

Efficacy of intralesional vitamin D3 injection in the treatment of palmoplantar and periungual warts

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ABSTRACT

Background: Warts are highly contagious benign lesions caused by HPV occurring in various forms, such as flat warts, palmar and plantar warts, etc. Immunotherapy offers a safe and effective method for the treatment of warts by stimulating cell-mediated immunity in these locations. **Materials and Methods:** Twenty cases of palmoplantar/periungual warts of varying size and duration who underwent a vitamin D3 injection immunotherapy procedure were included in the present study, irrespective of age and sex. 0.2 to 0.4 ml of vitamin D3 injection was infiltrated at the base of each wart to a maximum of five warts in each sitting in two-week intervals for about four sessions or till their complete clearance. The response was graded as complete resolution, partial (50–99% resolution), or no or mild (50%) response. The patients were followed up for six months for any recurrence. **Results:** Complete resolution was seen in nine (45%) patients, partial resolution in eight (40%), and no response in three (15%). **Conclusion:** Injection vitamin D3 immunotherapy offers a better alternative method of therapy for recalcitrant/multiple warts.

Key words: Palmoplantar warts, Periungual warts, Immunotherapy, Intralesional vitamin D3

INTRODUCTION

Warts are highly contagious benign lesions caused by the human papillomavirus (HPV) [1]. The various types are flat warts, palmar and plantar warts, common warts, and periungual, filiform, and anogenital warts [2,3]. The spontaneous resolution rate for warts is around 65–78%. The main reasons why patients seek treatment are their contagious nature and the associated poor quality of life [4]. Multiple recalcitrant warts, palmoplantar, and periungual warts impose a serious challenge to the treating physician as they do not respond to treatments such as electrocoagulation and cryotherapy. Recently, intralesional immunotherapy with skin test antigens and vaccines has been effective in the management of such warts without scarring and decreased recurrences [5]. Immunotherapy antigens such as measles, mumps, rubella (MMR) vaccine, tuberculin (purified protein derivative),

and vitamin D3 have been tried. Although not well elucidated, vitamin D3 employs the ability of the immune system to recognize the antigens that induce a delayed-type hypersensitivity reaction not only to the antigen yet also against HPV. The stimulated immune response clears all lesions on other body sites along with the treated lesions [6]. The present study highlights the importance of immunotherapy using the injection of vitamin D3 in the management of palmoplantar and periungual warts.

MATERIALS AND METHODS

A study was conducted at the Outpatient Department of Dermatology of PESIMSR in Kuppam on patients diagnosed with palmoplantar and periungual warts who received intralesional vitamin D3 immunotherapy between August 2018 and April 2019 after obtaining written informed consent from the participants. A documented clinical history regarding age, sex, site of

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warts, number of warts, duration of lesions, and clinical photographs was assessed for therapeutic response. Out of the 28 cases who received treatment during the stipulated period, about eight patients did not complete the follow-up period of six months. Hence, twenty cases were included in the study and assessed for therapeutic response. The treatment protocol followed was injection vitamin D₃ (6,00,000 IU, 15 mg/mL) at a dose of 0.2 to 0.4 mL injected at the base of a large wart to a maximum of five warts (in case of multiple warts) in each sitting in two-week intervals for about four sessions or till the complete clearance of lesions, whichever was earlier. Injection lignocaine 0.2 mL (20 mg/mL) was given before the procedure in apprehensive patients. The response was graded as complete resolution (complete disappearance of the lesion), partial (50–99% resolution), or no/mild (< 50%) response.

RESULTS

Out of the twenty patients included in the present study, the youngest patient was eleven years old, and the oldest patient was 51 years old. The mean age group was 31.5 years. The mean duration of the disease was 9.1 months. The M: F ratio was 2.3:1 (Table 1). Eleven patients (55%) were found to have palmar warts, five patients (25%) had plantar warts, and four patients (20%) had periungual warts. Out of the twenty patients, six (30%) were found to have warts at distant sites as well and twelve (60%) were observed to have multiple warts (> 5) (Table 2). Complete resolution was seen in nine (45%) patients with the clearance of distant warts (Figs. 1a – 1d). Partial resolution, that is, a reduction in wart size and number by more than 50–99% was noted in eight (40%) patients (Figs. 2a and 2b). No/mild response (< 50%) was noted in three (15%) patients. The average session required for the complete resolution of warts was 3.1. Adverse effects were documented in 65% of the patients, with no life-threatening complications.

Table 1: Demographic profile of the study group

Total patients	20
Sex ratio	2.3:1
Mean age in years	31.5 years
Mean duration of disease in months	9.1 months
Type of wart:	Percentage:
1. Palmar warts	11 patients (55%)
2. Plantar warts	5 patients (25%)
3. Periungual warts	4 patients (20%)
Distant warts/other sites	6 patients (30%)
Multiple warts (> 5)	12 patients (60%)

Swelling and pain at the site of injection were the only side effects seen in our patients, which resolved without treatment. Out of the nine patients who achieved complete clearance, none showed recurrence during the six months of their follow-up, and a further reduction in size and number of warts was noticed in the partial response group.

DISCUSSION

The treatment of multiple palmoplantar warts does not give immediate results, which necessitates multiple sittings by destructive methods, such as cryotherapy and electrocautery [6-8]. Although spontaneous resolution occurs within two years in 65–78% of warts, most patients seek treatment for warts as they are cosmetically disfiguring and sometimes painful, especially on the soles [9-12]. Local destruction of warts is a commonly used technique performed by laser therapy, electrocoagulation, cryotherapy, and topical keratolytics [13]. All these treatment modalities may be painful and have been known to cause scarring [14]. In addition, destructive modalities are not suitable for the treatment of multiple and refractory warts as they clear only treated lesions and not distant ones. Therefore, to overcome these disadvantages, immunotherapy has been widely used for the management of warts over the last couple of years. It acts on the basic principle of enhancing cell-mediated immunity for the clearance of warts [15]. In the present study, intralesional vitamin D immunotherapy was tried in the treatment of palmoplantar and periungual warts. Out of the twenty patients studied, fourteen (70%) were males, and six (30%) were females. The sex ratio was 2.3:1, and the mean age was 31.5 years. The mean duration of the disease was 9.1 months. The demographic profile was comparable to the study done by Manjunath Kavya et al. [5], who recruited 42 patients, among whom 27 were males and 15 were females, with a mean age of twenty years and a mean duration of six months. Singh et al. [6] conducted a comparative study between intralesional vitamin D₃ and intralesional PPD in eighty patients, among which males outnumbered females, with a ratio of 1.75:1. The mean age of the patient was 25.98 years, and the mean duration of illness was 6.7 months. Madhavi Latha Akula et al. [8] conducted a prospective comparative study on twenty patients, which consisted of thirteen males and seven females, with a sex ratio of 1.8:1. The mean age was 25.1 ± 4.41 years. In the present study, out of the

Table 2: Study group

Number	Age	Sex	Site	Number of warts	Number of sittings	Response
1	11 years	Female	Palmar with periungual	4	4	Partial
2	21 years	Male	Palmar	9	2	Complete
3	26 years	Male	Plantar	2	4	Complete
4	29 years	Female	Palmar	2	4	Mild
5	34 years	Female	Palmar	1	3	Complete
6	32 years	Male	Periungual+palmar	7	4	Partial
7	27 years	Male	Plantar	3	4	Complete
8	48 years	Female	Plantar	5	4	Partial
9	33 years	Female	Plantar	12	4	Mild
10	20 years	Male	Palmar/periungual	27	4	Complete
11	22 years	Male	Palmar	7	4	Partial
12	44 years	Male	Plantar	3	4	Partial
13	46 years	Male	Palmar	5	4	Mild
14	26 years	Female	Plantar	2	4	Partial
15	19 years	Male	Periungual	1	4	Complete
16	22 years	Male	Plantar	5	2	Complete
17	49 years	Female	Palmar	8	4	Partial
18	35 years	Male	Palmar	3	4	Complete
19	51 years	Male	Plantar	4	3	Complete
20	26 years	Female	Plantar	5	4	Partial



Figure 1: (a) Multiple palmar warts on the right palm. (b) Complete resolution of warts on the right palm after four sittings of injection vitamin D3 during the follow-up period. (c) A single palmar wart on the left ring finger. (d) Complete resolution of the wart on the left ring finger after three sittings of injection vitamin D3.



Figure 2: (a) Single palmar wart on the left thumb. (b) Partial resolution of the wart on the left thumb after four sittings of injection vitamin D3.

twenty patients, it was observed that 11 (55%) had palmar warts, 5 (25%) had plantar warts, and 4 (20%) had periungual warts. One patient was observed to have both palmar and periungual warts. Sites other than

the palmoplantar region were affected in 6 patients (30%). Twelve (60%) out of the twenty patients had multiple warts (more than five). In a study conducted by Manjunath Kavya et al. [5], 23 patients (54.76%) had palmoplantar warts, 18 patients had verruca vulgaris (42.85%), and one (2.38%) was observed to have a filiform wart. Multiple non-contiguous sites were involved in sixteen patients (38.09%). In our study, complete resolution was seen in nine (45%) patients, partial (moderate) resolution, that is, a reduction in wart size and number by more than 50–99% was noted in eight (40%) patients, and no or mild response (< 50%) in three (15%) patients. Out of the six patients with distant warts, complete disappearance was noted in four, who fell into the complete response group, and partial/no response was seen in two patients. The average session required for complete resolution of wart was 3.1, which was comparable to the study conducted by Manjunath Kavya et al. [5], in which the session

required was 3. In comparison with studies done by others [5-8], wherein the complete resolution was noted in more than 75% of cases, only 45% of cases in our study showed complete clearance. Manjunath Kavya et al. [5] found a complete response in 33 of 42 patients (78.57%), six patients (14.28%) with a moderate response, and three patients (7.14%) with a mild response. The mean number of intralesional injections required for complete clearance was three. Singh et al. [6] conducted a comparative study between intralesional vitamin D3 and intralesional PPD (purified protein derivative) in eighty patients, among which forty were treated with intralesional vitamin D3, among whom 29 (72.5%) showed a complete response, 8 patients (20%) showed a moderate to marked response, and 3 patients (7.5%) showed no response. In a study conducted by Naresh [7], complete clearance was seen in 48 out of 60 patients (80%), a moderate response in 6 patients (10%), and mild in 6 patients (10%). Madhavi Latha Akula et al. [8] conducted a prospective comparative study in which 14 out of 20 patients (70%) belonging to group A (vitamin D3) showed a complete response after four sessions, six patients (30%) showed a moderate response, and recurrence was noted in 1 patient after three months. No serious adverse effects were observed. The response achieved by our study was lesser (complete resolution was seen in 45%) when compared to other studies [5-8], which may be attributed to the relatively smaller sample size in our study, yet the overall response to vitamin D3 immunotherapy is satisfactory as the partial response group (8 patients) also achieved a marked response with 65–85% clearance of the lesions. Further large-scale studies are required to determine the exact therapeutic effectiveness of vitamin D3 immunotherapy.

CONCLUSION

Injection vitamin D3 immunotherapy provides a better alternative compared to other antigens used because of the fewer side effects, its cost-effectiveness, and the requirement of fewer sessions.

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Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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