

Efficacy of intralesional vitamin D3 injection in the treatment of cutaneous warts

Gotham Bhavika¹, Madhavi Latha Midde^{2*}, Praveena Thiriveedhi³

¹PG, ²Professor & HOD, ³Associate Professor, Department Of DVL, Santhiram Medical College and General Hospital, Nandyal, INDIA.

Email: bhavikagotham595@gmail.com

Abstract

Background: Cutaneous wart caused by human papilloma virus, is one of the most common presenting complaints among the patients attending DVL OPD. Even though various modalities of treatment are available, most of them are destructive in nature such as cryotherapy, photodynamic therapy, pulse dye lasers, kerolytic agents. Various topical and intralesional agents are used as immunotherapy of warts such as imiquimod, BCG, MMR vaccines, candida antigens, trichophyton skin antigens. Similarly, vitamin D₃ is an effective and recent immunotherapy used in the treatment of warts. **Objectives:** To evaluate the efficacy and safety profile of intralesional vitamin D₃ injection in the treatment of cutaneous warts. **Methods:** A Hospital based prospective interventional study was conducted from June 2021 to May 2022 among patients with cutaneous warts attending DVL OPD at our Hospital. A detailed history was recorded and thorough physical examination was done. Clinical photographs were taken during every visit. Vitamin D₃ (0.2-0.5 ml, 15 mg/ml) was injected intralesionally at the base of warts after applying topical anaesthesia. The injections were repeated at 2 weekly intervals until complete clearance or for a maximum of 4 injections. Patients were followed up for a maximum period of 4 months. **Results:** 22 patients with cutaneous warts (13 males and 9 females) were included in our study. Out of 22 patients, 19 patients had multiple warts and 3 patients had single wart. Of these, 16(72.73%) patients showed complete response, 5(22.7%) patients showed moderate response and 1(4.54%) patient showed mild response. None of them had any adverse effects except for the pain during injection. **Limitations:** small sample size and lack of control group. **Conclusion:** Intralesional vitamin D₃ injection is a safe and effective modality of treatment for cutaneous warts. **Keywords:** cutaneous warts, immunotherapy, vitamin D₃.

*Address for Correspondence:

Dr Madhavi Latha Midde, Professor & HOD, Department Of DVL, Santhiram Medical College And General Hospital, Nandyal, INDIA.

Email: bhavikagotham595@gmail.com

Received Date: 01/07/2022 Revised Date: 11/08/2022 Accepted Date: 18/09/2022

This work is licensed under a [Creative Commons Attribution-NonCommercial 4.0 International License](https://creativecommons.org/licenses/by-nc/4.0/). 

Access this article online

Quick Response Code:	Website: www.medpulse.in
	DOI: https://doi.org/10.26611/10212333

INTRODUCTION

Warts caused by Human Papilloma Virus are one of the most common skin conditions worldwide.¹⁻³ They are more common among children but can occur at any age^[1-3]. Despite of the availability of various modalities of treatment, no single therapy has been shown to completely cure the warts in every patient making it a therapeutic challenge for the treating physician.²⁻⁷ Most of the conventional treatments available are destructive in

nature which include cryotherapy, electrocautery, topical keratolytics, lasers etc.¹⁻¹⁰ All these methods are time consuming, needs multiple sessions in case of multiple warts, often associated with scarring, recurrences and do not clear the untreated or distant warts.⁴⁻¹² Immunotherapy is an emerging modality of treatment for warts which acts by enhancing the host immunity and includes methods like intralesional injection of candida albicans antigen, Measles, Mumps, Rubella vaccine, purified protein derivative (tuberculin) and vitamin D₃.⁴⁻¹² In this article, we discuss the effectiveness and safety profile of intralesional vitamin D₃ injection in the treatment of cutaneous Warts.⁴⁻¹²

MATERIALS AND METHODS

STUDY DESIGN

A Hospital based prospective interventional study was conducted among 22 patients with cutaneous warts attending DVL OPD at Santhiram Medical College and General Hospital, Nandyal, from June 2021 to May 2022.

Patients of both the sexes between the age group of 12-70 yrs, who were clinically diagnosed with single or multiple cutaneous warts (without prior history of treatment for warts) and willing to participate were enrolled in the study.

Exclusion criteria included systemic or local inflammation/ infection, pregnant and lactating women, immunosuppression including HIV and known hypersensitivity to vitamin D3.

MATERIALS

(As shown in the Figure 1)

1. Topical anaesthesia (lignocaine 25mg/gm + prilocaine 25mg/gm).
2. Micropore plaster for occlusion of topical anaesthesia.
3. 26 G needle and tuberculin syringe.
4. Vitamin d3 injection ampoule containing 6 lakhs IU (15mg/ml)

METHODOLOGY

After taking written informed consent a detailed history was recorded and a thorough physical examination was done for each patient. Clinical photographs were taken during every visit. Under aseptic precautions, after applying topical anaesthesia (lignocaine 25mg/gm + prilocaine 25mg/gm) for 45 minutes under occlusion, 0.2 – 0.5 ml of Vitamin D3 (15 mg/ml) was injected intralesionally at the base of each wart for a maximum of 5 warts in each session. (As shown in the Figure 2) Injections were repeated at 2 weekly intervals until complete clearance or for a maximum of 4 injections. Patients were followed up for a maximum period of 4 months and evaluated for clinical improvement, adverse effects and recurrences.

RESULTS

Out of 22 patients, 13(59.1%) were males and 9(40.9%) were females, with slight male preponderance. Majority of the patients were from the age group of 20- 30 years, the average age being 30.36 years. Duration of the disease ranged from 6 – 12 months in majority of them (45.5%). Among these 22 patients, most of the patients were asymptomatic (13) followed by the patients with symptoms like pain (8) and pruritus (1). Three patients (13.63%) had single wart, fourteen (63.63%) had two to five, three (13.63%) had six to ten, and two (9.1%) had more than ten warts. Three (13.63%) of the 22 patients had a prior history of similar lesions. 3 out of 22 patients had a positive family history, which accounted for 13.63%.



Figure 1

1. Topical anaesthesia- (lignocaine 25mg/gm + prilocaine 25mg/gm)
2. Micropore plaster- (for occlusion of topical anaesthesia)
3. Vitamin d3 injection ampoule- 6 lakhs IU(15mg/ml)
4. 26 G needle and tuberculin syringe



Figure 2: Injection of Vitamin D3 (15 mg/ml) intralesionally at the base of wart using 26 G needle and tuberculin syringe.

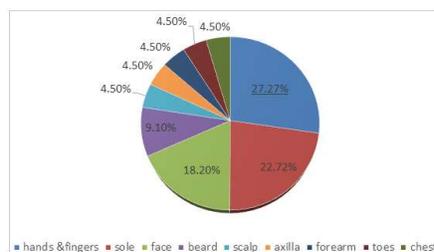


Figure 3

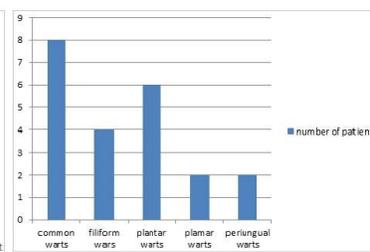


Figure 4

Figure 3: Pie chart showing percentage of distribution of warts in different sites; **Figure 4:** Bar diagram showing distribution of patients based on the type of warts

CLINICAL RESPONSE

Based on the reduction in size and number of warts, clinical response was graded as complete response (100% clearance of injected warts), moderate response (50 % to <100% reduction in size and number) and mild response (<50% reduction in size and number). The clinical response in our study is shown in Table 1.

Table 1

Clinical response	No. of patients (%)
Complete clearance (100%)	16 (72.73%)
Moderate response (50 % to <100%)	5 (22.7%)
Mild response (<50 %)	1 (4.54%)

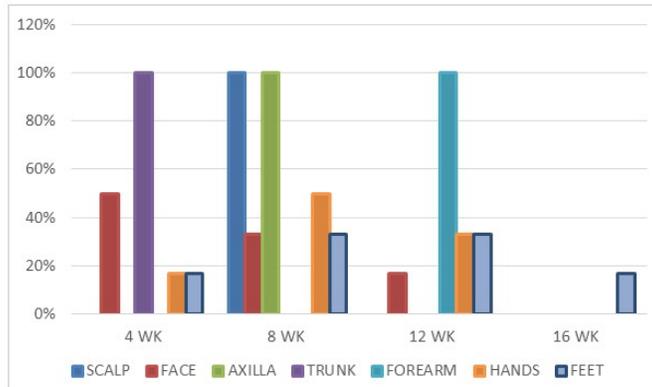


Figure 5: Column diagram showing percentage of improvement in each site at 4 weekly interval

Out of 22 patients, only 6 patients had distant warts, among them 3 patients (50 %) showed clearance of distant warts. Six patients complained of pain at the injection site among which only one patient needed management with analgesics. One patient developed swelling at the injection site one day after the injection which resolved spontaneously within 4 days. Percentage distribution of complications were as shown in the Table 2.

Table 2

Complications	No. of patients (%)
NIL	15 (68.2%)
PAIN	6(27.27%)
SWELLING	1(4.5%)

None of the 22 patients had a recurrence during the maximum follow up period of 4 months.



Figure 6: (A) Palmar wart before treatment (B) complete clearance after 2 injections



Figure 7: (A) Multiple warts before treatment (B) Moderate clearance after 4 injections



Figure 8: (A) Multiple warts before treatment (B) Mild clearance after 4 injections

DISCUSSION

Since viremia does not occur during the pathogenesis of warts, the virus escapes the systemic immune response. Immunotherapy act by boosting the host immune system against HPV virus leading to clearance of both treated and distant warts with less chance of recurrence and scarring. In our study, we used intralesional Vitamin D₃ which is one of the newer immunotherapies available for treating warts. Although the exact mechanism of action of Vitamin D in clearance of warts is not known, several studies suggest the following effects of vitamin D₃, it controls cell proliferation and differentiation, inhibits IL-6, IL-8, TNF- α and TNF- γ (**Immunomodulatory effect**) and induces antimicrobial peptide expression (**Immunoregulatory effect**) acts via VDR-dependent pathway by acting upon Vitamin D Receptors present on keratinocytes, melanocytes, fibroblasts, and immune system cells of the skin. In a study by Kavya *et al.* involving 42 patients with multiple warts, 33 (78.57%) patients showed complete response, 6 patients (14.28%) showed moderate response, and three patients (7.14%) showed mild response. Raghukumar *et al.* reported complete clearance in 54 (90%) patients, partial response in 4 (6.66%) patients, and no response in 2 (3.33) patients from their study involving 60 patients. Aktas *et al.*, used intralesional vitamin D₃ for plantar warts in 20 patients and reported complete clearance in 80% of the patients at the end of 8 weeks. In our study, out of 22 patients 16 patients (72.73%) showed complete response, 5 (22.7%) showed moderate response and 1 patient (4.54%) showed mild response.

CONCLUSION

In the present clinical study, we found that intralesional vitamin D₃ injection is an inexpensive, safe and effective treatment modality for cutaneous warts. It is a simple and easy OPD procedure and also a better treatment option than conventional modalities for treating multiple and

distant warts with minimal adverse effects. As our study was limited by small sample size and lack of control group, large randomized placebo controlled studies need to be conducted in future to confirm the efficacy of intralesional vitamin D₃ in treating cutaneous warts.

REFERENCES

1. K A Seetharam. Viral infections. IADVL Textbook Of Dermatology. 4th ed.2013 mar:vol 1 :595-607.
2. Jane C Sterling. Viral infections. Rooks Textbook Of Dermatology. 9th ed.2016 : vol 1:25.43-25.63.
3. Kang S, Amagai M, Margolis D. Fitzpatrick's Dermatology. 9th ed. New York: McGraw-Hill Education; 2019.
4. Aktaş H, Ergin C, Demir B, Ekiz Ö. Intralesional Vitamin D Injection May Be an Effective Treatment Option for Warts. J Cutan Med Surg. 2016 Mar-Apr;20(2):118-22. doi: 10.1177/1203475415602841. Epub 2015 Aug 20. PMID: 26294740.
5. Banoth S. Evaluation of therapeutic effectiveness of vitamin D₃ injections in common warts in a tertiary care centre. Int J Res Dermatol 2019;5:462-5.
6. Abdel-Azim ES, Abdel-Aziz RT, Ragaie MH, Mohamed EA. Clinical and dermoscopic evaluation of intralesional vitamin D₃ in treatment of cutaneous warts: a placebo-controlled study. J Egypt Womens Dermatol Soc 2020;17:6-12.
7. 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. doi: 10.4103/JCAS.JCAS_82_16. PMID: 28852295; PMCID: PMC5561717.
8. 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):320-324. doi:10.1177/1203475417704180. Epub 2017 Apr 6. PMID: 28384048.
9. Nofal, A., Adel, L., Fawzy, M., Elkholy, B. M. (2022). Intralesional immunotherapy for multiple recalcitrant plantar warts: Candida antigen is superior to intralesional purified protein derivative. Dermatologic Therapy, 6(35). <https://doi.org/10.1111/dth.15440>.
10. Kareem IMA, Ibrahim IM, Mohammed SFF, Ahmed AA-B. Effectiveness of intralesional vitamin D₃ injection in the treatment of common warts: Single-blinded placebo-controlled study. Dermatologic Therapy. 2019;32:e12882.
11. Gamil H, Elgharib I, Nofal A, Abd-Elaziz T. Intralesional immunotherapy of plantar warts: Report of a new antigen combination. J Am Acad Dermatol. 2010;63:40–3.
12. Imagawa I, Suzuki H. Successful treatment of refractory warts with topical Vitamin D₃ derivative (maxacalcitol, 1alpha, 25-dihydroxy-22-oxacalcitriol) in 17 patients. J Dermatol. 2007;34:264–6.

Source of Support: None Declared
Conflict of Interest: None Declared