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THE EFFICACY OF INTRALESIONAL VITAMIN D3 VERSUS INTRALESIONAL MEASLES, MUMPS AND RUBELLA VACCINE FOR THE MANAGEMENT OF WARTS: A COMPARATIVE STUDY.

Dermatology

Dr. Ramya B G Assistant Professor, Department Of Dermatology Navodaya Medical College Hospital And Research Centre, Raichur, Karnataka.

Dr. Snigdha Kodali Junior Resident, Department Of Dermatology Navodaya Medical College Hospital And Research Centre, Raichur, Karnataka.

Dr. Reynold Mangsatabam* Junior Resident, Department Of Dermatology Navodaya Medical College Hospital And Research Centre, Raichur, Karnataka. *Corresponding Author

Dr. Kallappa C Herakal Professor And Head, Department Of Dermatology Navodaya Medical College Hospital And Research Centre, Raichur, Karnataka.

ABSTRACT

Background: There are numerous documented therapeutic methods for the treatment of warts; nevertheless, no single approach is completely effective. Destructive modalities are associated with pain, scarring, and the possibility of recurrence. In order to address these issues, immunotherapy was introduced. **Aims And Objectives:** To compare the efficacy of intralesional MMR vaccine vs vitamin D in treatment of warts. **Materials And Methods:** In a prospective hospital based comparative study, 90 patients with warts were split randomly into equal groups, Group A and Group B. Group A received intralesional vitamin D and group B received intralesional MMR vaccine into the largest wart. The procedure was repeated every 2 weeks, requiring about 4-5 sittings or until complete clearance whichever was earlier. **Results:** All patients showed positive responses in group A. 41 out of 45 (91.1%) patients showed complete response, whereas 4(8.9%) showed partial response. In Group B, 33 out of 45 patients (73.3%) showed a complete response, 9(20%) patients showed partial response and 3(6.7%) showed no response. **Conclusion:** In addition to being safe and effective, intralesional MMR vaccine and vitamin D3 are also well tolerated by patients. However, vitamin3 D is more cost effective.

KEYWORDS

Immunotherapy, Warts, Intralesional, Vitamin D3, MMR vaccine.

INTRODUCTION

Warts or verrucae are benign tumours of the skin and mucosa caused by human papillomavirus (HPV), seen as distinctly defined hyperkeratotic protrusions. HPV can infect both keratinized(skin) and non-keratinized(mucosa) epithelia [1]. Some warts tend to regress spontaneously, while others persist and spread to other parts of the body [2].

Warts are often treated with a variety of ablative and destructive procedures. These traditional methods are associated with high recurrence, inadequate response and may need to treat each wart [3]. Consequently, immunotherapy gained significance. It functions primarily by boosting cell-mediated immunity (CMI) to clear warts [4]. The sensitization it produces may cause distant, not injected wart to disappear. Measles, mumps, rubella (MMR) vaccine, purified protein derivative, intralesional vitamin D3, candida antigen and mycobacterium vaccine are some of the antigens used in immunotherapy [4].

MATERIALS AND METHODS

The study was conducted in the Department of Dermatology of our institute for a duration of 6 months from June to December 2023. Ethical Committee approval was obtained, and 90 patients were included for this prospective study.

Patients with cutaneous warts (common, plantar or periungual warts) who have not received any therapy 4 weeks prior to the injection were selected. Patients were counselled about the pros and cons, potential outcomes. Written informed consent was obtained. Patients aged between 5 to 50 years were included.

The following patients were excluded from the study [2] –

- Patients with concurrent systemic illness, secondary infections
- Patients with genital warts
- Patients with allergic reaction to vitamin D3 injection or any component of MMR vaccine
- Patients with history of asthma or allergic skin disorders, keloidal tendency
- Pregnant and lactating women
- Patients on immunosuppressive drugs and immunocompromised patients

Every subject underwent a thorough history taking, comprehensive general and dermatological examination. At the initial visit, baseline assessment was done and demographic details like age, sex were recorded. Photographs were taken at initial and at each subsequent visit.

The patients were then randomly allocated into two groups, Group A and Group B, with 45 patients in each group. Participants in Group A received vitamin D3 injection and those in Group B received MMR vaccine.

Injection vitamin D3, available in vials containing 6,00,000 IU of cholecalciferol in 1 ml (15mg/ml) was used in the study. In each session, a maximum of two large warts were selected to be injected. Initially, 0.2 ml of lignocaine was injected into the targeted warts using a 27-gauge insulin syringe and 0.2 ml of vitamin D3 was then injected into the base of each wart after a few minutes. The injections were repeated every 2 weeks until complete clearance or for maximum of 4 injections whichever was earlier [3]. The patients were followed up for 6 months after complete clearance to document recurrence if any.

Patients in group B were administered MMR vaccine (freeze dried form). It was reconstituted with 0.5 ml distilled water and 0.3-0.5 ml of the vaccine was injected into the base of the largest wart. About 4 sessions were required for the procedure, which was repeated every 2 weeks [2]. Following each sitting, the patient was evaluated for immediate and late side effects like pain at site of injection, erythema, oedema, fever, or flu like symptoms.

In addition to comparing the photos, response was documented based on decrease in size of the wart. Response to treatment was graded as follows [5] –

(i) Complete response: Complete resolution of both treated and remote warts
(ii) Partial response: 50-99% reduction in size of warts
(iii) No response: 0-50% reduction in size of warts

RESULTS

A total of 90 patients were included in the study. Patients in Group A who received intralesional Vitamin D injection were between 5-50 years having a mean age of 26.11±9.25 Standard Deviation (SD). The patients of group B, who received MMR vaccine were aged between 15-45 years with a mean age of 31.58±7.93 (SD). Both groups had a higher number of female patients. In Group A, the male to female ratio was 0.8:1, while in Group B, it was 0.88:1.

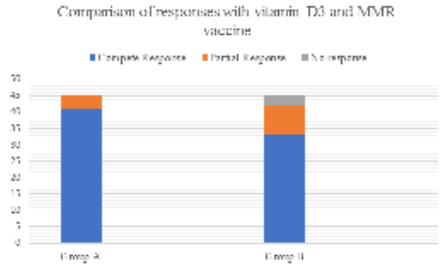
Amongst group A, 20(44.4%) of patients presented with verruca vulgaris, followed by 14(31.1%) patients with palmoplantar warts, 6(13.3%) with Mixed warts and lastly 5(11.1%) with periungual warts. Similarly in group B, 22(48.8%) had verruca vulgaris,17(37.7%) with palmoplantar warts, 4(8.8%) mixed warts and 2(4.4%) with periungual warts.

In group A, all patients showed positive responses. 41 out of 45 (91.1%) patients showed complete response, which was indicated by the presence of normal skin markings, 4(8.9%) showed partial response. In Group B, 33 out of 45 patients (73.3%) showed a complete response, 9(20%) patients showed partial response whereas 3(6.7%) patients showed no response. [Graph 1]

In group A, 20 (44.4%) patients showed complete resolution of wart after 2 injections, 12(26.7%) patients showed resolution after 3 injections, 8(17.8%) after 1 injection, and among the 5(11.1%) patients received 4 injections, 4 patients exhibited partial response. In group B, 4 sessions were given to 23(51.1%) patients, among which 11 had complete clearance of wart, 9 patients showed partial response and 3 patients were classified as no response. Additionally, 14(31.1%) patients showed clearance after 3 sessions, 6(13.3%) showed clearance after 2 sessions and 2(4.5%) patients improved after 1 session.

In group A, adverse effects were seen in 26(57.8%) of the patients overall, out of which 25 patients had localized pain and swelling at the site of injection, which resolved spontaneously. Hyperpigmentation was noted in 1 patient. In group B, overall, 12(26.7%) out of 45 patients showed adverse effect. Pain at the site of injection was seen in 9(20%) patients whereas 3(6.7%) patients developed fever which subsided within 12 hours with symptomatic treatment.

No recurrence was noted in both the groups after 6 months of follow up.



Graph 1: Comparison of responses with vitamin D3 and PPD

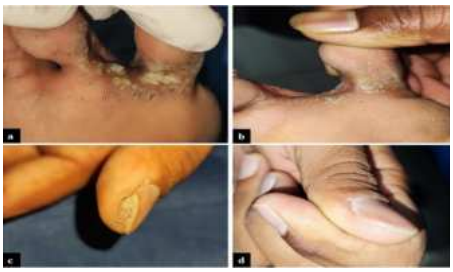


Figure 1- Response of warts to intralesional vitamin D injection. (a)plantar warts before injection (b) following 3 injections. (c) subungual wart before injection (d) after 2 injections.

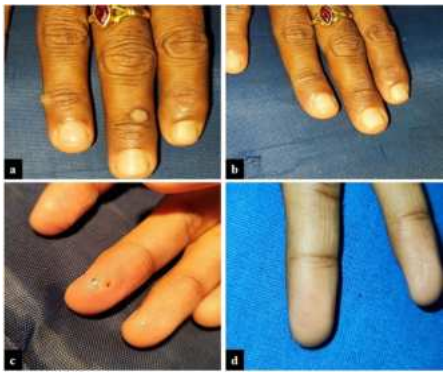


Figure 2- Response to Intralesional MMR injection. (a) Before injection and (b) After 3 injections. (c) before injection (d) after 2 injections.

DISCUSSION

Warts result from complex interactions between the host and pathogenic agents. In cases of strong immune systems, warts may vanish spontaneously without leaving visible evidence. However, they can recur despite treatment efforts. Warts are treated with ablative procedures like electrocauterization, cryotherapy, and surgical excision. Immunotherapy is preferred as it acts on the immune system, while other options focus on local clearance.

The exact mechanism of immunotherapy remains incompletely understood, but it is believed that injecting HPV-infected tissue triggers a strong nonspecific proinflammatory signal, attracting antigen-presenting cells [6]. Vitamin D plays a role in regulating cell proliferation and keratinocyte differentiation, inhibiting hyperkeratosis by suppressing cell replication. It also releases IL21, IL42, IFN-γ, and TNF-α, exerting an immunomodulatory effect. Additionally, TLR activation leads to upregulation of human macrophages and expression of VDR and VD1-hydroxylase genes, resulting in antimicrobial peptide production [7].

The MMR vaccine stimulates mononuclear cell proliferation in peripheral blood, triggering a delayed TH1-mediated response. This leads to the release of INFγ, IL2, and IL4, activating cytotoxic T cells that release TNFα and IL1. Consequently, both local and remote wart tissue are destroyed [7].

In Group A (Vitamin D), 91.1% of patients exhibited a complete response, while 8.9% demonstrated a partial response. Interestingly, these findings align with a study conducted by Raghukumar et al [6], where 90% of patients achieved a complete response, 6.66% showed a partial response, and 3.33% had no response. However, in our study, all participants exhibited a favorable response to the treatment. Mohta A et al [4] observed complete clearance in 77.4% of patients, partial clearance in 16.1%, and no response in 6.5%. Similar results were reported by Jartarkar SR et al [8] and Kavya et al [3].

In our present study, we observed a higher clearance rate compared to the findings reported by Jain S et al [9]. In their study, 60% of patients exhibited a complete response, 20% showed a partial response, and 20% had no response. These results align with the study conducted by Babu TN et al [10], where 65% showed a complete response, 15% demonstrated a moderate response, 10% had a partial response, and 10% showed no response.

In group B(MMR), patients 73.3% showed a complete response, 20% partial response and 6.7% showed no response which is lower than the results of previous studies. Our results closely resemble the results of Zamanian et al [11] where complete cure was seen in 75%, relative cure in 16.7%, no cure in 8.3% patients. Jain S et al [9], Mittal N et al [2] showed similar results with complete cure of 75% and 76% respectively. Jartarkar SR et al [8] observed complete resolution in 70% patient. Chauhan PS et al [12] observed better results with 82.4% complete clearance and 17.6% partial response. Mohta A et al [4] observed, 87.8% complete response, partial clearance in two (6.1%) patients, and no response in two (6.1%) patients.

In group A, maximum number of patients i.e., 20 (44.4%) showed complete resolution of wart with only 2 sessions. Only 5 patients required 4 sessions, of these 4 had partial response to the treatment. Most patients (23 or 51.1%) in group B needed 4 sessions, among which 3 patients did not respond to treatment and 9 showed partial response. Remarkably, 2 patients responded after only 1 session of MMR.

Most patients in group A (57.8%) experienced some mild, self-limiting adverse effects, such as pain and swelling at the injection site. Only 1 patient had hyperpigmentation at the injection site. All patients felt some pain and discomfort during the injection, which was likely due to the oily base of the Vitamin D injection [4]. These findings are consistent with other studies by Mittal N et al [2], Raghukumar S et al [6], Jain S et al [9], and Mohta A et al [4], who also reported itching at the injection site. Shaldoum DR et al [13] reported additional adverse effects, namely nail dystrophy and mild vasovagal symptoms, which we did not observe in our study.

Pain at the injection site was the most frequent adverse effect (20%) in group B, which resolved spontaneously. Fever was also reported by 3 patients, which lasted for 12 hours. These findings were consistent with previous studies by Mohta A et al [4], Dhope A et al [14], Jartarkar SR et al [8], and Mittal N et al [2], additionally observed 2 cases of numbness at injection site. Shaldoum DR et al [13] observed similar results, but with a higher incidence of adverse effects. Jain S et al [9] also reported itching at injection site, and one case of exacerbation of acute urticaria.

Adverse effects were more in Group A compared to Group B. All patients of Group A reported pain and discomfort during injection, despite prior lignocaine infiltration. Pain and swelling at the injection site were common in Group A, while Group B predominantly experienced pain at the injection site. Additionally, Group A had one case of hyperpigmentation, whereas Group B had three patients with post-MMR injection fever that resolved spontaneously

CONCLUSION

While the overall frequency of adverse effects, such as pain and swelling, was higher in Group A (Vitamin D), it's noteworthy that these effects were self-limiting. Moreover, clearance rates were better in Group A compared to Group B. Additionally, considering the cost of treatment, intralesional vitamin D therapy emerges as a more cost-effective option.

REFERENCES

[1] Sterling J C. Viral Infections. In Griffiths CE, Berker J, Bleiker T, Chalmers R, Creamer D, editors Rook's Textbook of Dermatology, 9th ed, Blackwell Science, 2016; 25: P25.43-62.

[2] Mittal N, Malhotra S, Singh NR, Relative efficacy and safety of intralesional measles mumps rubella vaccine (MMR) and intralesional vitamin D in multiple and recalcitrant verrucae vulgaris. IP Indian J Clin Exp Dermatol 2021;7(2):158-163.

[3] Kavya M, Shashikumar BM, Harish MR, Shweta BP. Safety and Efficacy of Intralesional Vitamin D3 in Cutaneous Warts: An Open Uncontrolled Trial. J Cutan Aesthet Surg. 2017 Apr-Jun;10(2):90-94.

[4] Mohta A, Kushwaha RK, Agrawal A, Sharma MK, Gautam U, Jain SK. Evaluation of the Efficacy of Intralesional Measles, Mumps, and Rubella Vaccine with Intralesional Vitamin D3 as Immunotherapies in the Treatment of Recalcitrant Cutaneous Warts in Adult- A Randomized Placebo-Controlled Study. Indian Dermatol Online J. 2021 Nov 22;12(6):879-887.

[5] Mohta A, Kushwaha RK, Gautam U, Sharma P, Nyati A, Jain SK. A comparative study of the efficacy and safety of intralesional measles, mumps, and rubella vaccine versus intralesional vitamin D3 for the treatment of warts in children. Pediatr Dermatol. 2020 Sep;37(5):853-859.

[6] Raghukumar S, Ravikumar BC, Vinay KN, Suresh MR, Aggarwal A, Yashovardhana DP. Intralesional Vitamin D3 Injection in the Treatment of Recalcitrant Warts: A Novel Proposition. J Cutan Med Surg. 2017 Jul/Aug;21(4):320-24.

[7] Babu TN, Sneha K, Ramadevi B, Pujitha BB, Ramadas K. Comparative study on the eff ectiveness of intralesional Measles, Mumps, and Rubella vaccine and intralesional vitamin D3 injection in the treatment of verruca. Our Dermatol Online. 2023;14(1):6-10.

[8] Jartarkar SR, Kadnur M, Mamatha P, Mishra SS, Spoorthy B. A comparative study of therapeutic efficacy of intralesional measles, mumps, and rubella vaccine and intralesional Vitamin D3 in the treatment of recurrent warts. J Dermatol Dermatol Surg 2021;25:14-7.

[9] Jain S, Marfatia YS. A Comparative Study of Intralesional Vitamin D3, Measles Mumps Rubella Vaccine, and Tuberculin Purified Protein Derivative in the Treatment of Recalcitrant Warts: An Approach to Solve a Therapeutic Conundrum. J Clin Aesthet Dermatol. 2021 Nov;14(11):26-34.

[10] Babu TN, Sneha K, Ramadevi B, Pujitha BB, Ramadas K. Comparative study on the eff ectiveness of intralesional Measles, Mumps, and Rubella vaccine and intralesional vitamin D3 injection in the treatment of verruca. Our Dermatol Online. 2023;14(1):6-10.

[11] Zamanian A, Mobasher P, Jazi GA. Efficacy of intralesional injection of mumps-measles-rubella vaccine in patients with wart. Adv Biomed Res. 2014 Mar 31;3:107.

[12] Chauhan PS, Mahajan VK, Mehta KS, Rawat R, Sharma V. The Efficacy and Safety of Intralesional Immunotherapy with Measles, Mumps, Rubella Virus Vaccine for the Treatment of Common Warts in Adults. Indian Dermatol Online J. 2019 Jan-Feb;10(1):19-26.

[13] Shaldoum DR, Hassan GFR, El Maadawy EH, El-Maghraby GM. Comparative clinical study of the efficacy of intralesional MMR vaccine vs intralesional vitamin D injection in treatment of warts. J Cosmet Dermatol. 2020;00:1-8.

[14] Dhope A, Madke B, Singh AL. Effect of measles mumps rubella vaccine in treatment of common warts. Indian J Drugs Dermatol 2017;3:14-9.