

Therapeutic Outcome and Safety of Intralesional Vitamin D3 in the Treatment of Cutaneous Warts

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Abstract:

Introduction: Cutaneous warts are a common but vexing condition with high recurrence rate and tendency to spread in spite of various therapeutic options. Intralesional immunotherapy is an attractive modality as it has an additional role of clearing both treated and distant warts by stimulating cell-mediated immunity against human papilloma virus.

Aims and Objectives: To evaluate efficacy and safety profile of intralesional Vitamin D3 formulation in the treatment of cutaneous warts.

Materials and Methods: Patients with multiple cutaneous warts were injected intralesionally with Vitamin D3 (0.2 ml, 15 mg/ml) at an interval of 2 weeks for maximum of 4 sessions, and patients were followed up for 6 months.

Results: Of the 106 patients included, complete clearance was seen in 26 (76.4 %) patients of verruca vulgaris, 20 (66.6 %) of palmoplantar warts, 18 (100 %) of plane warts, 6 (50 %) of genital and filiform warts each. Moderate response was seen in 14 (13.2%) patients while mild response was seen in 6 (5.7 %) patients. No response was seen in 10 (9.4 %) patients. No serious adverse effects were reported.

Conclusion: Intralesional Vitamin D3 is effective, safe, cheap and long lasting modality with a short downtime for the treatment of multiple cutaneous warts.

Keywords: Cutaneous Warts Intralesional treatment Vitamin D3 Immunotherapy.

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Introduction

Verrucae (Warts) are common epidermal proliferations caused by human papillomavirus, an epitheliotropic DNA virus. [1] Although spontaneous improvement is seen in 65-78% of cases, the cosmetic disfigurement, recurrent nature and pain (especially on the palms and soles) are frequent reasons for patients seeking treatment. [2] Till recently, local destruction was the commonly employed modality through topical keratolytics, electrocoagulation, cryotherapy, surgical excision or laser therapy. These modalities lead to significant tissue destruction, pain and frequent recurrences. Immunotherapy by various antigens is a new promising modality which has shown to clear both treated and distant warts by mounting a delayed hypersensitivity reaction to the viral antigen. Immunotherapy acts by enhancing cell mediated immunity against HPV, thus helping in clearance of both treated and distant warts. [3] The primary objective of this study was to evaluate the efficacy of intralesional vitamin D3 for the treatment of warts. The secondary objectives were

to study the side effect profile, correlation of efficacy with the wart subtype, correct dosage and median time of efficacy as well as the time of recurrence(if any).

A hospital based prospective interventional study was carried out in the Department of Dermatology of Pacific Institute of Medical Sciences, Udaipur which was followed by per protocol statistical analysis. Data and records of patients (5 – 70 years) with multiple (>= 2) warts over a period of 2 years from 1st April 2021 to 31st March 2023 were studied. Written informed consent of the patients had been taken. Patients whose data was available and who were followed up till 6 months of the last injection were included in the study.

Patients receiving any other treatment for warts, pregnant and lactating females and those with history of immunosuppression or hypersensitivity to Vitamin D3 were excluded from the study. The study was approved by the Institutional Ethical Committee. Method of injection and outcome

evaluation: Vitamin D3 (0.2 ml, 15 mg/ml) was injected into the base of two warts/per session (largest in size) after injecting lignocaine (0.2 ml, 20mg/ml). Injections were repeated every 2 weeks for a maximum of 4 sessions or until complete clearance, whichever was earlier. Patients were followed up for 6 months after the last injection to study for any side effects or recurrence. Serum calcium levels were monitored. Records and data were recorded at treatment session for resolution of the treated wart and the distant warts, reduction in the size and number of warts and any immediate or delayed complications or side effects. Results were graded as complete clearance, moderate response, mild response and no response by comparing with the baseline clinical photographs. Complete clearance implied clearance of all distant and treated warts, moderate response denoted 50-100% reduction in size and/or number of warts, while mild response indicated 1- 50% reduction in size and/or number of warts. Patients showing no reduction in size or number of warts after 4 injections were classified as no response. After completion of the 4 sessions or in case of complete clearance before completion of the sessions, patients were followed up for 6 months (at two monthly interval) to look for recurrence or any delayed complication

Results

The study included 106 patients including 58 males and 48 females (M: F- 1.2: 1). Patients ranged from 6 – 65 years with a mean of 28.64 years. The number of warts ranged from 2 to 26 warts with a mean of 10.28 warts. Of the 106 patients, 34 (32.08 %) had verruca vulgaris, 30(28.03 %) had palmoplantar warts, 18(16.98 %) had plane warts and 12(11.32%) had genital and filiform warts each.

Complete clearance was seen in 76.4 % of verruca vulgaris, 66.6 % of palmoplantar warts, 100 % of plane warts and 50 % of genital and filiform warts each. Moderate response was seen in 13.2% while mild response was seen in 6 patients 5.7 %. No response was seen in 9.4 % Patients of the 76 patients showing complete clearance, 56 required 4 sessions of Vitamin D3, 16 required 3 sessions while 4 patients required only 2 sessions of Vitamin D3 injections. The average number of injections required for complete clearance was 3.68. Complications were seen in 23 patients (18.8%), which included swelling at the site of injection in 16 patients (15.09%) and hyperpigmentation after injection in 4 patients (3.8%). Swelling subsided in 2 -3 weeks without complications. Recurrence was not seen in any patient during the 6 month follow up period. There was no increase in serum calcium level above the normal reference range in any of the patients during the entire study period.

Discussion

Local destructive procedures are the commonly available treatment modality for warts which include electrocautery, lasers or cryotherapy. However, all these procedures are tedious and painful and not practical in case of multiple warts. These also cause destruction of the surrounding tissue and hence may lead to scarring. Moreover, there can be recurrence of warts even after complete removal by these procedures. Hence immunotherapy by use of various agents is a good option for treatment of warts. Immunotherapy acts by boosting immunity to HPV virus as a result of which both treated and distal warts are cleared. [8] Various agents have been used for immunotherapy such as Mycobacterium vaccine, [4] Candida albicans antigen, [5] MMR (measles, mumps, rubella) vaccine, [6] Purified Protein Derivative (PPD) etc. [7] the advantage with immunotherapy is its low recurrence rate compared to the normal destructive procedures.

In the present study, we have used Vitamin D3 for immunotherapy for the treatment of multiple warts. The exact mechanism of action of Vitamin D3 as an immunomodulator is not known. Studies suggest that it can regulate proliferation and differentiation of keratinocytes and hence modulates cytokine production. It inhibits the expression of tumor necrosis factor (TNF)- α , TNF- γ , interleukin-6 (IL-6) and IL-8, mediated through Vitamin D receptor (VDR)-dependent pathway. [9] Hence topical Vitamin D3 has been used in the treatment of warts in various studies. [10,11]

Kavya et. al. Used intralesional vitamin D3 for the treatment of palmoplantar and common warts. [2] A total of 42 patients were included in the study and maximum of 4 injections were given at 2 weekly intervals. They achieved a clearance of 78.6% with recurrence in 2.38% patients. Similarly, Raghukumar et.al. Studied the effect of Vitamin D3 in verruca vulgaris, palmoplantar, filiform and plane warts. [12] Sixty patients were included in the study and a maximum of 4 sessions of Vitamin D3 injections intralesionally were given at 2 weekly intervals. Ninety percent of the patients responded while recurrence was seen in 3.33%. The results of both the studies were similar to our study.

The response rate achieved in our study was 71.7 % in maximum of 4 sessions which was superior to the results achieved with Mycobacterium w vaccine, Candida albicans and MMR vaccine. However, treatment with PPD was superior to that of Vitamin D3, but the complications and side effects during injection were more in the form of pain, severe swelling, eczematous changes, constitutional symptoms like fever and bodyache. However, in our study we did not experience any

major systemic or local side effects requiring any form of treatment. Also, there was no recurrence seen in our study during the 6 month follow up period.

Conclusion

Intralesional Vitamin D3 injection is cheap and effective approach for the treatment of multiple warts. Our study concludes its high efficacy in plane warts followed by verruca vulgarise. It is safe as compared to other immunotherapy agents with no major local or systemic side effects. It can be easily used in children as it is safe and painless compared to other locally destructive procedures.

The limitations of this study were its lack of a control group. However, the results are encouraging. Large well designed; randomised case control study is required to confirm the efficacy of intralesional Vitamin D3 in the treatment of multiple warts.

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