to treat many or stubborn warts when conventional techniques are ineffective. Immunotherapy given straight into the wart allows the immune system to target HPV-infected cells and leads to their destruction. Our study looked at how effective and responsive intralesional Vitamin D3 and vaccines that target MMR are in stimulating cellular Immune responses. Vitamin D3 is able to affect the immune system through the Vitamin D receptor (VDR), present in T cells, dendritic cells, and macrophages [11]. Altogether, this explains why Vitamin D3 acts as an important immunomodulator by lessening IL-6, IL-8, TNF- α , and IFN- γ production when regulated by the VDR. Evidence from this study demonstrates that out of seventeen cases, one patient improved with one dose, another one with two doses, and five patients recovered after three to four doses [12]. This finding suggests that Vitamin D3 becomes more effective in therapy after several exposures to the local immune system. The MMR vaccine ensures that the immune system responds both from cells and bodily fluids [13]. By exposing the infection to the immune system inside the lesion, the vaccine is believed to induce a strong Th1 immune response, resulting in more IL-2 and IFN- γ , which activate the body's cytotoxic T cells to fight HPV-infected cells. Sixty percent of the

patients got rid of all their warts after receiving the MMR vaccine, 20% of them responded partially, and 20% did not respond at all to the vaccine [14]. These findings are consistent with those of Raghukumar et al., indicating that five injections of MMR via the intralesional approach usually result in clearing the lesions and distant parts not treated with injections [15]. Both of these agents were safe, as no major adverse impacts were observed, which is why they are preferred over cryotherapy and electrocautery [16]. Because it helps resolve both injected and non-injected warts, intralesional immunotherapy is considered valuable for patients with multiple or widespread warts [17]. Even with these good results, there are some things that we must consider. The research included only 40 participants, out of the original 50. Since the time covered was short, the risk of relapse long after the surgery could not be measured. Long-term studies on bigger groups over time are required to compare the success and safety. Also, determining immunophenotype could be useful for selecting treatments in the future.

Conclusion

It is concluded that intralesional immunotherapy represents a safe, effective, and patient-friendly approach to the treatment of cutaneous warts. In this

study, both Vitamin D3 and MMR vaccine showed clinical efficacy, but with differing response dynamics. As per the present study, the maximum number of patients showing complete response belonged to the VITAMIN D3 group (15 of 20, 75%), compared to the MMR vaccine (12 of 20, 65%). Adverse effects were reported by the majority of patients in the vitamin D3 group. Intralesional Vitamin D and MMR vaccine exhibit promising wart treatment outcomes. Vitamin D demonstrated higher complete response and lower recurrence rates, suggesting superior efficacy. These findings underscore the potential of intralesional immunotherapy, particularly Vitamin D, in wart management. Further research is needed for optimized protocols.

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