

Efficacy and Safety of Intralesional Vitamin D3 in the Treatment of Cutaneous Warts: A Prospective Interventional Study

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ABSTRACT

Background:

Cutaneous warts are common benign epidermal proliferations caused by human papillomavirus infection. Conventional destructive treatments may be painful, require repeated sessions, and are associated with recurrence, scarring, and pigmentary alteration. Intralesional vitamin D3 has emerged as a potentially effective immunotherapeutic treatment, but clinical evidence remains heterogeneous.

Objectives:

To evaluate the efficacy and safety of intralesional vitamin D3 in patients with multiple cutaneous warts.

Methods:

This prospective interventional study included 41 adult patients with multiple cutaneous warts attending the dermatology outpatient department of a tertiary-care hospital in Chhatrapati Sambhajanagar, India, between April 2024 and April 2026. Intralesional cholecalciferol, at a concentration of 600,000 IU/mL, was administered in a dose of 0.2–0.5 mL into the base of up to four of the largest warts. Injections were repeated at two-week intervals for a maximum of four sessions. Clinical response was assessed according to the reduction in the number and size of treated and distant warts. Patients were followed for treatment-related adverse effects and recurrence.

Results:

The study included 22 males and 19 females. Most patients, 25/41 (60.98%), were aged 21–40 years. Verruca vulgaris was the predominant clinical type, occurring alone in 35 (85.36%) patients. Complete resolution was achieved in 27 (65.85%) patients, partial resolution in 10 (24.39%), and no significant change in 4 (9.76%). Thus, 37 (90.24%) patients demonstrated some degree of clinical improvement. Treatment response differed significantly according to wart type in the original analysis ($p=0.02$). Two patients (4.88%) developed painful injection-site nodules.

Conclusion:

Intralesional vitamin D3 produced complete resolution in approximately two-thirds of patients and some clinical improvement in more than 90%, with few local adverse effects and a low observed recurrence rate. It may be considered a useful therapeutic option for multiple cutaneous warts. Controlled studies with larger samples and standardized dosing and outcome definitions are required.

Keywords: Cutaneous warts; human papillomavirus; intralesional immunotherapy; vitamin D3.

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INTRODUCTION:

Cutaneous warts are benign epidermal proliferations caused by infection with human papillomavirus. They affect individuals across all age groups but are particularly frequent among children, adolescents, and young adults. Although warts are benign, persistent or multiple lesions may cause pain, functional limitation, cosmetic concern, social embarrassment, and impaired quality of life. Their tendency to persist, recur, and spread to adjacent or distant sites makes treatment challenging.^{1,2}

Human papillomavirus enters the epidermis through microscopic disruption of the skin barrier and infects basal keratinocytes. Viral replication is closely linked to keratinocyte differentiation. The relatively limited inflammation accompanying infection and the capacity of the virus to interfere with local antigen presentation permit prolonged persistence within the epidermis.^{3,4} Spontaneous regression of warts is primarily mediated by cell-mediated immunity against virus-infected keratinocytes, emphasising the importance of host immune responses in disease clearance.⁵

Available treatments include salicylic acid, cryotherapy, electrocautery, curettage, laser ablation, and topical immunomodulatory agents. However, no single treatment is consistently effective for all patients. Destructive therapies may require repeated procedures and can cause pain, blistering, scarring, and post-inflammatory pigmentary changes. They also remove visible lesions without necessarily inducing immunity against human papillomavirus, which may contribute to recurrence.⁶

Intralesional immunotherapy attempts to induce a local inflammatory response and enhance systemic recognition of viral antigens. Agents investigated for this purpose include measles-mumps-rubella vaccine, purified protein derivative, *Candida* antigen, and vitamin D3. Intralesional therapy may produce resolution not only of injected lesions but also of distant untreated warts, suggesting activation of systemic cell-mediated immunity.⁷

Vitamin D has regulatory effects on keratinocyte proliferation and differentiation and exerts immunomodulatory actions through the vitamin D receptor. It affects macrophages, dendritic cells, and lymphocytes and promotes the expression of antimicrobial peptides such as cathelicidin and defensins.^{8,9} These actions provide a plausible basis

for the use of intralesional vitamin D3 in human papillomavirus-associated lesions.

Several uncontrolled and comparative studies have reported promising clearance rates following intralesional vitamin D3 treatment. However, variations in patient selection, vitamin D concentration, injected volume, treatment interval, number of lesions injected, response definition, and duration of follow-up have resulted in considerable heterogeneity.¹⁰⁻¹⁴ The present study was therefore undertaken to evaluate the efficacy and safety of intralesional vitamin D3 in adult patients with multiple cutaneous warts.

Objectives: The primary objective was to determine the clinical efficacy of intralesional vitamin D3 in cutaneous warts. The secondary objective was to assess treatment-related local adverse effects and recurrence following therapy.

MATERIALS AND METHODS:

Study design and setting

This prospective interventional study was conducted in the outpatient department of Dermatology, Venereology and Leprosy at MGM Medical College and Hospital, Chhatrapati Sambhajinagar, Maharashtra, India, between April 2024 and April 2026.

Study population

Adult male and female patients clinically diagnosed with multiple cutaneous warts were screened for eligibility. A total of 41 eligible patients were enrolled.

Sample-size calculation

The sample size was calculated using the single-proportion formula:

$$n = Z^2 pq / d^2$$

Where:

n= sample size.

Z2= value for the selected alpha level (1.96 at 95% confidence level)

d= desired level of precision (10%)

p= prevalence of cutaneous warts was 12%.

Ref : Zhu P, et al. Clinical guideline for the diagnosis and treatment of cutaneous warts. *J Evid Based Med.* 2022 Sep;15(3):284-301.⁷

A prevalence of cutaneous warts of 12%, a 95% confidence level, and an absolute precision of 10% were considered. The calculated sample size was approximately 41 patients.

Inclusion criteria:

Patients of either sex aged 18 years or older with multiple cutaneous warts were included.

Exclusion criteria:

The following patients were excluded:

- Patients younger than 18 years
- Pregnant or lactating women
- Patients with a tendency for keloid formation
- Patients with evidence of immunosuppression
- Patients with a significant systemic or dermatological disorder affecting assessment
- Patients with known hypersensitivity to vitamin D3 or any component of the preparation

Data collection and clinical assessment:

A detailed history was recorded using a predesigned proforma. Clinical examination included assessment of the number, size, duration, distribution, and morphological type of warts. Possible precipitating factors, including minor trauma, were documented. Standard clinical photographs were obtained before treatment and after completion of therapy.

Treatment protocol: A commercially available cholecalciferol preparation containing 600,000 IU/mL, equivalent to 15 mg/mL in an arachis-oil base, was used.

Following appropriate aseptic precautions and local anaesthesia, 0.2–0.5 mL of vitamin D3 was injected longitudinally into the base of each selected wart using an insulin syringe. Up to four of the largest warts were treated during each session. The injections were repeated at two-week intervals for a maximum of four sessions.

The dose administered to an individual wart depended on its size, with the total injected volume limited according to the study protocol.

Outcome assessment: The number and size of warts were evaluated at each visit. The final response included the response of both injected and distant untreated lesions.

Clinical response was classified as:

- **Complete resolution:** complete disappearance of all treated and distant warts
- **Partial resolution:** clinically appreciable reduction in the size or number of lesions without complete disappearance
- **No significant change:** absence of a meaningful reduction in wart size or number

For consistency with the thesis dataset, moderate and mild responses were combined under partial resolution for manuscript reporting. Patients were observed for local adverse effects, including pain, erythema, swelling, nodules, scarring, and pigmentary alteration. Follow-up was planned for up to six months after the final treatment session to identify recurrence.

Ethical considerations

The study was approved by the Ethics Committee for Research on Human Subjects of MGM Medical College and Hospital. Written informed consent was obtained from every participant before enrolment. Separate consent was obtained for clinical photography and use of anonymised images for academic or scientific publication.

Statistical analysis: Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics for Windows, version 24.0. Categorical variables were summarised as frequencies and percentages. Associations between categorical variables were evaluated using the chi-square test. A p-value below 0.05 was considered statistically significant.

Because several cells in the wart-type-versus-response table contained small expected frequencies, the association should preferably be rechecked using the Fisher–Freeman–Halton exact test before journal submission.

RESULTS:

A total of 41 patients completed the study and were included in the analysis.

Demographic characteristics: The study included 22 (53.66%) males and 19 (46.34%) females. The largest age group was 21–30 years, accounting for 14 (34.15%) patients, followed by 31–40 years with 11 (26.83%) patients. Overall, 25 (60.98%) participants were between 21 and 40 years of age.

Insert table 1 here

Clinical characteristics: Fifteen patients (36.59%) had warts for six months or less. Eleven (26.83%) had lesions for 7–12 months, another 11 (26.83%) for 13–24 months, and 4 (9.76%) for more than 24 months. Minor trauma was reported as a possible precipitating factor by 20 (48.78%) patients. Verruca vulgaris was the most frequent clinical type and occurred alone in 35 (85.36%) patients. Three (7.32%) had plane warts alone and 3 (7.32%) had a mixed presentation of plane warts and verruca vulgaris.

Treatment response: Complete resolution was observed in 27 (65.85%) patients. Partial resolution was recorded in 10 (24.39%), while 4 (9.76%) demonstrated no significant change. Overall, 37 (90.24%) patients experienced at least some clinical improvement.

Among patients with verruca vulgaris, 23/35 (65.71%) achieved complete resolution, 8/35 (22.86%) had partial resolution, and 4/35 (11.43%) had no significant change.

All patients with plane or mixed warts showed at least some improvement, although these subgroups were very small. The original analysis reported a statistically significant association between wart type and treatment response ($p=0.02$).

Safety and recurrence: Two patients (4.88%) developed painful nodules at the injection site. No major systemic adverse event was reported. One patient (2.44%) experienced recurrence after initial

improvement. Thirty-eight patients (92.68%) had no reported adverse effects.

DISCUSSION:

The present study evaluated intralesional vitamin D3 in 41 adults with multiple cutaneous warts. Complete resolution was achieved in 65.85% of patients, while a further 24.39% experienced partial resolution. Thus, more than 90% of participants demonstrated some degree of clinical benefit. Treatment was generally well tolerated, with painful local nodules occurring in two patients and recurrence recorded in one patient.

Most participants were young adults, with approximately 61% aged 21–40 years. The predominance of younger patients is consistent with the known epidemiological distribution of cutaneous warts. Younger individuals may have greater exposure to minor trauma, close physical contact, communal environments, occupational activities, and practices that facilitate viral inoculation. However, the study was hospital based, and its age distribution should not be interpreted as an estimate of population prevalence.

A small male predominance was observed, with males accounting for 53.66% of participants. Similar near-balanced sex distributions have been reported in several wart-treatment studies. Sex is not generally regarded as a strong independent determinant of cutaneous wart development, and differences between studies may reflect health-seeking patterns, occupational exposure, or sampling variation.

Minor trauma was reported by almost half of the participants. Disruption of the epidermal barrier facilitates entry of human papillomavirus into basal keratinocytes and therefore represents a biologically plausible antecedent. Nevertheless, because exposure was self-reported and a substantial proportion of patients could not specify a precipitating event, a causal association cannot be inferred.

Verruca vulgaris was the predominant clinical morphology. This finding is clinically expected because common warts are among the most frequently encountered extragenital warts in dermatology practice. The small numbers of patients with plane and mixed warts limit meaningful comparison of response between individual morphological categories.

The complete resolution rate of 65.85% observed in the present study lies within the broad range reported in previous intralesional vitamin D3 studies. Aktaş et al. treated 20 patients with plantar warts and reported complete resolution in 80%.¹⁰ Kavya et al. reported complete clearance in 78.57% of patients with multiple warts following intralesional cholecalciferol administered at two-week intervals.¹¹ Raghukumar et al. observed complete response in 90% of patients with recalcitrant warts

and also described resolution of distant untreated lesions.¹²

The lower complete-clearance rate in our study compared with these early investigations may reflect differences in wart type, duration, disease burden, treatment protocol, endpoint definition, or host immune response. The combination of mild and moderate improvement as partial resolution also produced a more conservative classification than studies using “excellent,” “good,” or “moderate” response categories.

Studies comparing vitamin D3 with other intralesional immunotherapies have reported variable findings. Singh et al. found complete clearance in 72.5% of patients receiving vitamin D3 compared with 80% among those receiving purified protein derivative. Other studies have suggested comparable or greater efficacy with measles-mumps-rubella vaccine or Candida antigen. This variability indicates that intralesional vitamin D3 is a potentially useful option but cannot yet be considered uniformly superior to established immunotherapeutic agents.

A placebo-controlled study by Kareem et al. demonstrated greater clearance with vitamin D3 than with saline, supporting a treatment-specific immunological effect. Conversely, a more recent double-blind placebo-controlled trial using a substantially lower dose reported no meaningful difference between vitamin D3 and placebo.¹⁴ Differences in concentration, injected dose, formulation, treatment frequency, lesion selection, and baseline vitamin D status may partly explain these conflicting results.

The present study used a high-concentration cholecalciferol formulation and injected up to four of the largest warts at two-week intervals. The injection of several lesions may provide a greater local antigenic stimulus than protocols that inject only a single index wart. However, the absence of a comparator group prevents differentiation between the treatment effect, natural regression, procedural stimulation, and other unmeasured influences.

Vitamin D may act through several complementary pathways. Binding of active vitamin D to the vitamin D receptor influences keratinocyte proliferation and differentiation. Vitamin D also modifies innate and adaptive immune responses, induces antimicrobial peptides, and influences dendritic cells and T-lymphocyte activity.^{8,9} These actions may promote recognition and clearance of human papillomavirus-infected keratinocytes. Regression of non-injected warts reported in previous studies further supports the possibility of systemic immune activation after local treatment, although distant-wart clearance was not separately quantified in the current dataset.

The safety findings were favourable. Only two patients developed painful local nodules, and no serious systemic adverse effect was recorded. Local

pain, swelling, erythema, and transient nodules are among the most frequently described adverse effects of intralesional therapy. The absence of scarring and major pigmentary alteration is clinically important, especially in patients with darker skin types. Nevertheless, serum calcium and vitamin D concentrations were not systematically evaluated, and the study therefore cannot fully exclude biochemical effects of high-dose local vitamin D3. Only one recurrence was recorded. This suggests the possibility of a durable response, but recurrence should be interpreted cautiously because follow-up completeness and duration were not reported separately for each participant. Studies with standardised six- or twelve-month follow-up are required to determine whether immunotherapy provides lower recurrence than destructive treatments.

The statistically significant association reported between clinical wart type and response should also be interpreted carefully. The plane-wart and mixed-wart groups contained only three patients each, and several expected cell frequencies were below the assumptions required for the Pearson chi-square test. The association should therefore be recalculated using an exact test. The finding should not be presented as evidence that vitamin D3 is more effective for a particular wart morphology unless confirmed in a larger study.

Strengths

The study assessed both efficacy and safety in a real-world dermatology outpatient setting. A clearly defined intralesional treatment protocol was followed, and both the number and size of lesions were considered during response assessment. Follow-up for recurrence was also incorporated into the study design.

REFERENCES:

1. Bruggink SC, Eekhof JAH, Egberts PF, van Blijswijk SCE, Assendelft WJJ, Gussekloo J. Warts transmitted in families and schools: a prospective cohort. *Pediatrics*. 2013;131(5):928-934.
2. Sterling JC, Gibbs S, Haque Hussain SS, Mohd Mustapa MF, Handfield-Jones SE. British Association of Dermatologists' guidelines for the management of cutaneous warts 2014. *Br J Dermatol*. 2014;171(4):696-712. doi:10.1111/bjd.13310.
3. Doorbar J, Quint W, Banks L, Bravo IG, Stoler M, Broker TR, et al. The biology and life-cycle of human papillomaviruses. *Vaccine*. 2012;30 Suppl 5:F55-F70.
4. Steinbach A, Riemer AB. Immune evasion mechanisms of human papillomavirus: an update. *Int J Cancer*. 2018;142(2):224-229.
5. Aiba S, Tagami H. Immunohistologic studies in regressing common warts and condylomata acuminata. *Cancer*. 1986;58(6):1246-1251.
6. Kwok CS, Gibbs S, Bennett C, Holland R, Abbott R. Topical treatments for cutaneous warts. *Cochrane Database Syst Rev*. 2012;(9):CD001781.
7. Zhu P, Qi RQ, Yang Y, Huo W, Zhang Y, He L, et al. Clinical guideline for the diagnosis and treatment of cutaneous warts. *J Evid Based Med*. 2022;15(3):284-301.
8. Aranow C. Vitamin D and the immune system. *J Investig Med*. 2011;59(6):881-886.
9. Gombart AF. The vitamin D-antimicrobial peptide pathway and its role in protection against infection. *FASEB J*. 2009;23(9):2819-2828.
10. Schaubert J, Gallo RL. Antimicrobial peptides and the skin immune defense system. *J Allergy Clin Immunol*. 2008;122(2):261-266.

LIMITATIONS:

The principal limitations were the small sample size, single-centre design, absence of a placebo or active comparator group, and lack of randomisation and blinding. Baseline serum vitamin D and calcium levels were not documented. The number and size of individual lesions, response of injected versus distant warts, number of sessions required for clearance, and participant-wise follow-up duration were not separately reported. The small numbers in some wart subgroups limited assessment of factors associated with response. Spontaneous regression could not be distinguished from treatment-related clearance.

CONCLUSION:

Intralesional vitamin D3 resulted in complete resolution of cutaneous warts in approximately two-thirds of patients and produced at least partial improvement in more than 90%. The treatment was associated with few local adverse effects and a low observed recurrence rate. Intralesional vitamin D3 may therefore represent a convenient and relatively safe treatment option for adults with multiple cutaneous warts. However, these findings should be confirmed through adequately powered randomised controlled trials using standardised dosing, objective lesion-level assessment, biochemical safety monitoring, and longer follow-up.

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11. 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;20(2):118-122.
12. 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):90-94.
13. 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;21(4):320-324.
14. El Sayed MH, Hassan AS, El-Sayed DS, El-Mesidy MS. Intralesional zinc sulfate 2% versus intralesional vitamin D in plantar warts: a three-armed randomized clinical trial. *Dermatol Ther.* 2020;33(3):e13340.
15. Ibrahim NA, Nada EA, El-Gilany AH. Intralesional vitamin D3 versus topical photodynamic therapy in recalcitrant palmoplantar warts: a randomized comparative controlled study. *Photodiagnosis Photodyn Ther.* 2020;32:101979.
16. Abdel Razik LH, Rashad MA, Aboel-Fetoh NM. Intralesional Candida antigen versus intralesional vitamin D3 in the treatment of multiple recalcitrant common warts. *J Cosmet Dermatol.* 2021;20(10):3342-3348.
17. Muse ME, Stiff KM, Glines KR, Cline A, Feldman SR. A review of intralesional wart therapy. *Dermatol Online J.* 2020;26(3):13030/qt3md9z8gj.
18. Martin A, Parsi KK, Schachner LA, Keri JE. Emerging intralesional treatments for plantar warts: a systematic review. *J Drugs Dermatol.* 2022;21(12):1322-1329.
19. Al-Sabak H, Mohammed GF, Gomaa AHA, Hassan AM. The efficacy of intralesional vitamin D3 injection in the treatment of cutaneous warts. *J Cosmet Dermatol.* 2023;22(10):2908-2914.
20. Merry SP, Smith ML, Hueston WJ, et al. Intralesional injection of vitamin D3 for treatment of cutaneous warts: a randomized, double-blind, placebo-controlled trial. *J Am Board Fam Med.* 2025;38(4):[pages to be confirmed before submission].

TABLES

Table 1. Demographic characteristics of the study participants

Characteristic	Number (n=41)	Percentage
Age group		
18–20 years*	1	2.44
21–30 years	14	34.15
31–40 years	11	26.83
41–50 years	9	21.95
51–60 years	6	14.63
Sex		
Male	22	53.66

Female	19	46.34
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Table 2. Duration and reported precipitating factors of cutaneous warts

Clinical variable	Number (n=41)	Percentage
Duration of warts		
≤6 months	15	36.59
7–12 months	11	26.83
13–24 months	11	26.83
>24 months	4	9.76
Reported precipitating factor		
Minor trauma	20	48.78
Not specified	16	39.02

Unknown	5	12.20
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Table 3. Clinical type of wart according to sex

Type of wart	Female, n	Male, n	Total, n (%)
Verruca vulgaris	16	19	35 (85.36)
Plane wart	2	1	3 (7.32)
Mixed plane wart and verruca vulgaris	1	2	3 (7.32)
Total	19	22	41 (100.00)

Association between sex and wart type: p=0.72.

Table 4. Overall clinical response to intralesional vitamin D3

Clinical response	Number (n=41)	Percentage
Complete resolution	27	65.85
Partial resolution	10	24.39
No significant change	4	9.76
Any clinical improvement	37	90.24
Total	41	100.00

Table 5. Clinical response according to wart type

Type of wart	Complete resolution, n (%)	Partial resolution, n (%)	No significant change, n (%)	Total
Verruca vulgaris	23 (65.71)	8 (22.86)	4 (11.43)	35
Plane wart	1 (33.33)	2 (66.67)	0	3
Mixed plane wart and verruca vulgaris	3 (100.00)	0	0	3
Total	27 (65.85)	10 (24.39)	4 (9.76)	41

Table 6. Adverse effects and recurrence following treatment

Outcome	Number (n=41)	Percentage
Painful injection-site nodule	2	4.88

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Recurrence after initial response	1	2.44
No reported adverse effects	38	92.68

Adverse effects and recurrence are not necessarily mutually exclusive categories. The patient-level master chart should be checked before presenting them as a single categorical distribution.