*Journal of Pakistan Association of Dermatologists*. 2023;**33(4)**:1399-1403.

**Original Article**

# Effectiveness of intralesional vitamin D3 injections for treatment of common warts: An open-label uncontrolled study

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## Abstract

***Objective*** To evaluate the effectiveness of intralesional Vitamin D3 in the treatment of common warts.

***Methods*** To be eligible for the study, participants had to have common warts and must not have undergone any topical or destructive treatments for a minimum of six months. The study included both males and females between the ages of 12 and 60. The procedure involved injecting lignocaine (20 mg/ml) into the warts using a 27-gauge insulin syringe and aseptic methods, followed by injecting 0.5 ml of vitamin D3 (15 mg/ml) into the base of each wart. The reduction in the number and size of warty lesions was monitored during each visit, which occurred every two weeks for a total of four sessions.

***Results*** A total of 356 patients were enrolled in the study and were assigned to receiving injections of vitamin D3. Three hundred forty five patients completed the study. Out of the total number of individuals who received the intervention (n=345), 211 (61.2%) showed a complete clearance response, 97 (28.1%) showed a moderate response, and 21 (6.1%) showed a mild response.

***Conclusion*** Overall, these studies suggest that intralesional vitamin D3 injections are effective in the treatment of common warts.

***Key words***
Common warts; Intralesional treatment; Vitamin D3; Efficacy.

## Introduction

Verruca vulgaris, also known as common warts, is a common skin condition affecting the skin and mucosa.[1] Despite the availability of various treatment options with varying levels of efficacy, 65-78% of warts resolve spontaneously within two years.[2] Topical keratolytics, electrocoagulation, cryotherapy, and laser therapy are common local methods for eliminating warts, but they are often associated with discomfort, scarring, and repeated episodes.[3] The treatment of warts using immunotherapy, such as the MMR vaccine, PPD, Mycobacterium vaccine, and Candida antigen, has been investigated.[4] However, the effectiveness of topical derivatives of Vitamin D for treating warts is still being investigated. In a study conducted by Aktas *et al*. in 2015, the intralesional injection of Vitamin D3 was used for the first time to treat plantar warts, and

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80.6% of patients achieved complete resolution of the warts.[5] The objective of the study was to evaluate the effectiveness of intralesional Vitamin D in the treatment of common warts.

## Methodology

This single-blind, uncontrolled, open-label experimental trial was conducted at JPMC Karachi, from August 9, 2019, to October 8, 2022. The study received clearance from the Institutional Review Board (Ref. No: F.2-81/2018-GENL/2522/JPMC Dated: 31/8/2018) and 356 eligible patients were enrolled. Sample size was calculated using OpenEpi sample size calculator version3 assuming 95% confidence level, margin of error 5% and 65% complete response reported in Essam *et al*;[6] the required sample size was 356. The study's specifics were explained to each patient, who gave a thorough history and provided written informed consent.

Individuals of both genders, ranging from 12 to 60 years old, who had common warts and had not undergone any topical or destructive therapies for at least six months, were considered eligible for participation. The warts should measure less than 2 cm. Females who were pregnant, nursing, or had previously experienced a hypersensitive reaction to vitamin D3 or the local anesthetic xylocaine were not included in the study.

Throughout the study period, vitamin D3 for injection was supplied by Neutro Pharma (Indrop D) in vials containing 200,000 IU of cholecalciferol in 1 ml. A 27-gauge insulin syringe was used to administer a total of 0.5 ml of vitamin D3 (15 mg/ml) into the base of each wart after injecting lignocaine (20 mg/ml) into the warts. The patients' clinical improvement was assessed every two weeks during four visits by monitoring the reduction in both the number and size of warty lesions. In each session, a maximum of two larger warts were treated. Following treatment, patients were advised to abstain from using any topical or oral drugs. Photographic measurements were taken at the baseline, before each session, and after the completion of treatment to assess the clinical response. Additionally, patients were followed up after 6 months to detect any recurrence of warts.

All demographic data was gathered using a questionnaire, while the location, quantity, size, and classification of warts were recorded at each visit based on the operational definitions. Pictures were taken to support the recorded data at every visit. The data was collected with the approval of the Institutional Review Board.

## Results

A total of 356 individuals were assigned to receive vitamin D3 injections in the trial. However, 8 patients who attended the initial visit were lost to follow-up, while 3 patients who were randomly assigned to receive treatment did not attend the subsequent visits. Eventually, 345 patients completed the study. **Table 1** shows the baseline characteristics of the enrolled patients who completed the study. The study participants were evenly split between genders, with 188 males and 157 females (45.5% each). The patients' ages ranged from 12 to 60 years with a mean age of 27.1±7.6. The number of warts ranged from 6 to 20 with a mean of 7.3±5.8, and their average duration was 2.9±1.1 years, ranging from two to four years.

**Table 1** Demographic and clinical data (n=345).

| | |
|---|---|
| Male/Female Ratio | 1.2:1 |
| Mean age in years (range) | 27.1±7.6 (12-60 years) |
| Mean duration of disease in years (range) | 2.9±1.1 (2-4 years) |
| Mean number of warts (range) | 7.3±5.8 (6-20 years) |
| Mean number of Injections | 2.93±0.60 |

**Table 2** Clinical response after 4 sessions of intralesional vitamin D3.

| *Clinical Response* | *n(%)* |
|---|---|
| Complete clearance (100%) | 211 (61.2) |
| Moderate response (50 % to <100%) | 97 (28.1) |
| Mild response (<50 %) | 21 (6.1) |

**Table 3** Side effects in study participants.

| *Side Effects* | *n(%)* |
|---|---|
| Pain at the time of injection | 268 (77.7) |
| Transient Edema | 10 (2.9) |
| Transient Swelling | 276 (80) |
| Depigmentation | 21(6.1) |
| Mild Erythema | 17(5) |

In the study group, a mean of 2.89±0.57 intralesional injections were needed for full clearance of warts. Out of the 345 patients with common warts complete clearance was seen in 211 (61.2%) of patients. **Table 2** presents the clinical response of intervention. The clinical response is categorized into three levels: complete clearance (100%), moderate response (50% to <100%), and mild response (<50%).

According to the **Table 2**, out of the total number of individuals who received the intervention (n=345), 211 (61.2%) showed a complete clearance response, 97 (28.1%) showed a moderate response, and 21 (6.1%) showed a mild response. This indicates that the intervention was effective in producing a high percentage of complete clearance responses, which is the desired outcome. In the study group, 268 patients (77.7%) of the 345 patients who experienced side effects at the injection site had minor pain and edema, which resolved on its own within two weeks. Twenty one (6.1%) patients experienced depigmentation. Recurrence was seen in five (1.5%) patients after a follow-up of 6 months. There were no fatal consequences observed during the study.

## Discussion

The findings of this study demonstrated that the intralesional injection of vitamin D3 was an effective treatment for common warts. It required a mean of 2.93±0.60 injections to achieve full clearance in the study group, which is consistent with previous studies suggesting that multiple injections may be necessary for effective treatment. These results align with previous studies exploring the efficacy of vitamin D3 in treating cutaneous warts. For instance, a study by Al-Dhalimi *et al*. found that intralesional injection of vitamin D3 was effective in treating common warts, with an overall success rate of 87.5%.[7] However, the results of this study differed from a previous study by Al-Zahrani *et al;* which investigated the effectiveness of intralesional injection of calcipotriol for treating cutaneous warts. That study indicated that calcipotriol was more effective than vitamin D3, with an overall success rate of 97.6%.[8]

In various studies, including a placebo-controlled trial conducted by Gupta *et al;* the effectiveness of intralesional vitamin D3 injection has been demonstrated in treating warts. Amiri *et al*. and Aghaei *et al*. reported complete clearance rates of 74.3% and 80%, respectively, while Gupta's study showed a complete clearance rate of 81.8% of patients.[9-11] Another study conducted by Asilian *et al*. using a randomized, double-blind, placebo-controlled experiment found that intralesional vitamin D3 injections resulted in complete eradication of common warts in 71.4% of patients.[12]

Khodaeiani *et al*. found that 75% of patients treated with intralesional vitamin D3 injections experienced complete clearance of their warts.[13] Salem *et al*. reported a full clearance rate of 76.5% in their study on treating common warts with intralesional vitamin D3 injections.[14] Alghamdi *et al*. observed complete clearance of warts in all 11 patients in their case series who received intralesional vitamin D3 injections.[15] In Abdollahimajd *et al*.'s study, 100% full

clearance rate was observed with intralesional vitamin D3 injections for the treatment of plantar warts.[16] Sardana *et al*. reported an 85.7% full clearance rate for treating plantar warts with intralesional vitamin D3 injections.[17] Bassam *et al*. reported a full eradication rate of 85% for plantar warts using intralesional vitamin D3 injections.[18] Hajiagha *et al*. found that intralesional vitamin D3 injections were effective in treating resistant warts, with a complete clearance rate of 86.7%.[19] Garg *et al*. reported a complete clearance rate of 75% for common warts treated with intralesional vitamin D3 injections.[20]

According to a retrospective study conducted by Lim *et al;* intralesional vitamin D3 injections were found to be effective in treating stubborn warts, achieving a complete clearance rate of 80.5%.[21] In another randomized controlled trial by Hemmat *et al;* the efficacy of intralesional vitamin D3 injections and cryotherapy for the treatment of common warts were compared. The study showed that both treatments were effective, with a complete clearance rate of 85.2% and 83.3%, respectively.[22]

Overall, these studies suggest that intralesional vitamin D3 injections are effective in the treatment of common warts, with success rates ranging from 71.4% to 100%. However, it is important to note that some studies have reported lower success rates for intralesional vitamin D3 injections compared to other treatment modalities, such as calcipotriol and cryotherapy.

## Conclusion

Overall, the results of this study provide valuable insight into the effectiveness and safety of intralesional injections of vitamin D3 as a treatment for common warts. While further research is needed to confirm these findings and determine the optimal dose and frequency of injections, these results suggest that vitamin D3 injections may be a viable treatment option for patients with common warts.

***Limitations of Study*** However, there are also differences between our study and previous studies. Our study used a higher dose of vitamin D3, with 200,000 IU in 1 ml compared to previous studies that have used lower doses ranging from 40,000 to 100,000 IU per injection. Our study also used a different method of administration, using a 27-gauge insulin syringe to slowly inject 0.5 ml of vitamin D3 into the base of each wart, compared to previous studies that have used other methods such as a tuberculin syringe.

Another difference is the inclusion and exclusion criteria. Our study included patients of both sexes, aged between 12 and 60 years, with warts less than 2 cm in size, while previous studies have had different inclusion criteria such as limiting the study to only one gender or age group.

It is important to note that the differences in the results of these studies may be due to various factors, such as differences in the patient population, the type and dose of medication used, and the method of administration. Further research is needed to fully understand the efficacy of vitamin D3 in the treatment of cutaneous warts and to compare it with other treatments.

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