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Role of Intralesional Vitamin D3 in the Treatment of Cutaneous Warts - At a Tertiary Care Center in Central Karnataka

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Abstract: ***Background: Cutaneous warts are common benign epidermal proliferations caused by human papillomavirus (HPV) infection. Although several treatment modalities are available, none is universally effective and recurrence remains a challenge. Intralesional Vitamin D3 has emerged as a promising immunotherapeutic option owing to its immunomodulatory properties and favorable safety profile. Objectives: To evaluate the efficacy and safety of intralesional Vitamin D3 in the treatment of cutaneous warts and to assess recurrence during follow-up. Methods: A prospective interventional study was conducted on 25 patients with cutaneous warts who fulfilled the inclusion and exclusion criteria. Intralesional Vitamin D3 was administered at two-week intervals until complete clearance or for a maximum of four sessions initially, with additional sessions provided when required. Clinical response was assessed at each visit and categorized as complete clearance, partial response, or poor/no response. Adverse effects and recurrence were recorded during a 6-month follow-up period. Results: The mean age of the study participants was 27.6 ± 9.4 years, with the majority belonging to the 21–30 years age group (44%). Males constituted 56% of the study population. Common warts were the most frequent clinical subtype (52%), followed by plantar (28%), periungual (12%), and flat warts (8%). Complete clearance was achieved in 18 patients (76%), while 5 patients (16%) showed a partial response and 2 patients (8%) demonstrated poor or no response. Most patients achieved clearance within 2–3 treatment sessions, with a mean of 3.1 ± 1.1 sessions required for complete resolution. Common warts showed the highest complete response rate (84.6%). Pain during injection was the most common adverse effect (88%), followed by swelling (76%) and erythema (72%). One patient (4%) developed keloid. No serious systemic adverse effects were observed. During the 6-month follow-up period, recurrence was noted in one patient (4%). Conclusion: Intralesional Vitamin D3 is an effective, safe, and well-tolerated therapeutic modality for cutaneous warts, producing high clearance rates with minimal adverse effects and low recurrence. It may serve as a useful alternative treatment option for patients with cutaneous warts.***

Keywords: Cutaneous warts; Intralesional Vitamin D3; Immunotherapy; Human papillomavirus; Wart clearance; Recurrence.

1. Introduction

Warts or verrucae are benign epidermal proliferations of the skin and mucosa caused by human papillomavirus (HPV). They are among the most common dermatological conditions encountered in clinical practice and can affect individuals of all age groups. Cutaneous warts may present as common, plantar, flat, filiform, or periungual lesions depending on the site and HPV subtype involved. Although many lesions remain asymptomatic, some may become painful, cosmetically disfiguring, and psychologically distressing, thereby affecting the quality of life of patients[1, 2].

Spontaneous resolution occurs within two years in approximately 65–78% of cases due to host immune response[1]. However, most patients seek treatment because of persistence of lesions, cosmetic concerns, pain, and recurrence. Various modalities including topical agents such as salicylic acid, trichloroacetic acid, silver nitrate, and phenol, as well as physical destructive methods like electrocoagulation, cryotherapy, and laser therapy, are available for the treatment of warts[3, 4]. Despite the availability of several treatment options, recurrence and incomplete clearance remain major therapeutic challenges.

Immunotherapeutic modalities are becoming increasingly popular in the treatment of warts because they stimulate host cell-mediated immunity to eliminate the virus rather than merely destroying the visible lesions[5]. Immunotherapy has the additional advantage of clearing both treated and distant untreated lesions with a lower recurrence rate compared to conventional destructive methods.

Several immunotherapeutic agents have been used via topical, intralesional, and systemic routes in the treatment of warts. These include imiquimod, Mycobacterium w vaccine, Bacillus Calmette–Guérin (BCG) vaccine, measles-mumps-rubella (MMR) vaccine, Candida antigen, Trichophyton antigen, tuberculin, zinc, cimetidine, levamisole, HPV vaccine, and autoimplantation therapy[6, 7]. Among these newer modalities, intralesional Vitamin D3 has emerged as a promising therapeutic option because of its immunomodulatory and antiproliferative properties. Vitamin D3 enhances innate immunity by regulating epidermal cell proliferation and differentiation and by modulating cytokine production, thereby contributing to viral clearance. Intralesional Vitamin D3 therapy is simple, minimally invasive, cost-effective, and associated with fewer adverse effects compared to conventional destructive procedures. However, limited studies are available regarding

its efficacy and safety in the treatment of cutaneous warts, particularly in the Indian population. Hence, the present study is undertaken to evaluate the efficacy of intralesional Vitamin D3 in the treatment of cutaneous warts.

2. Materials and Methods

The present study was conducted among patients attending the Outpatient Department of Dermatology at Chigateri General Hospital and Bapuji Hospital attached to J.J.M. Medical College. This was a prospective interventional study conducted over a period of one year from November 2024 to October 2025. A total sample size of 25 patients was included in the study using convenient sampling. All patients meeting the inclusion and exclusion criteria and willing to participate during the study period were enrolled.

Patients with clinically diagnosed cutaneous warts who were willing to participate in the study were included. Pregnant and lactating women, immunosuppressed individuals, and patients with known allergy to Vitamin D3 were excluded from the study.

After obtaining approval from the Institutional Ethical Committee, written informed consent was obtained from all study participants prior to enrolment.

Diagnosis of cutaneous warts was made based on clinical history and examination findings. Baseline assessment was performed during the first visit, and clinical photographs were taken at each follow-up visit to document treatment response. Clinical response was assessed by recording reduction in the number and size of warty lesions at 2-week intervals for a maximum of four treatment sessions and during follow-up at 6 months after the final injection. Larger warts were selected for injection. Treatment sessions were repeated every 2 weeks up to a maximum of four injections. In patients achieving complete clearance before four sessions, treatment was discontinued and follow-up was continued to assess recurrence.

Vitamin D3 injection was administered using vials containing 6,00,000 IU of cholecalciferol in 1 ml (15 mg/ml). Initially, 0.2 ml of lignocaine (20 mg/ml) was injected into the selected wart, followed after a few minutes by slow intralesional injection of 0.2 ml of Vitamin D3 at the base of the wart using a 27-gauge insulin syringe. Patients were advised not to use any topical or systemic medications for warts during the study period.

The collected data were entered into Microsoft Excel and analyzed using SPSS version 25.0. Descriptive statistics such as proportion, mean, standard deviation, and standard error were used wherever appropriate. Inferential statistical tests including independent t-test and Chi-square test were applied for analysis, and a p-value of less than 0.05 was considered statistically significant.

3. Results

A total of 25 patients with cutaneous warts who satisfied the inclusion and exclusion criteria were enrolled in the study. The age of the participants ranged from 12 to 52 years, with a mean age of 27.6 ± 9.4 years. The majority of patients belonged to the 21–30 years age group. Males constituted a slight majority of the study population.

Common warts were the most frequently encountered clinical type, followed by plantar warts, periungual warts, and flat warts. The duration of warts before treatment ranged from 2 months to 3 years, with most patients presenting within the first 6 months of disease onset.

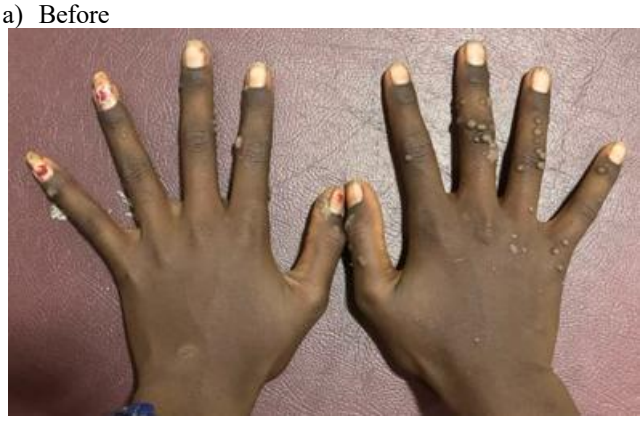
Clinical response was assessed at regular two-week intervals following intralesional Vitamin D3 therapy. A favorable therapeutic response was observed in the majority of patients. Among the 18 patients who achieved complete clinical clearance, 2 responded after one session, 5 after two sessions, 7 after three sessions, 3 after four sessions, and 1 after six sessions. Most patients attained complete clearance after two to three treatment sessions, although some required additional sessions to achieve complete resolution. The mean number of treatment sessions required for complete clearance was 3.1 ± 1.1.

When treatment outcomes were analyzed according to wart type, common warts demonstrated the best response to therapy, with most patients achieving complete clearance. Periungual and flat warts also showed encouraging responses, whereas plantar warts exhibited comparatively lower clearance rates and accounted for the majority of partial and non-responders.

Intralesional Vitamin D3 therapy was generally well tolerated. The most commonly reported adverse effect was pain at the injection site. Local reactions such as swelling and erythema were also frequently observed but were mild and self-limiting. One patient developed keloid formation following treatment. No serious systemic adverse effects or treatment-related complications were recorded during the study period.

Patients were followed up for six months after completion of therapy to assess recurrence. The majority of patients remained free of recurrence throughout the follow-up period. Recurrence was observed in only one patient, occurring at the same site approximately two months after complete clearance. A small proportion of patients were lost to follow-up.

a) Before



b) After

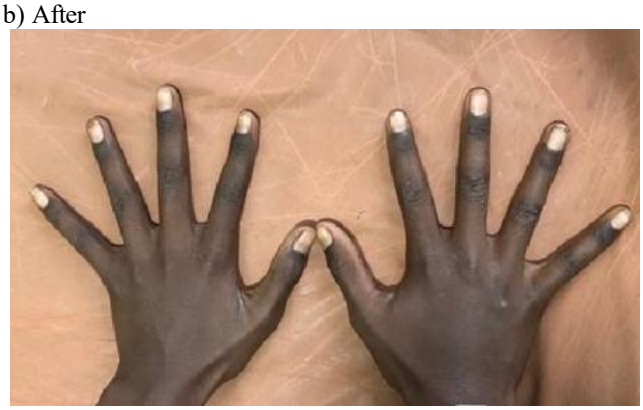
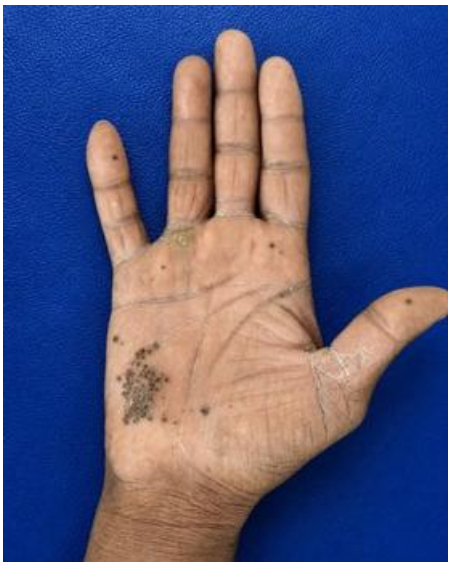


Figure 1: (a, b) Common warts before IL Vit d3 treatment. Complete resolution after four sessions of IL Vit D3.

a) Before



b) After

Figure 2: (a, b) Multiple Palmar warts before IL Vit d3 treatment. Complete resolution after two sessions of IL Vit D3.

Table 1: Baseline Characteristics of Study Participants (n = 25)

Variable		Number (%)
Age group (years)	<20	5 (20)
	21–30	11 (44)
	31–40	6 (24)
	>40	3 (12)
Gender	Male	14 (56)
	Female	11 (44)
Type of wart	Common warts	13 (52)
	Plantar warts	7 (28)
	Periungual warts	3 (12)
	Flat warts	2 (8)
Duration of warts before treatment	<6 months	10 (40)
	6–12 months	8 (32)
	>12 months	7 (28)

Table 2: Treatment Response According to Type of Wart

Type of Wart	Complete Response	Partial Response	No Response
Common warts (n=13)	11	1	1
Plantar warts (n=7)	4	2	1
Periungual warts (n=3)	2	1	0
Flat warts (n=2)	1	1	0

Table 3: Adverse Effects Observed Following Intralesional Vitamin D3 Therapy

Adverse Effect	Number (%)
Pain during injection	22 (88)
Swelling	19 (76)
Erythema	18 (72)
Keloid formation	1 (4)
Systemic adverse effects	0 (0)

Table 4: Recurrence During Follow-up

Follow-up Outcome	Number (%)
Recurrence present	1 (4)
No recurrence	19 (76)
Lost to follow-up	5 (20)
Total	25 (100)

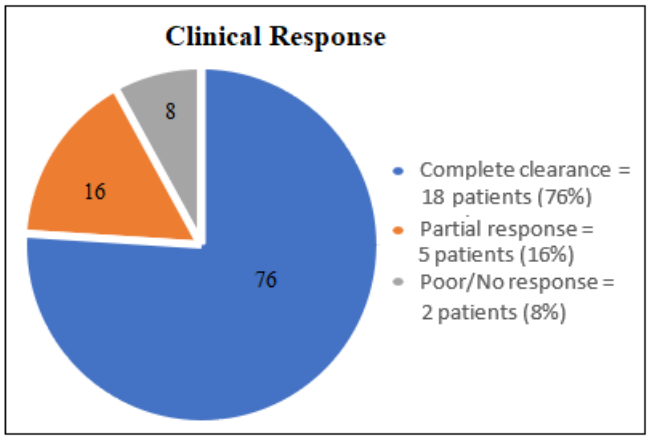


Figure 1: Clinical Response to Intralesional Vitamin D3 Therapy (n = 25)

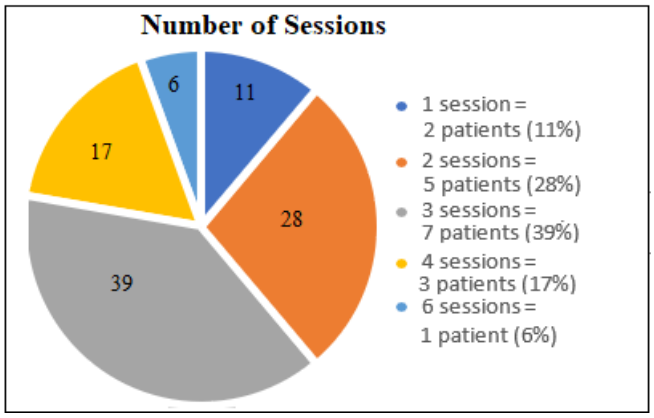


Figure 2: Number of Treatment Sessions Required

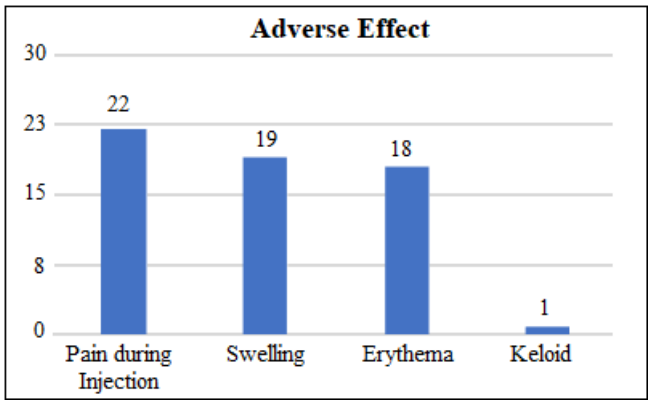


Figure 3: Adverse Effects Observed Following Intralesional Vitamin D3 Therapy

4. Discussion

Demographic Characteristics

In our study, the majority of patients belonged to the 21–30 years age group (44%), with a mean age of 27.6 ± 9.4 years, and males constituted 56% of the study population. Similar findings were reported by Manikandan et al.[9], where the mean age was 27 years and 46.67% of patients belonged to the 21–30 years age group, with males accounting for 63.33% of cases. Sharma et al.[12] and Munshi et al.[13] also reported comparable mean ages of 25 and 29 years, respectively, with male predominance of 69.1% and 76%. Al-Sabak et al.[8], Kavya et al.[10], and Abdel-Azim et al.[15] reported relatively younger study populations, with mean ages of 20.1 ± 12.8, 20, and 21.8 ± 9.9 years, respectively. Male predominance was a consistent finding across most studies, ranging from 56.3% to 90%, although Al-Sabak et al.[8] reported a female predominance (65%). These observations suggest that cutaneous warts predominantly affect young adults and are more common among males.

Clinical Profile of Warts

In our study, common warts were the predominant clinical subtype (52%), followed by plantar warts (28%), periungual warts (12%), and flat warts (8%). Similar findings were reported by Al-Sabak et al.[8], who observed common warts in 71.6% of lesions, and by Manikandan et al.[9], Sharma et al.[12], Munshi et al.[13], and Latif et al.[14], who reported common warts or verruca vulgaris in 56.67%, 76.5%, 58%, and 56.1% of cases, respectively. In contrast, palmoplantar warts were the predominant subtype in the studies by Kavya et al.[10] (54.8%) and Suganthi et al.[11] (60%). These findings indicate that common and palmoplantar warts constitute the majority of lesions encountered in clinical practice.

Duration of Disease

In our study, the duration of warts ranged from 2 months to 3 years, with 40% of patients presenting within 6 months of onset. Similar findings were reported by Suganthi et al.[11], where 50% of patients presented within 6 months. Manikandan et al.[9] reported a mean disease duration of 8.13 months, with 53.33% of patients having lesions for 7–12 months. Sharma et al.[12] and Kavya et al.[10] reported mean durations of 6 months, whereas Latif et al.[14] and Abdel-Azim et al.[15] reported shorter mean durations of 4.46 ± 2.58 months and 4.88 ± 2.17 months, respectively. Al-Sabak et al.[8] observed a longer mean disease duration of 1.4 ± 0.8 years. These findings suggest that intralesional Vitamin D3 therapy has been studied across patients with both relatively recent and long-standing disease.

Therapeutic Response

In our study, complete clearance was achieved in 76% of patients (18/25), while 16% (5/25) showed partial response and 8% (2/25) showed poor or no response. Comparable clearance rates were reported by Al-Sabak et al.[8] (81.9%), Kavya et al.[10] (78.6%), and Suganthi et al.[11] (75%). Slightly lower complete clearance rates were reported by Munshi et al.[13] (70%), Manikandan et al.[9] (66.67%), Latif et al.[14] (65.85%), and Sharma et al.[12] (63.63%). Abdel-Azim et al.[15] reported complete clinical and dermoscopic clearance in 56.25% of patients, while 28.13% failed to respond. Despite variations in study populations and methodologies, the majority of studies demonstrated complete clearance rates exceeding 60%, supporting the efficacy of intralesional Vitamin D3 in the treatment of cutaneous warts.

Treatment Sessions Required

Among the 18 patients who achieved complete clinical clearance, 2 (11%) responded after one session, 5 (28%) after two sessions, 7 (39%) after three sessions, 3 (17%) after four sessions, and 1 (6%) after six sessions. In our study, most patients achieved complete clearance within 2–3 treatment sessions (60%), with a mean of 3.1± 1.1 sessions.

Similar findings were reported by Kavya et al.[10] and Munshi et al.[13], who observed a mean of three treatment sessions for complete clearance. Abdel-Azim et al.[15] reported a mean of 3.56 ± 0.76 sessions, whereas Sharma et al.[12] and Latif et al.[14] reported a mean requirement of four sessions. Al-Sabak et al.[8] demonstrated progressive improvement with treatment, with cumulative complete clearance rates of 12.7%, 29.9%, 54.9%, and 81.9% after the first, second, third, and fourth sessions, respectively. Suganthi et al.[11] reported that 30% of complete responders achieved clearance after two sessions. These findings suggest that most patients achieve optimal clinical outcomes within three to four treatment sessions.

Response According to Wart Type

In our study, common warts demonstrated the highest complete clearance rate (84.6%), followed by periungual warts (66.7%), plantar warts (57.1%), and flat warts (50%). The better response observed in common warts may be

related to their relatively superficial location and easier diffusion of intralesional Vitamin D3, whereas plantar warts often require deeper penetration because of thick stratum corneum.

Al-Sabak et al.[8] reported the highest response among periungual warts (100%), followed by plantar warts (91.5%) and common warts (77.4%), with wart type significantly influencing treatment outcome ($p<0.001$). Suganthi et al.[11] observed complete clearance in 100% of plane warts, 75% of palmoplantar warts, 70% of common warts, and 66.7% of periungual warts. Kavya et al.[10] reported complete clearance in 82.6% of palmoplantar warts and 77.8% of verruca vulgaris. Similarly, Latif et al.[14] observed complete response rates of 71.4% for plantar warts, 69.6% for verruca vulgaris, and 54.5% for periungual warts. These findings indicate that intralesional Vitamin D3 is effective across different wart subtypes, although response rates may vary according to the lesion type.

Adverse Effects

In our study, pain during injection was the most common adverse effect (88%), followed by swelling (76%) and erythema (72%).

Similar findings were reported by Munshi et al.[13], where pain during injection occurred in 86% of patients. Swelling was the most frequently reported adverse event in studies by Kavya et al.[10] (78.6%), Al-Sabak et al.[8] (53.8%), and Manikandan et al.[9] (36.67%). Other reported adverse effects included itching (38.5%) and dyspigmentation (7.7%) in the study by Al-Sabak et al.[8], induration (20%) and erythema (5%) in the study by Suganthi et al.[11], and nodule formation (58.2%) in the study by Sharma et al.[12]. Keloid formation was observed in one patient (4%) in our study and similarly reported in one patient by Latif et al.[14]. Importantly, no serious systemic adverse effects were reported in our study or in the majority of previous studies, highlighting the favorable safety profile of intralesional Vitamin D3 therapy.

Recurrence During Follow-up

In our study, recurrence was observed in only one patient (4%) during the 6-month follow-up period. Similar findings were reported by Kavya et al.[10] and Suganthi et al.[11], who each observed recurrence in one patient. Latif et al.[14] reported recurrence in 2 patients (4.88%) during a 3-month follow-up period, while Munshi et al.[13] observed recurrence in 10% of patients. Sharma et al.[12] reported recurrence in four patients after treatment. In contrast, Abdel-Azim et al.[15] reported no recurrence during 6 months of follow-up. The consistently low recurrence rates observed across studies suggest that intralesional Vitamin D3 provides sustained clinical remission following successful wart clearance.

5. Conclusion

The present study demonstrated that intralesional Vitamin D3 is an effective, safe, and well-tolerated therapeutic modality for the treatment of cutaneous warts. A majority of the patients showed complete clearance of lesions with minimal adverse effects and low recurrence rates during follow-up. Common warts showed better therapeutic response compared to other types of warts. The immunomodulatory action of Vitamin D3 appears to play an important role in achieving viral clearance and reducing recurrence. Owing to its simplicity, cost-effectiveness, and favorable safety profile, intralesional Vitamin D3 may be considered a promising alternative treatment option for cutaneous warts.

The limitations of the present study include the small sample size, single - centre design, absence of a control group and relatively short follow-up period.

However, further studies with larger sample sizes and longer follow-up periods are required to validate these findings and establish standardized treatment protocols.

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