The Role of Intralesional Vitamin D3 injection in Treatment of Cutaneous Warts

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ABSTRACT:

Background: Cutaneous warts are treated primarily with destructive methods such as cryotherapy or electro-cautery. These modalities of treatment are time-consuming and may be associated with scarring in multiple warts. Immunotherapy is emerging as a new modality of treatment that acts on enhancing cell-mediated immunity against human papillomavirus for clearance of both treated and distant warts.
Aim of the study: To show the efficacy of Intralesional vitamin D3 in treating cutaneous warts.
Methods: A total of 50 patients were included in the study. They were injected with vitamin D3 300000 IU (up to 0.5 ml for each wart) at two weeks intervals for maximum of 4 sessions. The clinical response was assessed by photographic measurements at baseline, before each session, and after the completion of treatment and they were followed after 6 months for discovering any recurrence.
Results: in this study among 50 patients the response rate to vitamin D3 intralesionally was 94% in general, the mild response was seen in 20(40%) patients and moderate response was seen in 16 (32%) patients while the complete response was 11 (22%) patients. No serious side effects were observed except for pain at the site of injection which most of the patients had.
Limitation: small sample size with lack of control group.
Conclusions: Intralesional vitamin D shows a good response in the treatment of viral warts.

Keywords: human papillomavirus, viral wart, vitamin D3.

دور حقن فيتامين دور حقن فيتامين د-3 داخل الافة في علاج التأليل الجلدية

الخلاصة:

المدخل: يتم التعامل مع الثاليل الجلدية بالمقام الاول بطرق مدمرة مثل العلاج بالتبريد أو الكي الكهربائي، تستغرق طرق العلاج وقتا طويلا وقد ترافق مع تندب في الثاليل المتعددة. يظهر العلاج المناعي كطريقة جديدة للعلاج تعمل على تعزيز المناعة الخلوية ضد فايروس الورم الحليمي البشري لإزالة كل من الثاليل المعالجة والبعيدة.
الهدف من الدراسة: أظهار فاعلية فيتامين د-3 داخل الافة في علاج الثاليل الجلدية.
الطرق: تم تضمين مجموعه 50 مريضا في هذه الدراسة، تم حقنهم بفيتامين د-3 (30000 وحدة دولية ، ما يعادل (0.5 مل لكل ثؤلول) على فترات اسبوعين كحد أقصى 4 جلسات . تم تقييم الاستجابة السريرية من خلال قياس الصور الفوتوغرافية في الاساس قبل كل جلسة ، وبعد الانتهاء من العلاج وتم مطابقتها بعد 6 أشهر لاكتشاف أي تكرار.
النتائج: تمت هذه الدراسة على 50 مريضا ، كان معدل الاستجابة لفيتامين د -3 داخليا 94% بشكل عام ، وشوهد استجابة خفيفة في 20 مريضا (40%) ، بينما الاستجابة معتدلة في 16 (32%) مريضا. اما الاستجابة الكاملة 11 (22 %) مريضا. لم يلاحظ اي تأثيرات جانبية خطيرة باستثناء الالم في موقع الحقن الذي يعاني منه معظم المرضى. اان حجم العينة صغير مع عدم

وجود مجموعه تحكم.
الاستنتاج: يظهر فيتامين د-3 داخل الافة استجابة جيدة في علاج الثاليل الفيروسية.

الكلمات المفتاحية: فيروس الورم الحليمي البشري، ثؤلول فيروسي، حقن فيتامين د-3

INTRODUCTION:

Warts or verrucae are benign epidermal proliferations of the skin and mucous membrane caused by human papillomavirus (HPV) (1). Cutaneous warts have varied clinical presentations that include verruca vulgaris, verruca plana, verruca Palmaris and plantaris, and genital warts and the most common types of cutaneous warts are caused by HPV 1, 2, 3, 4, 7, 10, 27, and 57(2).warts are usually diagnosed clinically; Characteristic warty appearance with a rough, dry stippled surface, paring the surface of the wart will reveal capillary loops close to the surface and often causes bleeding (3).there are many modalities to treat warts like salicylic acid, glycolic acid and retinoic acid, these are regarded as first-line treatment , the 2nd line is destructive methods includes cryotherapy, laser and surgery, the third line is immunotherapy as imiquimod, intralesional interferon, PPD, candida antigen and etc. (4).The first and 2nd line of modalities of treatment can be painful and may be associated with scarring and frequent recurrences. In addition, destructive methods are not appropriate for the treatment of multiple and refractory warts as they clear only lesions that have been treated and not the distant ones. Hence, to overcome these shortcomings, immunotherapy is being tried widely for the treatment of warts over the last years (5). The immunity had a vital role in the pathogenesis of the disease and is specifically elated to cell-mediated immune response. Immunotherapy seems to enhance the immune system's recognition of the virus that enables the elimination of treated warts and sometimes warts at distant locations, thereby protecting against potential recurrence by inducting long-term HPV immunity (6).

Vitamin D; Is a group of fat-soluble secosteroids responsible for enhancing intestinal absorption of calcium, magnesium, and phosphate, and has multiple other biological effects (7). Cells in the skin have receptors for Vitamin D3 analogues are keratinocytes, Langerhans' cells, melanocytes, fibroblasts, and endothelial cells (8), so:

1. It works through Vitamin D receptor (VDR) to regulate cell growth, differentiation and immune function. It inhibits the proliferation of keratinocytes and modulates epidermal differentiation
2. Vitamin D prevents the production of several proinflammatory cytokines by T-cell clones, including IL-2 and IFN-γ.
3. It inhibits interleukin-6 (from B cell) and interleukin-8 (that produced by macrophage).
4. It inhibits transcription of granulocyte-macrophage colony-stimulating factor and messenger ribonucleic acid.
5. It blocks the activity of cytotoxic T cells and Natural Killer cells (9).

Aim of the study:

To show the efficacy of intralesional vitamin D3 injections in the treatment of cutaneous warts.

- To determine the efficacy of intralesional vitamin D3 injection in treating cutaneous warts.
- To find out any complications of intralesional vitamin D3.
- To show the difference in clinical

response to intralesional vitamin D3 among different types of cutaneous wart.

METHODS:

Study design:

This interventional study was conducted in Erbil Dermatology Teaching Center over a period of 8 months from May 2021 to January 2022.

Sample collection:

50 patients had been diagnosed clinically with cutaneous warts were included in this study.

Inclusion criteria

- Male and female patients with cutaneous wart
- Age of patient between 10-60 years

Exclusion criteria

- Patients who are currently on other treatment modalities of wart
- Patients with genital and facial wart
- Those who are allergic to vitamin D3
- Immunocompromised patients
- Pregnant and lactating women

The diagnosis was made by history and clinical examination. A questionnaire was prepared and each patient was given a number and all demographic data were recorded. The number, type, site, and size of warts for each patient were recorded. Photographs were taken at each visit for assessing the response to treatment. Informed verbal consent was obtained from each patient after an explanation of the procedure.

Administration of vitamin D3

The vitamin D3 vial 300000 IU is used. For each patient maximum of 5 warts were treated in each session. 0.2 to 0.5 ml (according to the size of the wart) of vitamin D3 was injected by insulin syringe at the base of each wart. The treatment was repeated each 2 weeks apart for maximum of 4 sessions.

Clinical response assessment

Clinical response was checked at each visit by recording any decrease in size and number of warts as follows:

- Complete response 100% clearance of warts
- The moderate response between 50%-100% clearance of warts.
- A mild response less than 50% clearance of wart.
- No response no lesion cured

Informed consent was obtained from all of the participants.

Statistical analysis:

The data collected during the study were summarized in sheets of Microsoft Excel version 2007. The statistical analysis was performed by using IBM-SPSS version 26. The normality of these data was tested by the Shapiro-Wilk test, and the nonparametric Kruskal-Wallis H test was decided to be used to find the difference between the three study groups regarding the age, number, and duration of Wart. Frequencies, medians, 25^{th}, and 75^{th} percentile values were calculated. The Chi- square test and Freeman Halton exact test were performed instead of Chi-square test to measure the association between the three groups' nominal data when any cell was present with an expected value less than 5. P-value ≤ 0.05 is considered significant.

RESULTS:

55 patients participated in the study and 5 patients were lost to follow-up due to various reasons.

Table (1) demonstrates the statistical characteristics of the sample's age and shows that the median age is 21.5 years with a minimum of 11 years and a maximum of 59 years, the 25^{th} and 75^{th} percentile are 17 and 31 years respectively.

Table (1): The statistical characteristics of the sample's age.

Median		21.50
Range		48.00
Minimum		11.00
Maximum		59.00
Percentiles	25	17.00
	50	21.50
	75	31.00

Figure (1) illustrates the distribution of the study sample according to gender and shows that 46.0% are males and 54.0% are females.

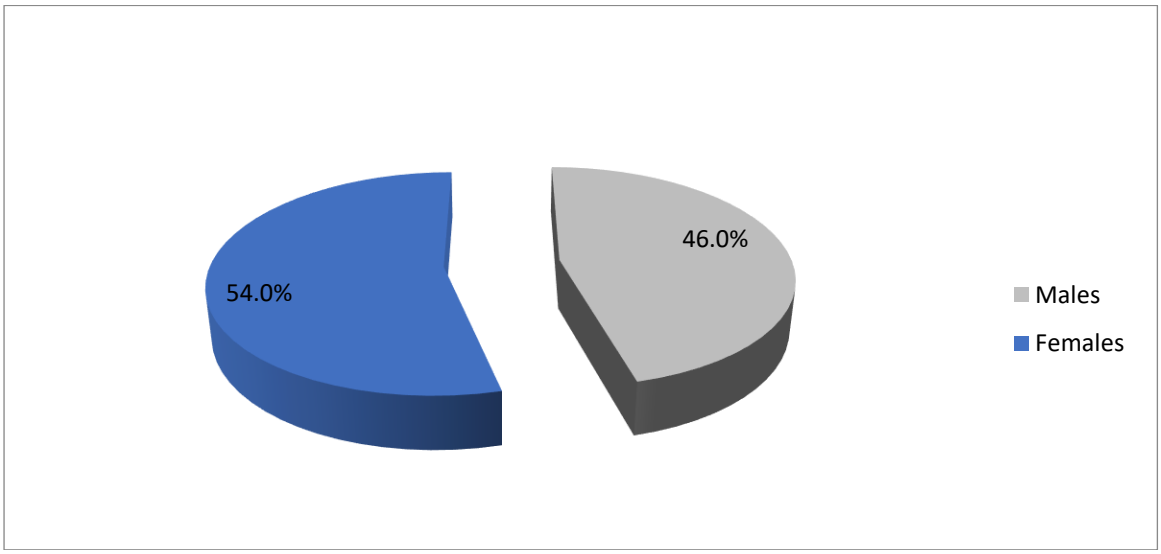

Figure (1): The distribution of the study sample according to gender.

Table (2) demonstrates the comparison of the socio-demographic characteristics among the study groups and reveals that the age medians of the common group (19.0) years, Palmo-planter group (24.5) years, and periungual group (20.0) years are statistically of non-significant difference (p=0.383).

The male gender represents 56.0% of a common group, 41.7% of the palmoplanter 30.8% of the Periungual group, and does not significantly differ (p=0.315) from the female gender which constitutes 44.0%, 58.3%, and 69.2% respectively. The difference among the study groups concerning residence is statistically not significant (p=1.000) although the urban residence is more frequent than the rural in the three study groups. Regarding the occupation, the common group distributed as 48.0% student, 24.0% housewife, and 28.0% employee, while the among palmoplanter, 41.7% student, 16.6% housewife, and 41.7%. Furthermore, most of the periungual group is students 53.8%; 15.4% housewives, and

30.8% employees. The difference in occupation among the study groups is statistically non-significant (p=0.673).

Table (2): The comparison of the socio-demographic characteristics among the study groups.

		Common n=25	Palmoplanter n=12	Periungual n=13	p-value
Age Median (25^{th} , 75^{th})Q		19.0 (17.0, 29.5)	24.5 (18.25, 34.0)	20.0 (12.5, 28.0)	0.383*
		No. (%)	No. (%)	No. (%)	
Gender	Males	14(56.0%)	5(41.7%)	4(30.8%)	0.315**
	Females	11(44.0%)	7(58.3%)	9(69.2%)	
Residence	Urban	18(72.0%)	9(75.0%)	10(76.9%)	1.000***
	Rural	7(28.0%)	3(25.0%)	3(23.1%)	
Occupation	Student	12(48.0%)	5(41.7%)	7(53.8%)	0.831**
	Housewife	6(24.0%)	2(16.6%)	2(15.4%)	0.902***
	Employee	7(28.0%)	5(41.7%)	4(30.8%)	0.673***

*Kruskal-Wallis test, **Chi-square test, *** Freeman-Halton exact test

Table (3) shows the comparison of the Wart characteristics among the study groups and depicts that the median number of the Wart are 4.0, 3.5, and 5.0 among the common, palmoplanter, and periungual groups respectively and the difference is statistically not significant (p=0.701). The duration of the Wart is longer among the palmoplanter group (median =30.0) than that of common and periungual groups but the difference is statistically non-significant (p=0.068).

All the clinical sites have no significant statistical differences among the study groups apart from the foot site that presents in 36.0% of the common group, 66.7% of palmoplanter group, and 7.8% of periungual group with a statistically significant difference at (p=0.009).

Additionally, only the size of 11-15 appears to be significantly different among the study groups with (p=0.032) that constitute 4.0%, 33.3%, and 15.2% of common, palmoplanter, and periungual groups respectively.

Table (3): The comparison of the socio-demographic characteristics among the study groups.

		Common n=25	**Palmoplanter n=12**	**Periungual n=13**	**p-value**
No. of Wart Median (25^{th} , 75^{th})Q		4.0 (1.5, 6.5)	3.5 (2.25, 7.0)	5.0 (2.0, 9.0)	0.701*
Duration of Wart Median (25^{th} , 75^{th})Q		12.0 (6.0, 24.0)	30.0 (10.5, 61.5)	12.0 (4.5, 21.0)	0.068*
		No. (%)	No. (%)	No. (%)	
Site	Finger	7(28.0%)	0(0.0%)	3(23.1%)	0.136**
	Hand	5(20.0%)	0(0.0%)	4(30.8%)	0.134**
	Toe	2(8.0%)	3(25.0%)	3(23.1%)	0.310**

	Foot	9(36.0%)	8(66.7%)	1(7.8%)	**0.009****
	Multiple area	2(8.0%)	1(8.3%)	2(15.2%)	0.830**
Size	1-5	7(28.0%)	2(16.7%)	4(30.8%)	0.765**
	6-10	12(48.0%)	4(33.3%)	7(53.8%)	0.566***
	11-15	1(4.0%)	4(33.3%)	2(15.2%)	**0.032****
	16-20	2(8.0%)	2(16.7%)	0(0.0%)	0.250**
	21-25	1(4.0%)	0(0.0%)	0(0.0%)	1.000**
	26-30	2(8.0%)	0(0.0%)	0(0.0%)	0.734**

*Kruskal-Wallis test, **Freeman-Halton exact test, ***Chi-square test

Table (4) shows the comparison of the previous treatment characteristics among the study groups and demonstrates that the history of previous treatment used by the patients presents in 64.0% of the common group, 75.0% of palmoplanter group, and 69.2% of periungual group with a statistically non-significant difference (0.922) .22 patients (44%) used topical treatment and only 2 patients(4%) used cryotherapy.11 patients (22%) showed complete response fig 2 and 3,16((32%) showed moderate response fig 4 ,20 patients (40%) showed a mild response and only 3 patients (6%) showed no response. No significant statistical difference was found among the study groups regarding types of previous treatment, responses, side effects, and reasons for seeking another treatment.

Table (4): The comparison of the previous treatment characteristics among the study groups.

Treatment		Common n=25	Palmoplanter n=12	Periungual n=13	p-value*
History	Yes	16(64.0%)	9(75.0%)	9(69.2%)	0.922
	No	9(36.0%)	3(25.0%)	4(30.8%)	
		n=16	n=9	n=9	
Types of treatment	Topical	9(56.3%)	5(55.6%)	8(88.9%)	0.244
	Surgical	2(12.5%)	0(0.0%)	0(0.0%)	0.486
	Multiple treatment	3(18.7%)	2(22.2%)	0(0.0%)	0.483
	Cryotherapy	2(12.5%)	2(22.2%)	1(11.1%)	0.836
		n=25	n=12	n=13	
Response to treatment	No response	2(8.0%)	1(8.3%)	0(0.0%)	0.602
	Mild	10(40.0%)	3(25.0%)	7(53.8%)	0.389
	Moderate	9(36.0%)	5(41.7%)	2(15.2%)	0.330
	Complete	4(16.0%)	3(25.0%)	4(30.8%)	0.551
Side effects		n=25	n=12	n=13	
No side effects		3(12.0%)	1(8.3%)	3(23.1%)	0.571
Itching		2(8.0%)	3(25.0%)	2(15.2%)	0.369
Pain		8(32.0%)	4(33.4%)	33(23.1%)	0.848
Swelling		1(4.0%)	0(0.0%)	1(7.8%)	0.999
Pain + Itching		4(16.0%)	1(8.3%)	0(0.0%)0	0.414
Pain + Swelling		2(8.0%)	3(25.0%)	4(30.8%)	0.186
Pain + Itching + Swelling		5(20.0%)	0(0.0%)	0(0.0%)	0.064

		n=16	n=9	n=9	
Reasons for seek another treatment	No response	12(75.0%)	7(77.8%)	7(77.8%)	0.999
	Recurrence	4(25.0%)	0(0.0%)	1(11.1%)	0.338
	Multiple	0(0.0%)	0(0.0%)	1(11.1%)	0.529
	Pain	0(0.0%)	2(22.2%)	0(0.0%)	0.128

* Freeman-Halton exact test

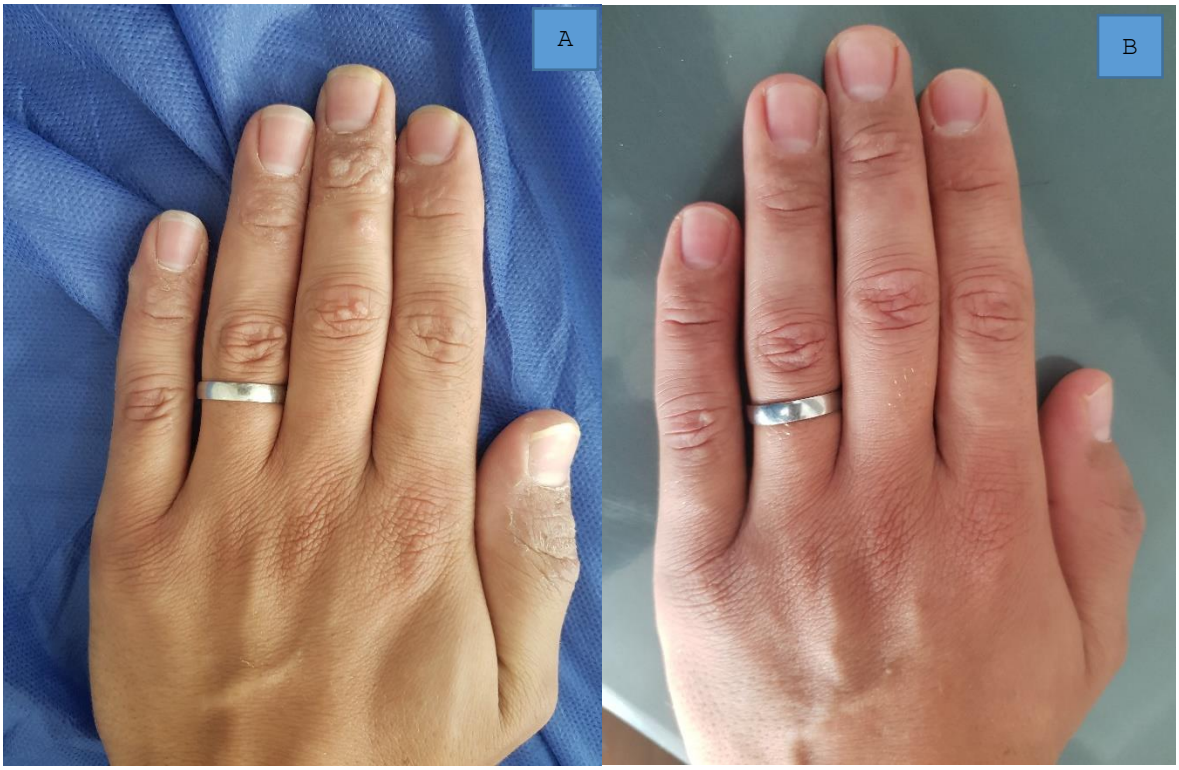

Figure (2): A. Showing multiple common warts before treatment, B. showing complete clearance of warts after 4 sessions of treatment with intralesional vitamin D3.

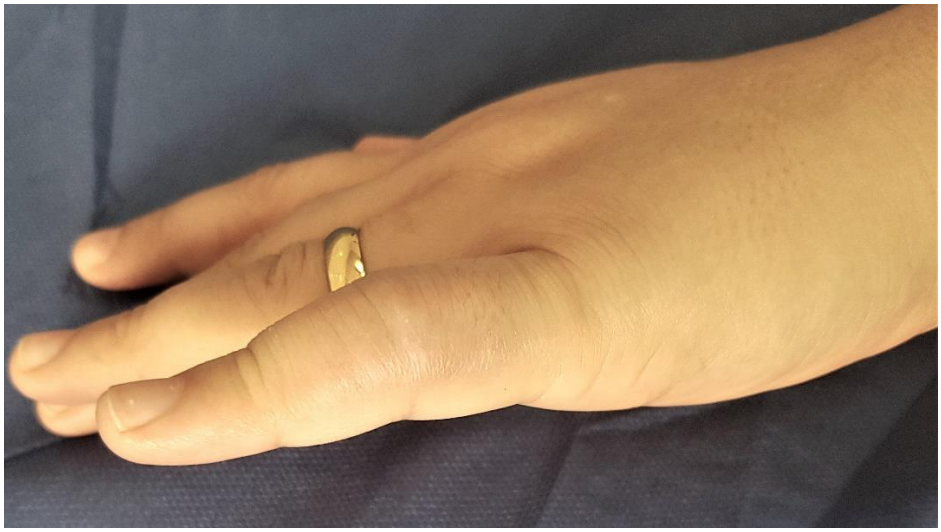

Figure (3): A. Showing a Single wart on the little finger before treatment B. showing complete clearance after 2 sessions of intralesional vitamin D3

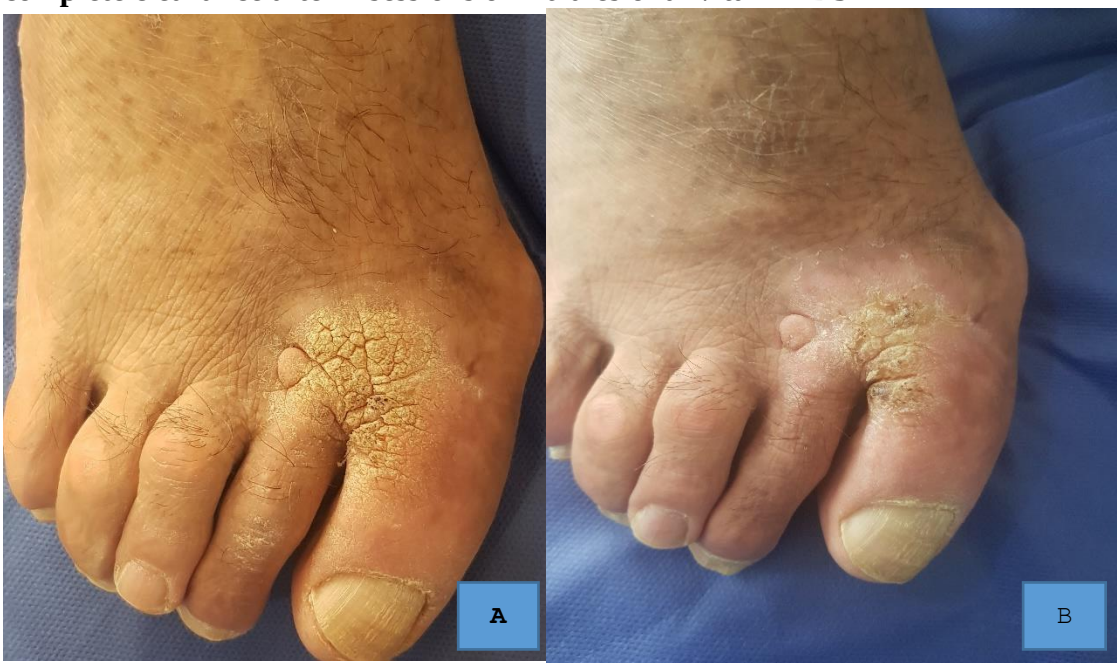

Figure (4): A. Showing a wart of 15 years' duration before treatment. B. Showing partial response after 4 sessions of intralesional vitamin D3

DISCUSSION:

Warts are non-cancerous (benign) skin growths that develop in different parts of the body and come in various forms. They are caused by viruses. Warts are contagious and very common: Most people will have one at some point in their lives. Although they can affect people at any age, warts are most common among children and teenagers (10). The present study involved 50 patients who had cutaneous warts with a median age of 21.50 years old ranging from 11.00 to 59.0 years, and the 25th percentile below 17.0 years. That was corresponding to the findings of Rübben *et al.* (11) who reported that patients aged between 10 and 30 years were most affected and they typically displayed a

long disease history (mean duration of warts at the time of first clinical examination, 22 months). Different age distribution was observed in HPV-1 serotype warts, most of which occurred in children 6-10 years of age. Common wart cases had the oldest mean age, with a mean of 51.3 (standard deviation of 19.3), while the youngest mean age was that of flat warts, with a mean age of 26.9 (standard deviation of 4.2). Moreover, the mean age of palmar and plantar wart cases was 34.1 (standard deviation 11.3) and 29.5 (standard deviation 5.7), respectively (12). Hongal *et al.,* study (13) found that most of the patients with palmoplanter warts belonged to the age group of 21-30 years (25.30%). Among the periungual wart, the patients' ages ranged from 22 to 89 years as reported by Riddel *et al.* (14).

In the current study, the male gender constituted 56.0% of common wart, 41.7% of palmoplanter, and 30.8% of periungual warts in comparison to females. The prevalence of common Wart was significantly higher in male than in female students (2.0% *vs*. 0.9%, $P < 0.0001$) (15). Moreover, Essa *et al*.,a study found that the gender distribution of common wart were 55% boys and 45% girls (16).

The association of gender with the type of wart was clearly noted in Ghadgepatil *et al.,* study (17) in which 61.9% of common wart was males and 38.1% females. Among the palmoplanter type, 80.0% were males and 20.0% females.

Additionally, the prevalence was significantly higher in male than in female students (2.0% *vs*. 0.9%, $P < 0.0001$) (15) and in students from rural than those from urban areas (1.7% *vs*. 1.3%, $P = 0.03$).

In the Hongal *et al.,* (13) study, the pattern of sex distribution of patients in palmoplanter showed 54.7% females and 45.3% males with female to male ratio of 1.2:1; while there was a male preponderance in a study by Kang *et al.,* with F:M = 1:1.01(18). While among the periungual warts men were affected twice as often as women as concluded by Riddel *et al.*,(14).

No statistical difference was found among the study groups in the present work regarding the residence in spite of the high proportion of urban residence among the study groups that constituted 72.0%, 70.0%, and 76.9% of common, palmoplanter, and periungual groups respectively.

Allayali *et al*.,the study ound that the total prevalence of warts was 10.3% and this agrees with the finding reported in Medinah and Jeddah regions, Saudi Arabia (19). On the other hand, a much lower prevalence rate (4.5%) was reported in Al Hassa rural area, Saudi Arabia (20), whereas a higher prevalence (13.1%) was reported in Kuwait (21). Moreover, the impact of socioeconomic status on the prevalence of warts is evident in several studies as the prevalence was higher in children from rural areas, public schools, and big families (19, 20, 22, 23). Factors like overcrowding, lower hygiene with sharing of personal fomites, and reluctance to seek medical advice are more common in children from rural areas, public schools, and big families which reflect lower socioeconomic levels.

Concerning the occupation effects on the different types of warts, the present study found that 48.0% of common warts, 41.7% of palmoplanter, and 53.8% of periungual were students followed by an employee who associated with 28.0%, 41.7%, and 30.8% among common, palmoplanter, periungual and the least frequent for all the groups was being housewives. Corresponding findings were reported by Ghadgepatil *et al.,* study (17) in which, among the common wart, 28.6% were students, 23.8% were workers, and 14.3% were housewives while among palmoplanter, 25.0% were 45.0% 20.0%. Also, common wart was the most common type of warts among students (49.0%) followed by plantar and plane warts (24.1%

each) while genital wart was the least frequent (2.8%) (16). Some studies from other areas in the world reported variable results. The prevalence of warts in primary school children in Romania and Taiwan was 6.9%, 2.4%, and 2.8%, respectively (24, 26). The highest reported prevalence was 33% among Dutch primary school students (27). While the palmoplanter wart in Hongal *et al,* study (12) showed that housewives constituted the majority (30%) followed by students (22.3%), agriculturists (17.3%), skilled laborers (10.3%), unskilled laborers (5.7%), elderly retired personnel (5.3%), professional workers (5%), business personnel (3%), children (0.7%) and un-employed (0.3%) and this reflects the functional importance of the palms and soles in one's occupation.

The wart might present as single or multiple with variable numbers as the present study showed, the median number of common warts was 4.0, palmoplanter wart was 3.5, and the Periungual wart was 5. Up to the knowledge, no study was found while searching the entire available website for a comparable parameter evaluating the differences in the numbers of the different wart types. Ahmed *et al.,* reported that the number of warts on the hands and feet varied from one to 80 (mean 5) (28).

Although the medians of the duration f the common wart and periungual were equal the 25th quartile of the common wart was longer. The median of the palmoplanter wart duration was 30. Ahmed *et al*.,a Study found that the mean duration of the common warts was 98 weeks (median 78, range 2-936) (28). In the current study, the frequent sites for the common wart were the foot in (36.0%), fingers in (28.0%) and hand in (20.0%); the palmoplanter wart (66.7%) in the foot, 25.0% in toes, and 8.3% in multiple areas. The commonest sites for periungual warts were hand were the 30.8%, 23.1% for each finger and toes. Essa *et al.,* study (16) showed that the hand was the most commonly affected (42.6%) followed by the face (28.7%) and feet (24.1%). The palmoplanter and periungual warts, and imbs (upper, 38%, and lower, 28%) were by far the commonest site of involvement in patients. Theng *et al.* (29) in their study that 39% of the cases involved hands and 38% involved feet. Face (23%) was the next commonly involved site whereas the trunk was affected the least (3%) in our study. Frequent involvement of the face is probably attributable to the increased cosmetic procedures like waxing, threading, facials, shaving, and so forth, in the saloons.

Additionally, the correlation of the clinical types with the sites of warts revealed that upper limbs including palms were affected in 28 (25.9%) patients and lower limbs including soles, in 24 (22.2%). With the addition of the periungual/subungual sites, overall involvement of extremities extended to 2/3rd (66.7%) of the cases. The next common site was the face (23%), which was the site of 72.2% of plane warts. The trunk was the least (3%) affected site. The majority (84.6%) of the cases of common warts involved extremities. Mosaic warts were seen in over two sites, soles (4; 66.7%) and Periungual. Two (2; 33.3%) of each of the four cases of filiform warts were present over the face and trunk (17).

The difference in the prevalence rate of warts between different studies may reflect the difference in socio-demographic patterns and distribution of risk factors among studied children in addition to differences in the inclusion criteria of the target population.

The size of warts was widely varied in the present study it was found that 48.0% of common wart, 33.3% of palmoplanter wart, and 53.8% of periungual wart had the size of 6-10 mm. A result that corresponds to a previous study where the wart may range in size from 1 mm to several centimeters (30).

Among those who have a history of previous

treatment for their warts, topical treatment was found to be the most frequent choice among the current study groups, in which 56.3% of common warts, 55.6% of palmoplanter warts, and 88.9% of periungual warts were used for. The surgical option was used for 12.5% of common warts only. Cryotherapy appeared to be the least frequent option pursed for the treatment of the different types of warts.

Salicylic acid topical application was found by Kwok *et al*., (31) to significantly increased the chance of clearing warts at all sites in trials compared to placebo (RR (risk ratio) 1.56, 95 percent CI (confidence interval) 1.20 to 2.03). Hands (RR 2.67, 95 percent CI 1.43 to 5.01) and feet (RR 1.29, 95 percent CI 1.07 to 1.55) subgroup analysis revealed it would be more effective for hands than feet. In a meta-analysis of cryotherapy versus placebo for warts across all sites, neither intervention nor controls were found to be superior (RR 1.45, 95 percent CI 0.65 to 3.23).

According to a previous study, topical agents were utilized first in most cases, Salicylic acid was often a first-line agent for the common wart. It required no prescription and can be used by the patient at home and has cure rates of 50% to 70% (30).

The commonest side effect among the current study group are pain which occurred in 34 patients (68%) and this is similar to the study done by Priya A et al 2019(32) and Jakhar D et al 2019 (33),Mohta A et al 2021(34).

Several studies have proposed the effectiveness of intralesional vitamin D in cutaneous warts treatment and through comparing our findings with the findings of those studies we can pinpoint the following notes; In a study involving 60 patients by RaghuKumar *et al., 2017* (35) reported complete clearance in 54 (90%) patients which is a huge percentage regarding the study's sample size, and partial response in four out of 60 (6.66%) patients, and no response in two (3.33) patients. The difference in the percentage of complete clearance may be related to the higher concentration of vitamin D3 (600000 IU) and or longer session intervals which were 3 weeks in this study in comparison to our study which was 2 weeks. In another study by Kavya *et al.* (36) involving 42 patients with multiple warts total responses were seen in 33 (78.57%) patients, six patients (14.28%) showed a moderate response, and three patients (7.14%) showed mild responses without a single patient showing no response at all and also this may be due to higher concentration of vitamin D3 which they used 600000 I.U.

A study by Priya A et al 2019(32) which used vitamin D3 intralesionally only in palmoplanter and periungual warts showed complete clearance in 56 (88.9%) out of 63 cases which is closer to our study as a more complete clearance rate was seen in these two types of a wart I mean out of 25 patients with palmoplanter and periungual wart 7 patients showed complete clearance in comparison to the common wart group only 4 patients showed complete clearance out of 25 patients and maybe this is another factor affecting the overall clearance rate, as in our study, half of the patients have common warts. In our study though 94% of the patients showed positive responses to the intra-lesional vitamin D3 injection but complete clearance was observed only in 11 patients out of 50 which is about only 22% of our actual sample size which means that the complete clearance rate in our study is relatively lower than previous studies. May be due to lower concentration of vitamin D3 or shorter duration between sessions, different types of wart involved in our study, and lastly increasing the number of sessions may have a better impact on clearance rate.

CONCLUSION:

Intralesional injection of Vitamin D3 is an extremely safe, recent, and creative method for the treatment of warts in general which also happens to be both inexpensive (cost-effective) and highly tolerable by most if not all patients (as its relatively not that painful to get rejected by the patient as a treatment and the injection site usually heals without scarring) also extremely practical when it comes to treating multiple cutaneous warts.

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The questionnaire includes the following

Code
Age:
ender: 1. male 2. female
Residency: 1. urban 2. rural
occupation: 1. student 2. housewife 3. Employee 4. not employee
Type of wart: common periungual palmoplantar
Number of warts:
Size of wart in mm:
Site of wart:
Duration in month:
History of previous treatment: 1. Yes 2. No
If yes:
What was the treatment: 1. Topical 2. cryotherapy 3. surgical
Why you seek for other modalities:
Pain not respond to treatments expensive recurrent
Clinical response

Session	No of lesions	Size	Side effects
1st			
2nd			
3rd			
4th			

Consent form

Research: The role of intralesional vitamin D3 injection in treatment of cutaneous warts
I…….
Herby consent to participate in above research study. The research project, which I am asked to participate, has been explained fully to me verbally and all my questions regarding the project have been answered to my satisfaction.

I understand that:

1. All information I will provide will be treated with strict confidence.
2. The result of the study will be used for research purposes and may be reported in scientific and academic journals.
3. I am free to withdraw from the project at any time during the study in which event my participations in the research will immediately cease and any information obtained from me will not be used in the study.

Signature :…… Date:…….