Open Access

Original Article

Efficacy and Safety of Intralesional Vitamin D3 in the Treatment of Plantar Warts

Mahrukh Javed, Moizza Tahir, Sumera Hanif*, Muhammad Sufyan, Najia Ahmed, Atiya Rahman*****

Combined Military Hospital, Multan/National University of Medical Sciences (NUMS) Pakistan, *Lahore Medical & Dental College, Lahore Pakistan, **Pakistan Naval Ship Shifa Hospital, Karachi Pakistan, ***Combined Military Hospital, Lahore/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To explore the effectiveness and safety of intralesional cholecalciferol (vitamin D3) for the treatment of plantar warts.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Tertiary Care Hospital, Multan Pakistan, from Sep 2019 to Aug 2020.

Methodology: Sixty-two patients with warts of varying sizes and duration were included in the study. Intralesional lignocaine was used to anaesthetize the skin. About 0.2ml injection of cholecalciferol (vitamin D3) solution (600,000 IU, 15mg/mL) was injected with a 30-gauge needle to the base of the wart under aseptic measures. A maximum of 4 warts were injected per session at 3-week intervals until resolution or for a maximum of 6 treatments. Patients were followed up for six months after the last injection for recurrence.

Results: Sixty-two patients completed the study, including 45(72.58%), patients who had complete clearance of warts following injection 14(22.5%) which showed partial response and 3(4%) cases had no response.

Conclusions: Intralesional vitamin D3 is a safe and effective treatment for plantar warts.

Keywords: Immunotherapy, Intralesional, Recalcitrant warts, Vitamin D3.

How to Cite This Article: *Javed M, Tahir M, Hanif S, Sufyan M, Ahmed N, Rahman A. Efficacy and Safety of Intralesional Vitamin D3 in the Treatment of Plantar Warts. Pak Armed Forces Med J 2022; 72(6): 2055-2058. DOI: https://doi.org/10.51253/pafmj.v72i6.7559*

INTRODUCTION

Plantar warts or verrucae are caused by human papillomavirus (HPV). Plantar warts are asymptomatic. 2% of the population seeks consulta-tion for its treatment annually. Plantar warts shed HPV, which infects other plantar sites and spreads to others. The pervasive nature of the virus makes it difficult to prevent its spread. Asymptomatic infection of HPV is very common.[1,2]

Treatment modalities of plantar warts are cryotherapy, electrocoagulation, laser therapy, photodynamic therapy, keratolytic-like salicylic acid, immune stimulation and anti-mitotic therapies.[3] However, they are cosmetically disfiguring and sometimes painful, especially on the soles. There is the possibility of spontaneous resolution within two years of treatment in 65%–78% of warts. The destructive treatment modalities for plantar warts are ineffective as recurrences are frequent.[4,5] Therefore, to overcome these shortcomings, during past decades, immuno-therapy has been tried widely to treat warts that act on the basic principle of enhancing cell-mediated immunity.[6] Tuberculin purified protein derivative (PPD), Measles, mumps, rubella vaccine, and Candida albicans antigen immunotherapy have been used to treat warts.[7]

The recurrence of warts is frequently observed. Risk factors for recurrence are age>25 years, increase in size, distribution and duration of warts. In addition, smokers have a five-fold increased risk of recurrence due to its effects on inflammation and immune response.[8,9]

Recently few studies have been published that highlight the efficacy of intralesional Vitamin D3 in the treatment of warts in comparison to cryotherapy.[10] The current study explored the effectiveness of intralesional Vitamin D3 for treating plantar warts and thus finds effective and economical treatment. This study would inform practice in resource-limited health setups.

METHODOLOGY

This prospective longitudinal study was conducted from September 2019 to August 2020 at the Dermatology Department of the Tertiary Care Hospital, Multan Pakistan. The Institutional Ethical Committee approved the study. Patients with the clinical diagnosis of plantar warts during the study period were enrolled by non-probability consecutive sampling technique after informed consent.

Inclusion Criteria: Patients of either gender, with plantar warts and no past treatment in the last six months were included in the study.

Correspondence: Dr Mahrukh Javed, Department of Dermatology, Combined Military Hospital, Multan, Pakistan

Received: 25 Mar 2021; revision received: 02 Feb 2022; accepted: 23 Feb 2022

Exclusion Criteria: Patients of less than 15 years and more than 55 years, pregnant patients, lactation women, patients with immunosuppressive therapies or diseases were excluded from the study.

Demographic data of patients' age, gender, number, size and type of warts were recorded. The plantar wart was cleaned with a 70% alcohol swab. Intralesional 0.2 ml lignocaine (20mg/ml) was then injected. After 2-3 min, 0.2ml of intralesional vitamin D3 600,00IU (15mg/ml) was injected at the base of the wart with a 30-gauge insulin syringe. The patient was advised to follow-up visits at 03 weeks intervals. Each patient was advised to continue the visit till the warts were completely cleared. A maximum of six injections were done 03 weeks apart. Efficacy of treatment was recorded as complete if all warts resolved, moderate for 60 to less than 100% reduction in both size and number of lesions, whereas minimal response was between 1% to 59%. Injections were prescribed for larger warts, and a maximum of 4 were treated at each session. Patients were evaluated for untoward reactions every third week for four sessions and later monthly to record for any recurrence for six months.

Data were analyzed by Statistical Package for the social sciences (SPSS) version 21.00. Descriptive statistics were used for continuous quantitative variables of age, number, duration, number of intralesional vitamin D3 and efficacy of treatment. The chi-square test was employed for treatment response with intralesional vitamin D3. The *p*-value of <0.05 was taken as significant.

RESULTS

Sixty-two patients, including 37(59.67%) males and 25(40.32%) females with plantar warts, were injected with vitamin D3. The mean age of the patients was 20.00±2.02 years. The duration of warts was from one month to 20 years. The distribution of age with the gender of the total patients was shown in Table-I. Wart sizes ranged from 1.5 x 2.5mm to 30x 36mm, respectively.

Table-I: Age and Gender of Patients with Plantar Warts (n=62)

Age Distribution (years)	Gender	
	Male	Female
15-24	23(65.7%)	12(34.3%)
25-34	9(60.0%)	6(40.0%)
35-44	8(80.0%)	2(20.0%)
45-55	2(100.0%)	0(0.0%)

The therapeutic response of plantar warts with vitamin D3 injections was graded as complete in 44(71.0%) cases, moderate in 15(24.2%) and minimum in 3(4.8%) cases. Total of 3 sessions of IL vit D3 were given in 15(24.2%) and 4 sessions in 44(71.0%).Several sessions and therapeutic responses were listed in Table-II. Intralesional Vit D3 therapeutic response in the treatment of plantar warts was effective (*p*-value <0.001).

Table-II: Treatment Response with Intralesional Vit D3 in Plantar Warts (n=60)

Treatment Response	IL Vit D3 Sessions		
	3 n (%)	4 n (%)	*p*-value
Complete Response	18(29.03%)	25(40.30%)	<0.001
Moderate Response	5(8.06%)	10(16.12%)	
Minimum Response	1(1.61%)	1(1.61%)	

The patients were followed up for six months after the last injection, and no patients showed recurrence (Figure-1A & 1B).

Figure-1A: Planter wart 1B.Plantar wart IL Vit D3 Third Session

Twenty-five (40.6%/) had an uneventful recovery. Adverse effects were observed in 37(60.0%) patients. Swelling at the injection site was the most commonly reported adverse effect in 30(75.3%) patients that resolved in three weeks without treatment (Figure-2A&2B).

Figure-2A: Plantar wart 2B: Plantar wart IL Vit D3 injection third Session

DISCUSSION

Human papillomavirus (HPV) causes warts; HPV2/27/57 and HPV11–7 are the most prevalent strains. Most patients are asymptomatic; few may suffer physical or psychological distress.[9] Conventional treatments are used to treat plantar warts. Recently immunotherapy has gained popularity in the treatment of plantar warts. It boosts host immunity so that not only targeted wart but also distant wart is treated. Intralesional vitamin D3 plays an important role in the proliferation and differentiation of keratinocytes. We found complete clearance in 72.58% of plantar warts. *Priya et al.* documented complete clearance of plantar warts in 86.2% of patients following intralesional vitamin D3.[10] Aktas *et al.* in Turkey found 80% clearance of plantar warts with no recurrence.[11] Close to our study, a therapeutic response of Intralesional injections of vitamin D3 with complete resolution was found by Akula *et al.*[12] Potlapati *et al.* found complete resolution of plantar warts in (76.6%), no response in 3.4% of cases.[13] Intralesional vitamin D3 is an effective treatment modality in treating plantar warts. Differences in complete clearance rates are attributed to host immunity and strain of HPV.

The average number of intralesional injections of vitamin D3 was 4 in our study. Ghaly *et al.* in a comparative study of therapeutic response in Egypt in plantar warts, found that intralesional vit.D3 injection was superior to PPD. They documented three sessions four weeks apart as adequate for recalcitrant plantar warts.[14] Raghukumar *et al.* found a treatment response with 3.66 injections, a complete response in 90% of patients in a study conducted in Karnataka state.[15] Differences in the number of vitamin D3 injections are due to host factors such as smoking and ageing, as it reduces the efficacy of intralesional vitamin D3.[16] However, in the past few years, many cases of viral warts have been treated successfully with topical vitamin D3. It regulates epidermal cell proliferation, differentiation and cytokine production.[17]

Untoward effects noted during treatment sessions were minimal and included only pain and localized swelling in 50(80.6%) patients that resolved in two to three days. Three patients (4%) developed nodules as post-injection side effects, which settled as intralesional vitamin D3 injection was discontinued. Pain after vitamin D3 injection was found in 40(64.51) findings in our study. This is consistent with the finding of other studies where 80% of patients suffered mild pain after Intralesional vitamin D3.[18]

Other commonly used treatments are topical keratolytic, electrocoagulation, cryotherapy and laser therapy, but they are cosmetically disfiguring, painful, especially on the soles and cause skin atrophy and paraesthesia.[19] Destructive treatments are not suitable for multiple and refractory warts. They only help to treat the treated lesions.[20] Intralesional vitamin D3 alone in the treatment of refractory plantar warts is effective in outdoor settings with minimum downtime.

ACKNOWLEDGEMENT

Authors acknowledge the contribution of paramedical staff for their support in the selection of patients and collection of data for this research.

CONCLUSION

Intralesional vitamin D3 is a safe and effective treatment for plantar warts.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MJ & MT: Data acquisition, data analysis, critical review, approval of the final version to be published.

SH & MS: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

NA & AR: Concept, critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFRENCES

1. Witchey DJ, Witchey NB, Roth-Kauffman MM, Kauffman MK. Plantar Warts: Epidemiology, Pathophysiology, and Clinical Management. J Am Osteopath Assoc 2018; 118(2): 92-105.
2. Leto Md, Santos Júnior GF, Porro AM, Tomimori J. Human papillomavirus infection: etiopathogenesis, molecular biology and clinical manifestations. An Bras Dermatol 2011; 86(2): 306-317. doi: 10.1590/s0365-05962011000200014.
3. Banoth S.Evaluation of therapeutic effectiveness of vitamin D3 injections in common warts in a tertiary care centre. Int J res Dermatol 2019; 5(3): 462-465. doi:10.18203/issn.2455-4529.
4. Nofal A, Albalat W, Ismail A, Khattab FM. Immunotherapeutic modalities for the treatment of recalcitrant plantar warts: a comparative study. J Dermatolog Treat 2022; 33(2): 922-927.
5. 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. doi: 10.4103/JCAS.JCAS_82_16.
6. Podder I, Bhattacharya S, Mishra V, Sarkar TK, Chandra S, Sil A et al. Immunotherapy in viral warts with intradermal Bacillus Calmette–Guerin vaccine versus intradermal tuberculin purified protein derivative: A double-blind, randomized controlled trial comparing effectiveness and safety in a tertiary care center in Eastern India. Ind J Dermatol Venere Leprol 2017; 83(3): 411-415.

7. Bencini PL, Guida S, Cazzaniga S, Pellacani G, Galimberti MG, Bencini M, et al. Risk factors for recurrence after successful treatment of warts: the role of smoking habits. J Eur Acad Dermatol Venereol 2017; 31(4): 712-716. doi: 10.1111/jdv.14086.
8. Yousaf F, Raza N, Ahmed N, Sadiq S, Anwar A. Comparison of Intralesional vit D3 versus cryotherapy for management of plantar warts. Pak Armed Forces Med J 2019; 69 (6): 1304-1308.
9. Liu J, Li H, Yang F, Ren Y, Xia T, Zhao Z, et al. Epidemiology and Clinical Profile of Cutaneous Warts in Chinese College Students: A Cross-Sectional and Follow-Up Study. Sci Rep 2018; 8(1):15450. doi: 10.1038/s41598-018-33511-x.
10. Priya A, Adil M, Amin SS, Mohtashim M, Bansal R, Alam M. Intralesional Vitamin D3 in Recalcitrant Palmoplantar and Periungual Warts: A Prospective, Observational Study. Acta Dermatovenerol Croat 2019; 27(4): 215-224.
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. doi: 10.1177/120347 5415602841.
12. Akula ML, Shetty M, Shetty V, Patel P, Basil A. Comparative study of therapeutic efficacy of intralesional vitamin D3 versus intralesional purified protein derivative in the treatment of warts. Indian J Clin Exp Dermatol 2018; 4(3): 226-231.doi: 10.182 31/2581-4729.2018.0048.
13. Potlapati A, Gangaiah N, George NM. A study on safety and efficacy of intralesional vitamin D3 in cutaneous warts. Int J Res Dermatol 2020; 6(5): 648-651.doi:10.18203/issn.2455-4529.
14. Ghaly NE, El-Ashmawy AA, Zeid MA,Shaker ESE. Efficacy and safety of intralesional injection of vitamin D3 versus tuberculin PPD in the treatment of plantar warts: A comparative controlled study. J Cosmet Dermatol 2021; 20(4): 1231-1240. doi: 10.1111/ jocd.13712.
15. 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. doi: 10.1177/1203475417704180.
16. El-Taweel AEA, Salem RM, Allam AH. Cigarette smoking reduces the efficacy of intralesional vitamin D in the treatment of warts. Dermatol Ther 2019; 32(2): e12816. doi: 10.1111/dth.12816.
17. Imagawa I, Suzuki H. Successful treatment of refractory warts with topical vitamin D3 derivative (maxacalcitol, 1α, 25-dihydroxy-22oxacalcitriol) in 17 patients. J Dermatol 2007; 34(4): 264-266. doi: 10.1111/j.1346-8138.2007.00266.x.
18. El Sayed MH, Sayed FS, Afify AA. Intralesional zinc sulfate 2% vs intralesional vitamin D in plantar warts: A clinicodermoscopic study. Dermatol Ther 2020; 33(3): e13308. doi: 10.1111/dth.13308.
19. Reichrath J, Zouboulis CC, Vogt T, Holick MF. Targeting the vitamin D endocrine system (VDES) for the management of inflammatory and malignant skin diseases: An historical view and outlook. Rev Endocr Metab Disord 2016; 17(3): 405-417.
20. Kareem IMA, Ibrahim IM, Mohammed SFF, Ahmed AA. Effectiveness of intralesional vitamin D3 injection in the treatment of common warts: Single-blinded placebo-controlled study. Dermatol Ther 2019; 32(3): e12882. doi: 10.1111/dth.12882.

.....