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Original Article

Efficacy of intralesional vitamin D3 in cutaneous warts

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Abstract

Objective The objective of this study was to determine the efficacy of intralesional vitamin D3 in cutaneous warts.

Methods The study comprised 226 patients with palmoplantar warts of various sizes and duration. After injecting lignocaine 0.2 ml (20 mg/ml), about 0.5 mL of vitamin D3 solution (200,000 IU, 15 mg/mL) was administered to the base of the warts. At 2-week intervals, up to 5 warts were injected in each session until they disappeared, which could take up to 4 treatments. Following the final injection, patients were monitored for 6 months to look for any recurrence.

Results The study included 226 patients. The average number of injections needed to obtain a complete resolution was 2.93±0.60. Complete response was observed in 185 (81.9%) patients.

Conclusion Cutaneous warts can be treated effectively, affordably, and safely with intralesional vitamin D3.

Key words
Plantar warts; Cutaneous warts; Intralesional treatment; Vitamin D3; Efficacy.

Introduction

The benign epidermal proliferations known as verruca vulgaris (viral warts) affect the skin and mucosa. It is a pretty common ailment with a wide range of treatments that have varying degrees of efficacy. Although 65-78% of warts spontaneously resolve within two years.[1] Patient sought therapy due to cosmetic disfigurement and pain, particularly in the soles. Common methods for eliminating warts locally include topical keratolytics, electrocoagulation, cryotherapy, and laser therapy.[2-5] All of these techniques cause discomfort, scarring, and repeated episodes. Over the past few years, many other types of immunotherapy have been tested to cure warts, including the measles, mumps, and rubella (MMR) vaccination, the tuberculin purified protein derivative (PPD), the Mycobacterium vaccine, and Candida antigen.[6-9]

In Pakistan, 10.05% of the population has warts.[10] There aren't many researches available that demonstrate how well topical Vitamin D derivatives work to treat warts.[11,12] In addition to its topical effects, vitamin D3 has been used intralesionaly to investigate its alleged role as an immunotherapeutic molecule. According to experimental data, it inhibits the expression of interleukin-6 (IL-6), IL-8, tumour necrosis factor (TNF), and TNF via a VDR-dependent mechanism, which may have immunomodulatory effects.[13] However, Aktas *et al*. attempted intralesional Vitamin D3 injection for the first time in 2015 for the treatment of plantar warts, and they found that 80.6% of patients saw a complete response.[14] To the best

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of our knowledge, there are no other local or international publications with data on this subject. This study aims to evaluate the effectiveness of intralesional vitamin D in the local community. This can aid those with cutaneous warts in decreasing their appearance concerns.

Methods

This descriptive case study series was conducted from August 9, 2018 to February 8, 2019 following permission from the Institutional Review Board (Ref. No:F.2-81/2018-GENL/2522/JPMC Dated: 31/8/2018). Two hundred and twenty six patients who met the criteria and were seen in the dermatology outpatient department at JPMC Karachi were chosen and given the study's specifics. Each patient gave a thorough history and gave written consent after being properly informed.

Patients of both sexes with cutaneous warts and ages between 12 and 70 years were eligible for inclusion. With no prior topical or destructive treatments for at least six months, the patient's history and clinical characteristics were evaluated. Common warts, plantar warts, and filiform warts were among the varieties. The study included warts that were less than 2 cm in size. Females who were pregnant, nursing, or had a history of hypersensitivity to vitamin D3 or the local anaesthetic xycolaine were excluded from the trial.

Under the company name Neutro pharma (Indrop D), vitamin D3 for injection was offered in vials containing 200,000 IU of cholecalciferol in 1 ml (15mg). After injecting lignocaine (20 mg/ml) into the warts initially, a 27-gauge insulin syringe was used to slowly inject 0.5 ml of vitamin D3 (15 mg/ml) into the base of each wart (using aseptic techniques). Clinical improvements were recorded by noting the reduction in the number and size of warty lesions at each visit, every two weeks, for a total of four sessions. In each session, a maximum of two warts were treated. The patients were instructed not to take any topical or oral drugs after therapy.

A questionnaire was used to collect all of the demographic information. At each visit, the location, number, size, and kind of warts were noted (as per operational definitions). At each visit, pictures were taken to support the data that had been recorded. Data were gathered after the Institutional Review Board's approval.

Results

A total of 226 patients received injections of vitamin D3. **Table 1** displays the demographic and clinical information for 226 patients. 81(35.8%) females and 145(64.2%) males participated in the study. The patients' ages varied between 12 to 70 years old, with a mean age of 26.77±9.69. About 3 to 30 warts were seen, with a mean of 14.5±7.5. There were 96 cases of verruca vulgaris, 6 cases of filiform warts, and 47 cases of plantar warts.

A mean of 2.93±0.60 intralesional injections were needed for full clearance. **Table 2** shows the patient that had complete eradication.

Table 1 Summary of demographic and clinical data (n=226)

Male : Female Ratio	0.88:1
Age (mean±SD)	26.77±9.69 yrs.
Age (range)	12-70 yrs.
Duration of disease in years (mean±SD)	4.5 ± 11.02
Duration of Disease (range)	(3-8 yrs.)
Number of warts (mean±SD)	14.5±7.47
Number of warts (range)	3-30
Type of Warts n (%)	
Common warts	96 (42.47)
Plantar warts	124(54.86)
Filiform warts	6 (2.65)
Mean Number of Injections	2.93 ± 0.60

Table 2 Treatment Response According to Types of Wart (n=226)

Types of Wart	*Efficacy n(%)*		*p-value*
	Yes	*No*	
Common Wart	79 (35)	17 (7.5)	
Planter Wart	101 (44.7)	23 (10.2)	0.908
Filliform Wart	5 (2.2)	1 (0.44)	

Patients who have fully recovered are shown in **Figures 1-4**. 33 patients (70.2%) of the 35 patients who experienced side effects at the injection site experienced minor pain and edema, that was relieved in two weeks. In 2 (4.25%) patients depigmentation was observed. There were no consequences that could have been fatal.

Discussion

Clinical signs of a human papillomavirus infection include cutaneous and anogenital warts (HPVs). More than 120 distinct HPV varieties have been thoroughly described so far. Both diseases are quite prevalent and can affect people of all ages. Cutaneous warts can affect any area of the skin, however they typically appear on the face, soles, and fingers. Anogenital warts are one of the most frequent sexually transmitted infections (STIs) in adolescents and adults, albeit they are more common in children.[15–21] Verruca plana (plantar warts) are brought on by HPV 1, 2, 4, 27, and 57. Small, granular papules at start, they quickly develop into well-defined, spherical lesions with keratotic surfaces.

The majority of plantar warts grow on pressure areas like the metatarsal heads or the heel. Walking-related pain is frequent but varies in degree.[19] There are numerous therapeutic alternatives, and before seeing a doctor, individuals frequently self-medicate.[15] Formic acid solution, cryotherapy with liquid nitrogen, salicylic acid or trichloroacetic acid products, as well as removal of the lesion with a punch and diathermy, are among the therapeutic alternatives available for such patients.[19] The sunshine vitamin (vitamin D) has recently been linked to a wide range of medical conditions. The main sources of vitamin D include adequate amounts of sunlight, an oil-rich diet, and fortified milk.

Table 3 Comparison with other studies.

	Aktas et al [2014]	*Raghukumar [2017]*	*Present Study*
No. of Patients	20	60	226
Types of Wart	Planter warts	Common and palmoplantar warts	Common and palmoplantar warts
Treatment	Vitamin D3+ lignocaine	Vitamin D3+ lignocaine	Vitamin D3+ lignocaine
Interval Between Sessions	2 Weeks	4 Weeks	2 Weeks
Maximum Injections	2	4	4
Complete Clearance n(%)	18(80)	54(90)	180(79.7)

Figure 1 A) Planter wart before treatment B) Near Complete clearance after 4 injections

Figure 2 A) Verruca vulgaris before treatment B) Complete clearance after 3 injections with swelling at injection site.

Figure 3 A) Verruca vulgaris before treatment B) Near Complete clearance after 3 injections.

Figure 4 A) Verruca vulgaris before treatment B) Complete clearance after 3 injections

The metabolism of parathyroid hormone (PTH), calcium, and phosphorus are regulated by vitamin D, which has significant effects on the health of the skeletal system.[25] Plantar warts have reportedly responded quite well to intralesional vitamin D3 injections, according to a recent study.[20] The present study was necessary because the evidence was scarce and there was no locally published information of this kind. This study's goal was to evaluate the effectiveness of intralesional vitamin-D injections for the treatment of plantar warts. The patients in the current study had a mean age of 26.77±9.69 years. In Indian patients with diabetes, Das *et al*. reported a comparable mean age of 28±8.7 years, although Gupta *et al*. reported it to be 31.9±6.7 years.[22,23]

Uyar *et al*.[26] observed a somewhat higher mean age of 33.4±8.81 years in such patients from Turkey, but Lal *et al*.[27] and Syed *et al*.[28] reported a substantially lower mean age of 24.29±8.36 years and 24.7±7.5 years in such patients from India and Pakistan, respectively. With a male to female ratio of 1:2:1, there were 145 (64.2%) men and 81 (35.8%) women among the patients. Our findings are consistent with those of Gharib *et al*.[24] who likewise noted a male predominance among these Egyptian patients, with a male to female ratio of 1:2:1. Similar male predominance (M:F, 1.3:1) was documented by Das *et al*. in Indian patients with genital warts.[22]

In the current study, the mean disease duration was 4.5±11.02 years, with disease durations ranging from 1 month to 12 months. Our findings are consistent with those of Gupta *et al*. who discovered a comparable mean disease duration at presentation among Indian patients with this condition and reported it to be 6.6±4.1 months. Similar mean disease duration (5.57 months) at presentation was also found by Das *et al*. in India[22] According to Huo *et al*. (2010), it was 8.0±5.6 months among Chinese patients with this condition.[28]

Vitamin D3 intralesional injection was successful in 185 (81.8%) patients. The frequency of efficacy did not change statistically significantly across age (p=0.666), gender (p=0.016), duration (p=0.724), or extent of lesion (p=0.645) groups. Our findings are consistent with those of Aktas *et al*. from 2015, who estimated that 80% of patients with plantar warts would benefit from intralesional injections of vitamin D.[14] The current study adds to the scant body of knowledge on the subject and is the first of its type among the local community. The current study's findings support the findings of the earlier study by Aktas *et al*.[14] and further demonstrate the effectiveness of intralesional Vitamin D3 injection in the treatment of plantar warts.

Given this information, it can be suggested that intralesional vitamin D3 injections should be used more frequently in the future to treat plantar warts because they are less expensive,

less invasive, simple to use, and more effective over the short term. The following study was severely constrained by the fact that we only looked at treatment results after a 30-day follow-up period. To assess the long-term role of intralesional vitamin D3 injection in treating plantar warts, studies with longer follow-up are needed. Future research is strongly encouraged to do such a study. The single-centre of our investigation was also the limitation of this study.

Conclusion

It can be stated that intralesional vitamin D3 injection was effective in curing cutaneous warts. Nevertheless, future research utilising large sample sizes and multiple institutes is required.

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