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A Study of Effectiveness of Intralesional Vitamin D3 in Treatment of Multiple Cutaneous Warts

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Abstract: *VerrucaVulgaris (viral warts) is a fairly common condition with manytherapeutic options having variable success rates. Few warts are refractory to treatment with often disappointing response and high recurrence. Intralesional immunotherapy has gained importance due to its effectiveness in clearing both treated and distant warts by stimulating the cell-mediated immunity against human papillomavirus.*
Aims and objectives: *This study aims to evaluate the effectiveness and safety of intralesional Vitamin D3 injections in the treatment of multiple cutaneous warts.*
Materials and Methods: *Patients with multiple cutaneous warts were selected and Vitamin D3 (0.2-0.4 ml, 15 mg/ml) was injected at the base of warts. The injections were repeated at an interval of3 weeksfor a maximum of 4 sessions or until complete clearance, whichever was earlier. A maximum of 5 warts was treated in one session and patients were followed up for a period of 6 months after the last injection.*
Results: *Sixty patients with multiple cutaneous warts were included in the study who completed the 6-month follow-up period and were available for analysis. Of these, 36 had palmoplantar warts, 12 had verruca vulgaris,6 patients had periungual warts and 6 patients had filiform warts. In total, 48 of 60 patients (80%) showed a complete response, 6 patients (10%) showed moderate response and 6 patients (10%) showed a mild or no response. Recurrence was seen in 4 patients. No serious adverse effects were reported.*
Conclusion: *Intralesional Vitamin D3 is effective and safe for the treatment of multiple cutaneous warts.*
Keywords:*Cutaneous Warts, Intralesional, Vitamin D3,Immunotherapy.*

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I. Introduction

Warts or verrucae are benign epidermal proliferations of the skin and mucosa caused by human papillomavirus (HPV1,2,4,27,57). Although spontaneous resolution occurs within 2 years in 65%–78% of warts, most patients seek treatment of warts as they are cosmetically disfiguring and sometimes painful, especially on the soles.[1] Local destruction of warts is a commonly employed treatment modality performed by using either electrocoagulation, cryotherapy,laser therapy ortopical keratolytics like salicylic acid, trichloro acetic acid.[2],[3],[4],[5] All these treatment options can be painful and may be associated with scarring and frequent recurrences. In addition, destructive modalities are not suitable for the treatment of multiple warts as they clear only treated lesions and has no effect on the distant ones. In order to improve outcome, intralesional immunotherapy is being tried widely for the treatment of multiple cutaneous warts over the last few years. It acts on the basic principle of enhancing the cell-mediated immunity against human papilloma virus and results in clearance of warts.[6] Various agents have been tried for intralesional immunotherapy including measles, mumps, rubella vaccine (MMR) ,Bleomycin ,Tuberculin purified protein derivative (PPD); *Mycobacterium* w vaccine and *Candida* antigen.[7],[8],[9],[10]

Few studies have been published showing the efficacy of topical Vitamin D3 derivatives in the treatment of warts.[11],[12] However, intralesional Vitamin D3 injection was tried first time by Aktas *et al*. for the treatment of plantar warts and reported improved results.[13]

II. Material And Methods

This is a prospective observational study conducted on 60 clinically diagnosed cases of cutaneous warts attending DVL OPD,Government General Hospital, Vijayawada betweenJanuary 2017 to June 2018.

Exclusion criteria consisted of mucosal warts, pregnancy, lactation, or immunosuppression.

They were also instructed not to use any other wart therapies duringthe study period. The characteristics of warts such as type, size, number, presence or absence of side effects, and clinical photographs were recorded at the start of the study and at each follow-up visit. Using an Insulin syringe with the bevel facing upward, 0.2 to 0.4 mL vitamin D3 solution (600,000 IU; 15 mg/mL) was slowly injected into the base of each

wart. A maximum of 5 warts were injected per session. The injections were performed at 3 weekly intervals until complete resolution or for a total of 4 sessions.

Depending on the decrease in wart size, the response rate was classified as complete response , moderate response , or mild response . The response was considered Complete or 100% if they showed a complete disappearance, moderate if some remained unchanged or regressed in size more than 50%, and mild or no response if the improvement was less than 50%. Patients were followed up for a period of 6 months after the last injection to detect any recurrence. Before starting treatment, Informed consent wastaken from each patient and institutional ethics committee clearance was obtained. Appropriate statistical tests were applied to analyse the results. The results were statistically significant with a p-value less than 0.05.

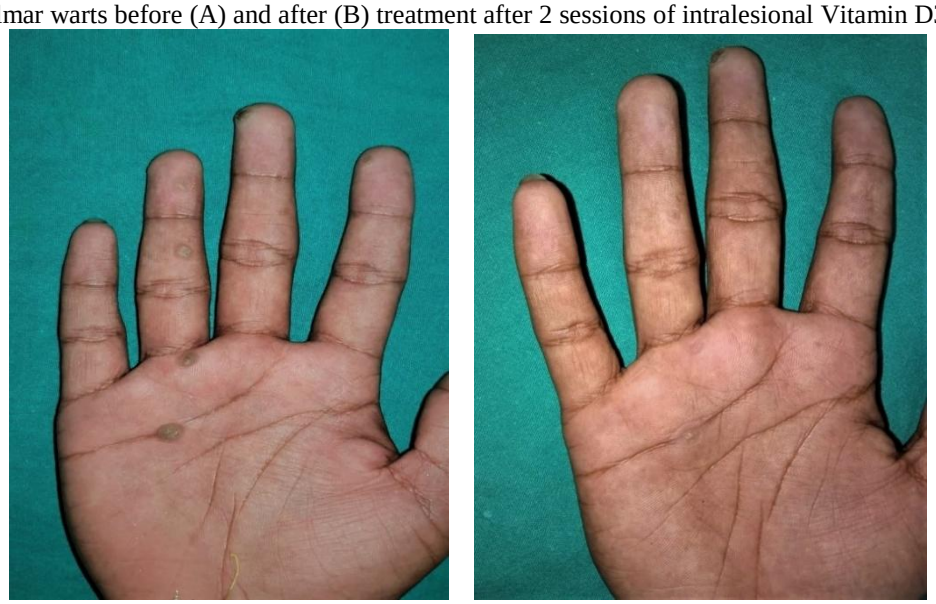
III. Results

Amongst the 60 patients enrolled 40 were males and 20 were females. Of these, 36 (60%) patients had palmoplantar warts, 12 (20%) had common warts, 6(10%) had periungual warts, and 6 (10%) patients had filiform warts. The mean age of the patients was 31 years (range, 10-60 years). The number of warts ranged from 1 to 30 (mean, 10). The duration of warts was a minimum of 6 months to a maximum of 5 years, with the mean duration being 15 months. The dimensions of the lesion ranged from 2 × 2 mm to 20 × 30 mm. 24(36%) patients had distant warts. Complete clearance was seen in 48 out of 60 patients (80%), the moderate response in 6 patients (10%), and mild in 6 patients (10%). The average number of injections required for total disappearance in the CR group was 3.66. All 24 patients with distant warts showed resolution of both primary and distant lesions.

Adverse effects were minor with no life-threatening complications. Pain during injection was seen in almost all cases , swelling at the site of injection was the second most common adverse effect seen in 36 (60%) patients which resolved later spontaneously in 4 - 6 weeks.

The patients were followed up for a period of 6 months following the last injection, during which 4 (6.66%) patients showed recurrence.

Figure 1. Palmar warts before (A) and after (B) treatment after 2 sessions of intralesional Vitamin D3 injections



A B

Figure 2. Cutaneous warts before (A) and after (B) treatment after 3 sessions

A B

Figure 3.Swelling of fingers following intralesional Vitamin D3 injection

IV. Discussion

Multiple cutaneous warts are difficult to treat, especially palmoplantar warts which cause morbidityand needs multiple sittings by destructive methods such as cryotherapy and electrocautery. These destructive procedures are usually associated with scarring, pigmentation and has no effects on distant warts. In addition, some warts are resistant to these treatments and the recurrence rate is also high. Hence, immunotherapy is the best available option in treating multiple warts as it boosts the immune system against HPV virus leading to clearance of both treated and untreated warts. Recurrence rate is also low when compared to destructive methods[1,15]. Immunotherapy has been tried with various antigens and vaccines such as bleomycin, PPD, MMR, Candida albicans and Mycobacterium w vaccine.

In this present study, we used intralesional Vitamin D3 injections which was a relatively new treatment option for warts. Intralesional immunotherapy reportedly causes the resolution of these longstanding benign proliferations at the primary as well as distant sites. The exact mechanism of immunotherapy has not been completely elucidated but is believed that the injection to the HPV-infected tissue induces a strong nonspecific proinflammatory signal and attracts the antigen-presenting cells. This is associated with the release of different cytokines such as IL-2, IL-8, IL-12, IL-I8, tumor necrosis factor–α, and interferon-γ. Significant peripheral mononuclear cell proliferation promotes a Th1 cytokine response. This successively activates the cytotoxic T cells and natural killer cells to eradicate the HPV-infected cells[16].Furthermore, the trauma of the injection may cause resolution in previously sensitised individuals.

Aktas et al[13]. used intralesional Vitamin D3 for plantar warts. Twenty patients were included in the study, and 7.5 mg of Vitamin D3 injection was given at monthly intervals for a maximum of 2 sessions. They reported complete clearance in 80% of patients at the end of 8 weeks. The results were similar to our study.

An Open Uncontrolled Trial conducted by Kavya, et al[14] "Safety and Efficacy of Intralesional Vitamin D3 in Cutaneous Warts" used intralesional vitamin D3 for various cutaneous warts and the positivetherapeutic effect was seen in 78.6% cases.The results were comparable to our study

Raghukumar et al [15] used intralesional vitamin D3 in treatment recalcitrant warts and complete clearance was seen in 90% of patients.

Treatment response in various types of Warts

Clinical response	Palmoplantar warts	VerrucaVulgaris	Filiform Warts	Periungual warts	Total
Complete clearance	32	10	2	4	48
Moderate clearance (50% - <100%)	2	2	---	2	6
Mild clearance (50%)	2	---	4	---	6

Comparison with various studies

Study	Number of patients	Type of warts	Treatment	Intervals between sessions	Maximum number of sessions	Adverse effects	Results
Aktas et al [13]	20	Plane warts	Vitamin D3 + lignocaine	4 weeks	2	Pain	CR-80% R-0
Kavya et al [14]	42	VerrucaVulgaris Palmo plantar warts	Vitamin D3 + lignocaine	2 weeks	4	Swelling Pigmentation	CR-78.5%
Present study	60	Veruccavulgaris, Palmoplantar warts, Filiform warts, Periungual warts	Vitamin D3 (6,00,000 IU)	3 weeks	4	Mild to moderate pain, Swelling	CR-80% R-6.6%

CR- Complete clearance
R- Recurrence

V. Conclusion

Intralesional vitamin D3 is a safe, cost-effective treatment option for multiple cutaneous warts.

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