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To evaluate efficacy and safety of intralesional vitamin D3 in cutaneous warts at a tertiary care centre, Rajasthan

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Abstract

Background: Warts or verrucae are benign epidermal proliferations of the skin and mucosa caused by human papilloma virus (HPV). Intralesional vitamin D3 injection is an innovative option for warts that are recalcitrant to conventional treatments**.**

This study was conducted in a tertiary care hospital. 100 patients (male and female) were included. Clinically diagnosed cases of multiple warts were given Vit D3 (15mg/ml) intralesionally at an interval of 2 weeks for 4 sittings. Maximum of 2 warts were treated at one time. Initially warts were injected with 0.2 ml of Lignocaine (20 mg/ml) followed by 0.2 ml of vitamin D3 into the base of wart using a 26 gauge needle and syringe. Follow up was done up to two months.

Results: Out of 100 enrolled patients it was found that Mean number of warts was 6.50±2.39 at 1st visit, 3.61±1.12 at 2nd visit, 2.20±0.89 at 3rd visit, 1.40±0.49 at 4th visit and 0.89±0.70 after 2 months. The change in number and size of warts in each visit found statistically significant ($p < 0.001$). Side effects were noted as 27 patients felt pain at the site of injection, 13 patients with swelling after intralesional injection and 5 patients showed pigmentation after resolution of wart which was persistent upto follow-up.

Conclusion: Intralesional vitamin D3 injection is an innovative option for warts that are recalcitrant to

conventional treatments. It is a simple, well-tolerated treatment method with minimal side effects that is easy to administer in outpatient clinics.

Keywords- Intralesional vitamin D3, Cutaneous Warts.

Introduction

Warts or verrucae are benign epidermal proliferations of the skin and mucosa caused by human papilloma virus (HPV).HPV initially targets the basal cells and undergoes a latent phase of slow replication. As the epidermis grows superficially the virus induces hyperplasia and hyperkeratosis.[1] 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.[2]

Treatment modalities includes local destruction of warts by using either topical keratolytics, electrocoagulation, cryotherapy or laser therapy. All these modalities of treatment are painful, associated with scarring and frequent recurrences and not suitable for the treatment of multiple and refractory warts as they clear only treated lesions and not the distant ones.[3]

Other therapies which are used for treatment for warts include diphenylcyclopropenone (DCP), squaric acid dibutyl ester (SADBE), imiquimod, tuberculin jelly and autologous vaccines but use of all these modalities are limited by their side effect profile. Exact mechanism of action of Vit D3 in management of warts is not clear but its supposed to be through immunomodulation by inhibiting the expression of IL-6 and IL-8, tumor necrosis factor- alpha and gamma through Vit D receptor dependent pathway.

Material & Methods

Written informed consent was taken from all the patients. Ethical clearance was taken from the institutional committee (52-/MC/EC/2020). Study was conducted over a period of 12 months (May 2019 to April 2020) in the department of Dermatology. This was an OPD based self financed project.

After obtaining written informed consent, 100 consecutive patients, both male and female age between 10 to 70 year, who had cutaneous warts diagnosed by clinical features and dermoscopy with no prior treatment with either topical or destructive modalities for at least 1 months prior were included. Patients with anogenital wart, mucosal wart, plane wart, pregnant and lactating females, any evidence of immuno suppression including HIV, prior history of hypersensitivity to Vitamin D3 and with keloidal skin tendency were excluded.

The socio-demographic parameters, detailed history and clinical examination was done and recorded in proforma. A graphical wart map was prepared for each patient; location, number, size and type of wart recorded on it at each visit. Photographs was taken at each visit to support the recorded data.

All consecutive patients diagnosed clinically as multiple cutaneous warts were treated with intralesional vitamin D3 [15mg/ml] at 2 week of interval for 4 maximum sessions.

Larger warts were selected for Vit D3 therapy in a dose as mentioned earlier. After injections patients were asked not to use any form of treatment; oral and/ or topical.

Assessment and analysis

To assess the clinical response photographs were taken at the beginning of the therapy and after 2 months of last therapy. Clinically assessment was done by the reduction in size and number of cutaneous warts then graded as per response rate, complete response will be considered if all the warts both treated and distant warts

were resolved completely. Marked response if there 75 to <100% reductions in both size and number of lesions. Moderate response if there 50 to <75% and Inadequate response <50% reductions in both size and number of lesions. Statistical analysis was performed with the SPSS, version 21 for Windows statistical software package (SPSS inc., Chicago, IL, USA). The Categorical data was presented as numbers (percent) and were compared among groups using Chi square test. The quantitative data was presented as mean and standard deviation and were compared by paired t-test. Probability was considered to be significant if less than 0.001.

Results

Mean age of patients was 31.36±12.89 years. Maximum patients (39.00%) belonged to 21-30 years age group. 63.00% patients were male and 37.00% patients were female. Mean Duration of disease was 2.41±0.83years. In 70.00% patients, disease duration was >2years and in 30.00% patients, duration was < 2 years.Out of 64 patients of verruca vulgaris, 33(51.56%) were situated on upper limb, 23(35.94%) on lower limb and 8(12.50%) on face. Out of 20 patients of palmoplantar wart, 13(65.00%) were situated on head and 7(35.00%) on face. Out of 10 patients of periungual wart, 7(70.00%) situated around fingernail and 3(30.00%) around toenail. Out of 6 patients of filliform wart, 3(50.00%) situated on upper limb and 3(50.00%) were on lower limb mentioned in Table-1.

Table 1: Distribution of study subjects according to Location

Type of Wart	Location	Number of Cases	%
Verruca Vulgaris (64)	Upper Limb	33	51.56
	Lower Limb	23	35.94
	Face	8	12.50
Palmoplantar wart (20)	Hand	13	65.00
	Feet	7	35.00
Periungual Wart (10)	Around fingernail	7	70.00
	Around toenail	3	30.00
Filiform wart (6)	Upper Limb	3	50.00
	Lower Limb	3	50.00

Mean and standard deviation (SD) of cutaneous wart in each visit was calculated.. Mean number of warts was 6.50±2.39 at 1st visit, 3.61±1.12 at 2nd visit, 2.20±0.89 at 3rd visit, 1.40±0.49 at 4th visit and 0.89±0.70 after 2 months. The analysis of results showed that the change of number of warts in each visit was found statistically significant (p value <0.001) [Table -2].

Table 2: Mean and standard deviation (SD) of cutaneous wart in each visit

Visit	Mean	SD	P value
1st visit	6.50	2.39	0.0003 (S)
2 visit	3.61	1.12	p<0.001 (S)
3 visit	2.20	0.89	p<0.001 (S)
4 visit	1.40	0.49	p<0.001 (S)
After 2 month	0.89	0.70	p<0.001 (S)

Distribution of study subjects according to type of wart was noted and 64.00% patients presented with verruca vulgaris,20.00% patients presented with palmoplantar wart, 10.00% patients presented with periungual wart and 6.00% patients presented with filiform wart.[Table -3].

Table 3: Distribution of study subjects according to type of wart

Type of Wart		Number of Cases	%
Verruca Vulgaris	Present	64	64.00
	Absent	36	36.00
Palmoplantar Wart	Present	20	20.00
	Absent	80	80.00
Periungual Wart	Present	10	10.00
	Absent	90	90.00
Filiform Wart	Present	6	6.00
	Absent	94	94.00

Out of 64 patients presented with verruca vulgaris, 31(51.56%) patients showed complete response, 21(32.81%) patients showed marked response, 6(9.37%) patients showed moderate response and 4(6.25%) showed inadequate response.Out of 20 patients presented with palmoplantar wart, 9(45.00%) patients showed complete response, 5(25.00%) patients showed marked response, 4(20.00%) patients showed moderate response and 1(10.00%) showed inadequate response. Out of 10 patients presented with periungual wart, 6(60.00%) patients showed complete response, 2(20.00%) patients showed marked response, 1(10.00%) patient showed moderate response and 1(10.00%) patient showed inadequate response. Out of 6 patients presented with filiform wart, 3(50.00%) patients showed complete response, 2(33.00%) patients showed marked response and 1(16.67%) patients showed moderate response.[Table -4].

Table 4: Distribution of study subjects according to treatment response in different type of warts

Response	Verruca vulgaris (n=64)		Palmoplantar wart (n=20)		Periungual wart (n=10)		Filiform wart (n=6)	
	No.	%	No.	%	No.	%	No.	%
Complete	33	51.56	9	45.00	6	60.0	3	50.00
Marked	21	32.81	5	25.00	2	20.0	2	33.33
Moderate	6	9.37	4	20.00	1	10.0	1	16.67
Inadequate	4	6.25	2	10.00	1	10.00	0	0.00

27 patients felt pain at site of injection, 13 patients presented with swelling after injection which remains maximum upto 7 days and 5 patients showed pigmentation after resolution of cutaneous wart which remained upto follow-up period. [Table -5]

Table 5: Distribution of study subjects according to duration of side effectT

Side effect	Duration (days)	No. of cases
Pain	at the time of injection	27
Swelling	Upto 7 days	13
Pigmentation	Upto follow up period	5

The overall results after 2 months of 4th visit of therapy indicated that there was significant improvement in wart.[figure-1 and 2]

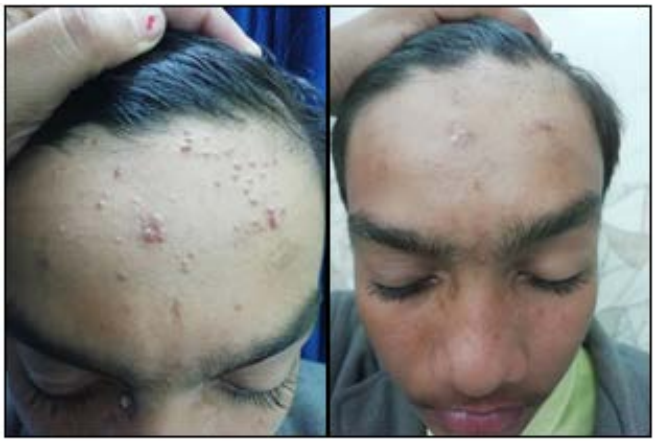

Figure 1 patient 1: Pre-treatment and Post-treatment after 4th visit

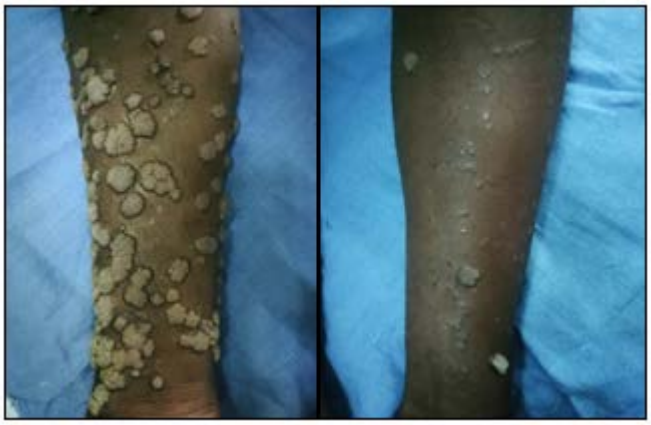

Figure 2 patient 2: Pre-treatment and Post-treatment after 2 months of 4th visit

Discussion

In the present study, the numbers of patients of cutaneous wart were 100 and mean number of warts was 6.50±2.39 at 1st visit, 3.61±1.12 at 2nd visit,

2.20±0.89 at 3rd visit, 1.40±0.49 at 4th visit and 0.89±0.70 after 2 months which was similar to the studyby Kumar SS et al (2020)[6]and Ahmed R et al (2020)[7]. Kavya M et al (2017)[8]

In our study out of 64 patients presented with verruca vulgaris, 31(51.56%) patients showed complete response, 21(32.81%) patients showed marked response, 6(9.37%) patients showed moderate response and 4(6.25%) showed inadequate response. Out of 20 patients presented with palmo-plantar wart, in 9(45.00%) patients complete response, in 5(25.00%) patients marked response, in 4(20.00%) patients moderate response and 1(10.00%) inadequate response was seen. Out of 10 patients presented with periungual wart, in 6(60.00%) patients complete response, in 2(20.00%) patients marked response, in 1(10.00%) patient moderate response and 1(10.00%) inadequate response was seen. Out of 6 patients presented with filiform wart, in 3(50.00%) patients complete response, in 2(33.00%) patients marked response and in 1(16.67%) patients moderate response was seen which was similar to the study by Kumar SS et al (2020)[6]

Kavya M et al (2017)[8] found complete disappearance of lesions in 82.60% patients of palmoplantar warts and in 77.77% of verruca vulgaris. While 14.28% patients showed moderate response. One in each subtype showed 1 to less than 50% change.

Kavya M et al (2017)[8] found adverse events in 80% patients but all were of minor grade, not life threatening and did not need much intervention. Swelling at the site of injection was the commonest (78.75) which subsided on its own. Dyspigmentation was observed in one patient only.

In our study, 27 patients complained of pain at the injection site, 13 patients had swelling which was transient and only in one patient; similar adverse effects observed by Kumar SS et al (2020)[6] in their study.

Conclusion

Intralesional vitamin D3 injection is an innovative option for warts that are recalcitrant to conventional treatments. It is a simple, well-tolerated treatment method with minimal side effects and is easy to administer in outpatient clinics. Intralesional vitamin D3 is very effective for cutaneous warts both for the treated recalcitrant and distant warts. However, Relatively less effacious for palmoplantar wart.

Limitations: This study is limited by its small sample size and lack of control group. Long terms follow-up is needed to ascertain the result.

Declaration of patient consent

The authors certify that they have obtained written informed consent from all the patients. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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