Role of Intralesional Vitamin D3 in the Treatment of Cutaneous Warts

Sabahat Shah, Seemab Khan and Noor Us Sabah

Department of Dermatology, P.N.S. Shifa Hospital, Karachi, Pakistan

ABSTRACT

Objective: To determine the effect of intralesional vitamin D3 injection in the treatment of cutaneous warts.
Study Design: Quasi-experimental study.
Place and Duration of the Study: Department of Dermatology, P.N.S. Shifa Hospital, Karachi, Pakistan, from May to November 2023.
Methodology: A total of 30 patients with cutaneous warts of various sizes and durations were selected. Vitamin D3 (0.2 ml, 15 mg/ml) was injected to the base of the warts after anaesthetising with lignocaine (0.2 ml, 20 mg/ml). The injections were repeated two weeks apart for a maximum of 4 sessions or until complete clearance, whichever was earlier. A maximum of two warts were treated per session, and patients were followed up for six months after the last injection.
Results: The patients' average age was 32.20 ± 11.9 years, and their average illness duration was 14.3 ± 6.5 months. Out of the 30 patients, 10 (33.4%) were females and 20 (66.6%) were males. Twenty cases (66.6%) showed complete clearance, seven cases (23.3%) showed a moderate response, and three (10%) showed a mild response. The only side effects observed in 17 (56.6%) cases were mild swelling and irritation at the injection site, both of which went away on their own within a few days.
Conclusion: Intralesional vitamin D3 is an effective and affordable treatment option for cutaneous warts.

Key Words: *Cutaneous warts, Common warts, Efficacy, Intralesional treatment, Vitamin D3*.

How to cite this article: Shah S, Khan S, Sabah NU. Role of Intralesional Vitamin D3 in the Treatment of Cutaneous Warts. *J Coll Physicians Surg Pak* 2025; **35(05)**:642-645.

INTRODUCTION

Warts are benign cutaneous tumours that are rarely found on mucosal membranes and are caused by the *Human Papillomavirus* (HPV). In the Western world, the incidence of warts is estimated to be between 3 and 13%. In Pakistan, around 10.05% of the population has warts.[1,2] It is quite a common condition for which there are several different therapies with differing levels of effectiveness. However, after two years, 65-78% of warts disappear spontaneously.[3] Patients seek therapy due to cosmetic disfigurement and pain, particularly in the soles.[4] The most prevalent treatment method for warts is local destruction, which can be achieved with topical keratolytics, electrocoagulation, cryotherapy, or laser therapy.[5] Each management approach carries a risk of pain, scarring, and frequent recurrences.[6] Furthermore, because they can only remove treated lesions and are ineffective for remote warts, these destructive methods are not appropriate to treat the many refractory warts.[7]

Correspondence to: Dr. Sabahat Shah, Department of Dermatology, P.N.S. Shifa Hospital, Karachi, Pakistan
E-mail: sabadoctor16@gmail.com

Received: November 28, 2023; Revised: August 27, 2024; Accepted: October 19, 2024
DOI: https://doi.org/10.29271/jcpsp.2025.05.642

Therefore, during the past few years, immunotherapy has frequently been used to treat warts to overcome these drawbacks. It functions primarily by strengthening cell-mediated immunity to eradicate warts.[8] Numerous antigens have been tested, such as *Candida* antigen, *Mycobacterium* vaccine, tuberculin PPD, MMR, *etc*.[9]

Aktas *et al*., attempted intralesional vitamin D3 injection for the first time in 2016 in order to cure plantar warts, and they reported positive outcomes.[10] Recently, various studies have shown intralesional vitamin D as a potential therapeutic option for the treatment of cutaneous warts. The majority of the previous studies were international, and local data about its significance are insufficient. Due to the scarcity of local data on this subject, the findings of this study would be a valuable addition to the existing pool of knowledge. This study was planned to assess the role of intralesional vitamin D3 injection in the treatment of cutaneous warts.

METHODOLOGY

This experimental study was conducted in the Outpatient Department of Dermatology, P.N.S. Shifa Hospital, Karachi, Pakistan, from May to November 2023 after obtaining the approval from the Institute's Ethical Review Committee.

The sample size was calculated by using the OpenEpi calculator, based on a prevalence of warts of 10.05%, margin of error of 8%, and a 95% confidence interval. The calculated sample size was 55. However, due to expensive treatment, a total of

30 patients were enrolled in the study meeting the eligibility criteria.

All patients of either gender, with cutaneous warts and no prior treatment of either topical or destructive modalities for at least six months prior to the study, were included *via* a non-probability consecutive sampling technique. The study excluded patients who were younger than 12 or older than 70 years, pregnant or nursing females, those with immunosuppression, including HIV, and those who had previously experienced vitamin D3 hypersensitivity. Clinical characteristics and history were used to diagnose cutaneous warts. A standardised questionnaire produced specifically for this research was used to record demographic information and conduct the baseline evaluation at the initial appointment. For every patient, a graphical wart map was created, and at every visit, the position, number, size, and type of warts were noted. At every visit, pictures were captured to supplement the data that were recorded.

Clinical response was assessed by noting the decrease in the number and size of warty lesions at each visit, that is, every two weeks for four sessions and six months following the last injection. Complete clearance was considered if all the warts, both treated and distant warts, resolved completely. Moderate response was considered if there were 50 to <100% reductions in both size and number of lesions; mild response was considered if the response was between 1% and <50%.[11] Larger warts were considered for the injection. A maximum of two warts were treated at each session. The injections were repeated at 2-week intervals for a maximum of four injections. If complete clearance was achieved before four injections, the treatment was stopped, and the patient was followed up for recurrence. Patients were evaluated for treatment efficacy every two weeks for the first two months and monthly, thereafter, to record any recurrence for six months.

Vitamin D3 for injection is available in vials containing 6,00,000 IU of cholecalciferol in 1 ml (15 mg). The selected warts were injected first with 0.2 ml of lignocaine (20 mg/ml); after a few minutes, 0.2 ml of vitamin D3 (15 mg/ml) was slowly injected into the base of each wart with a 27-gauge insulin syringe. Post-treatment, the patients were advised not to use any topical and oral medications.

Statistical Package for the Social Sciences (SPSS) version 26 was used to analyse the data. Quantitative variables were reported through mean ± SD. Frequency and percentages were calculated for qualitative data.

RESULTS

The patients' average age was 32.20 ± 11.9 years, and their average disease duration was 14.3 ± 6.5 months. Ten (33.4%) patients were females and 20 (66.6%) were males. Thirteen (43.4%) individuals had multiple warts, while 17 (56.3%) patients had a single wart. The most observed type of wart was plantar wart i.e., 21 cases (70%), followed by verruca vulgaris with 6 cases (20%), and filiform wart 3 cases (10%), as shown in Table I.

In terms of the treatment's outcome, 20 patients (66.6%) showed complete clearance, 7 cases (23.3%) showed a moderate response, and 3 cases (10%) showed a mild response. The only side effects observed in 17 (56.6%) cases were mild swelling and irritation at the injection site, both of which went away on their own within a few days (Figure 1). Fourteen (70%) of those cases who showed complete cure achieved it in 3 sessions, 3 (15%) achieved after 2 sessions, while another 3 (15%) achieved complete cure after 4 sessions.

Table I: Baseline characteristics of the patients (n = 30).

Baseline characteristics	Statistics
Age (mean ± SD)	32.20 ± 11.9 years
Duration of disease (mean ± SD)	14.3 ± 6.5 months
Gender	
Male	20 (66.6%)
Female	10 (33.4%)
Number of warts	
Single	17 (56.6%)
Multiple	13 (43.3%)
Type of wart	
Verruca vulgaris	06 (20%)
Filiform wart	03 (10%)
Plantar wart	21 (70%)

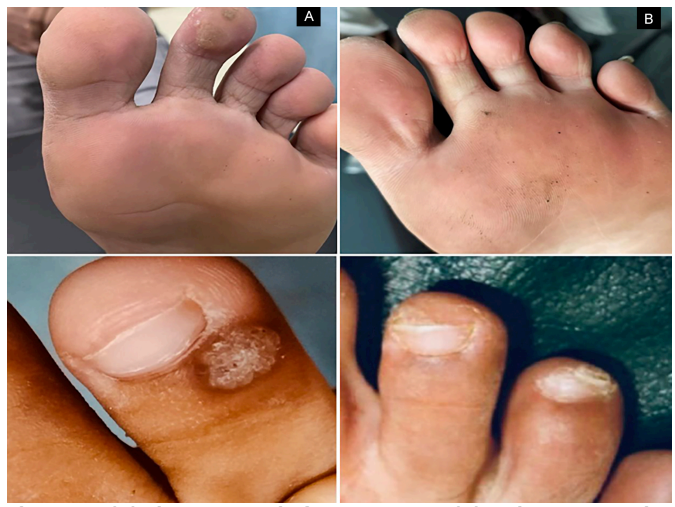

Figure 1: (A) Plantar warts before treatment (B) and near to resolve after four injections.

DISCUSSION

Wart is a common, innocuous, and often recurrent HPV infection of the skin and mucous membranes. The majority of people seek treatment for warts due to their unsightly appearance and sporadic pain, particularly when they are found on the soles of the feet.[11,12] When treating several warts at once, particularly palmoplantar, destructive treatments such as cryotherapy and electrocautery may be required. Such invasive operations may result in discolouration as well as scars. In addition to being ugly and potentially unpleasant, warts can resist popular treatments and have a high recurrence rate. Currently, immunotherapy is the most effective way to treat warts since it can boost the body's immune response against HPV. Comparatively few occurrences recur when compared to other destructive modalities.[13] Numerous antigens and vaccines, including bleomycin, *Candida albicans*, PPD, MMR, and the *Mycobacterium W* vaccine, have been investigated for use in immune therapy.[14]

According to this study, treating cutaneous warts with intralesional vitamin D3 was effective. In this study, mild response occurred in 10% of cases, moderate response in 23.3% of cases, and full clearance was noted in 66.6% of cases. The precise mechanism by which vitamin D eradicates warts is uncertain. Because of its capacity to regulate cytokine release, epidermal cell proliferation, and differentiation, vitamin D derivatives are believed to be efficacious against warts. When human macrophages are activated by toll-like receptors, it has been found that the expression of the VDR and vitamin D-1-hydroxylase gene is increased, which promotes the generation of antimicrobial peptides. It has been demonstrated in experimental settings that inhibiting the expressions of IL-6, IL-8, TNF-alpha, and TNF-gamma *via* a VDR-dependent pathway has immunomodulatory effects.[15]

These findings are consistent with a number of studies, including one by Shaldoum *et al*. in 2020, which found that 66.7% of patients had a complete response, 6.67% showed moderate response, 20% had a mild response, and 6.67% had no response.[16] Raghukumar *et al*., in 2017 reported complete response in 90%, moderate response in 6.66% cases, and no response in 3.33% cases.[17]According to Aktas *et al*., 70% of patients achieved total clearance, 15% had a partial response, and 15% had no response.[10]According to the Kavya *et al*.'s study, 78.57% of patients achieved complete clearance, 14.28% had a partial response, and 7.14% had a limited response.[18] Another study was conducted by Naseer *et al*. in which complete response was observed in 185 (81.9%) patients.[19]

The only side effects in the present study's experiment were minor swelling and irritation at the injection site, and both resolved on their own within a few days. The same has been documented in a study carried out by Al-Sabak *et al*.[20]

This study's main limitation was its very small sample size; so, greater sample sizes would be needed in future research. Another limitation comprised of a single-centre experience. It was conducted in an urban environment, therefore, the results might not generalise to mass population.

CONCLUSION

This study concludes that an intralesional injection of vitamin D3 is a highly successful and inexpensive immunotherapy option for treating the cutaneous warts option that can be used in simple set-ups as a useful method for the treatment of warts. Nevertheless, further researches with a larger sample size are required to firm up the conclusion.

ETHICAL APPROVAL:
Ethics Committee of P.N.S. Shifa Hospital gave its approval to the study (ERC/2023/DERMA/18; dated: 29-5-2023).

PATIENTS' CONSENT:
Informed consent was obtained from the patients to publish the data concerning this study.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
SS: Conception and design of work, data collection, analysis and interpretation of data, drafting, and revision of work.
SK: Conception of design, data collection, critical analysis, writing of the manuscript, and final review.
NS: Data collection and drafting.
All authors approved the final version of the manuscript to be published.

REFERENCES

1. Ashraf U, Ahmed N, Tahir M, Hasan F, Shah AH, Farooq O. Effectiveness of autoinoculation in patients with multiple warts presenting at a tertiary care hospital. *J Coll Physicians Surg Pak* 2023; **33(1)**:16-19. doi: 10.29271/jcpsp.2023.01.16.
2. Abdel Razik LH, Obaid ZM, Fouda I. Intralesional Candida antigen versus intralesional vitamin D3 in the treatment of recalcitrant multiple common warts. *J Cosmet Dermatol* 2021; **20(10)**:3341-46. doi: 10.1111/jocd.14335.
3. Ahmed R, Bhadbhade SP, Noojibail B, Shetty SM, Varghese A. Comparative study in efficacy and safety of intralesional injections of vitamin D3, measles rubella (MR) vaccine, and purified protein derivative (PPD) in the management of cutaneous warts. *J Cutan Aesthet Surg* 2020; **13(4)**:326-32. doi: 10.4103/JCAS.JCAS_39_20.
4. Kudligi C, Ramachandra ST, Kuntoji V, Chhangte MZ. Chovatiya KM, Khat N, *et al*. A study of homologous auto-implantation therapy for multiple warts. *J Pak Assoc Dermatol* 2020; **30(4)**. Available from: https://www.jpad.com.pk/index.php/jpad/article/view/1599.
5. Chhangte M, Verma S, Marak A, Thakur BK. Homologous auto-implantation; an effective modality in the treatment of multiple warts; a non-randomized interventional study at a tertiary care hospital in North-Eastern India. *Int J Res Dermatol* 2021; **7(6)**:835-9. doi: 10.18203/issn.2455-4529.IntJResDermatol20214210.
6. Taneja G, Hazarika N, Bhatia R. Effectiveness of auto-inoculation in viral warts: A single arm, open-label, and clinical trial. *Dermatol Ther* 2020; **33(6)**:e14122. doi: 10.1111/dth.14122.
7. Izumi Y, Kawase M, Egawa K. Human papillomavirus type 7 identified in digitated warts on facial seborrhoeic eczema of a non-butcher immunocompetent individual. *Skin Health Dis* 2022; **3(3)**:e184. doi: 10.1002/ski2.184.
8. Naresh M. A study of effectiveness of intralesional vitamin D3 in treatment of multiple cutaneous warts. *IOSR J Dent Med Sci* 2019; **18(3)**:84-7. Available from: www.iosrjournals.org.
9. Mohamed EEM, El Taieb MA, Abd El-Sabour GA. Intralesional vitamin D3 versus purified protein derivatives in the treatment of multiple cutaneous warts: Comparative study. *Egypt J Hosp Med* 2019; **76(2)**:3589-94. doi: 10.21608/EJHM.2019.39165.
10. Aktas H, Ergin C, Demir B, Ekiz O. Intralesional vitamin D injection may be an effective treatment option for warts. *J Cutan Med Surg* 2016; **20(2)**:118-22. doi: 10.1177/1203475415602841.
11. El Sayed MH, Sayed FS, Afify AA. Intralesional zinc sulfate 2% *vs* intralesional vitamin D in plantar warts: A clinic

dermoscopic study. *Dermatol Ther* 2020; **33(3)**:e13308. doi: 10.1111/dth.13308.

12. Kareem IMA, Ibrahim IM, Mohammed SFF, Ahmed AAB. Effectiveness of intralesional vitamin D3 injection in the treatment of common warts: Single-blinded placebo-controlled study. *Dermatol Therapy* 2019; **32(3)**:e12882. doi: 10.1111/dth.12882.
13. Moscarelli L, Annunziata F, Mjeshtri A. Successful treatment of refractory wart with a topical activated vitamin D in a renal transplant recipient. *Case Rep Transplant* 2022; **2022**:9838495. doi: 10.1155/2022/9838495.
14. Munshi N, Varma K. Role of intralesioal vitamin D in treatment of cutaneous warts. *IP Indian J Clin Exp Dermatol* 2022; **8(4)**:248-51. doi: 10.18231/j.ijced.2022.050.
15. Latif I, Sultan J, Aslam A, Hassan I, Devi R. Role of intralesional vitamin D3 in the treatment of cutaneous warts. *J Cutan Aesthet Surg* 2021; **14(4)**:404-8. doi: 10.4103/JCAS.JCAS_170_20.
16. 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; **19(8)**:2033-40. doi: 10.1111/jocd.13272.
17. 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 Cut Med Surg* 2017; **21(4)**:320-24. doi: 10.1177/1203475417704180.
18. 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; **10(2)**:90-4. doi: 10.4103/JCAS.JCAS_82_16.
19. Naseer M, Ghafoor R, Asad N. Efficacy of intralesional vitamin D3 in cutaneous warts. *J Pak Assoc Dermatol* 2023; **33(4)**. Available from: https://www.jpad.com.pk/index.php/jpad/article/view/2268.
20. Al-Sabak H, Al-Hattab M, Al-Rammahi M, Al-Dhalimi M. The efficacy of intralesional vitamin D3 injection in the treatment of cutaneous warts: A clinical therapeutic trial study. *Skin Res Technol* 2023; **29(8)**:e13442. doi: 10.1111/srt.13442.