

COMPARISON OF THE EFFICACY OF INTRALESIONAL VITAMIN D3 AND INTRALESIONAL 5 FLUOROURACIL IN TREATMENT OF CUTANEOUS WARTS

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ABSTRACT

Background: Cutaneous warts are common benign skin lesions caused by human papillomavirus (HPV) and can be resistant to conventional therapies. Intralesional therapies such as vitamin D3 and 5-fluorouracil (5-FU) have emerged as promising treatment options, yet their comparative efficacy remains under-investigated. **Objective:** To compare the efficacy of intralesional vitamin D3 and intralesional 5-FU in the treatment of cutaneous warts. **Study Design:** Randomized controlled trial. **Setting:** Department of Dermatology, Khyber Teaching Hospital, Peshawar, Pakistan. **Duration of Study:** 29-September-2024 to 29-March-2025. **Methods:** A total of 192 patients with clinically diagnosed cutaneous warts were included and randomly assigned into two equal groups. Group A received intralesional vitamin D3 (0.2–0.5 mL of 15 mg/mL) combined with lidocaine-adrenaline, while Group B received intralesional 5-FU (10 units of 250 mg/5 mL) in the same anesthetic solution. Treatment efficacy was defined as >50% reduction in lesion size and number assessed visually. Data were analyzed using appropriate statistical tests, with a p-value <0.05 considered significant. **Results:** The mean age of participants in Group A was 33.04 ± 11.89 years, while in Group B it was 33.30 ± 11.31 years. The efficacy rate was significantly higher in the 5-FU group (82%) compared to the vitamin D3 group (64%) (p < 0.05). **Conclusion:** Intralesional 5-FU demonstrated superior efficacy compared to vitamin D3 in the treatment of cutaneous warts, suggesting that 5-FU may be preferred in clinical practice.

Keywords: Cutaneous Warts, Intralesional Therapy, 5-Fluorouracil, Vitamin D3, Efficacy

INTRODUCTION

Cutaneous warts tend to be proliferative conditions resulting from human papillomavirus (HPV) infection in keratinocytes. Viral warts exhibit a prevalence rate of 7% (1, 2). HPVs can be divided into high-risk and low-risk types based on their risk for carcinogenesis. The life cycle of HPV is intricately linked to the proliferation and differentiation of epithelial cells. Cutaneous HPV infection usually appears as various types of warts, such as flat warts on hands as well as face, common warts, plantar warts on soles of feet, along with condyloma acuminatum affecting the genitalia or perianal region (3-5). Most cutaneous HPV infections lead to proliferative lesions with rare progression to cutaneous cancers, which include squamous cell carcinoma (6). Dermoscopy can enhance diagnostic accuracy; nevertheless, adequate training is needed for it to be an effective tool (7-9). Diagnosing warts can be challenging because they resemble various skin lesions, including seborrheic keratosis, calluses, acne, and folliculitis. Conversely, these lesions may also resemble warts (10, 11). The treatment methods commonly used for warts focus on eliminating the infected epidermis. The pain associated with treatment, side effects, and expense can significantly influence the choice of therapy. 5-Fluorouracil (FU) inhibits cell division as well as induces cell cycle arrest. Topical 5-FU is used for treating warts; however, its curative effect is limited. Intralesional injection of 5-FU allows for elevated drug concentrations in the lesion, and prior research has demonstrated its efficacy in wart therapy (12). A vitamin D derivative regulates the production of cytokines, differentiation, and proliferation of keratinocytes, while additionally improving cell-mediated immunity. Intralesional vitamin D3 for wart treatment has been recorded, showing favourable outcomes (13). A study reported the efficacy of intralesional vitamin D3 (64%) and intralesional 5-fluorouracil (82%) in the treatment of cutaneous warts (14). Cutaneous warts, caused by HPV infection, represent a common dermatological condition characterized by their recurrent nature,

varied clinical presentations, and limited treatment options. Due to the scarcity of literature on this subject at the local level, the goal of this study is to compare the efficacy of intralesional vitamin D3 and intralesional 5-fluorouracil in the treatment of cutaneous warts at our health setup. The results of this study will be helpful for our clinicians in optimizing dosing regimens and addressing the challenges associated with individual therapeutic modalities, which would ultimately contribute to the development of evidence-based treatment guidelines and improved clinical management strategies for this common dermatological condition.

METHODOLOGY

This randomized controlled trial was conducted in the Dermatology Department at Khyber Teaching Hospital in Peshawar, from 29 September 2024 to 29 March 2025, following ethical approval from the hospital. The sample size was estimated using the World Health Organization's sample size calculator, taking an anticipated efficacy rate of 64% (14) for intralesional vitamin D3 and 52% (14) for intralesional 5-fluorouracil in treating cutaneous warts with an 80% power and 95% confidence level resulting in 192 participants evenly divided into two groups of 96 each.

Participants were selected through consecutive non-probability sampling. Patients aged 18 to 60 years of either gender diagnosed with cutaneous warts based on clinical features such as raised or flat growths with rough or smooth surfaces confirmed via dermoscopic examination, showing vascular structures, keratotic plugs, and surrounding hyperpigmentation were included in the study. Exclusion protocols encompassed pregnant patients, those with bleeding disorders, individuals on immunosuppressive therapy, or those with active infections. After obtaining consent from all participants, baseline demographics were documented on a structured proforma. Participants were then randomly assigned to one of two groups using a blocked randomization technique. In Group A, patients received an

injection of 0.5 ml of 2% lidocaine with adrenaline (1:200000) followed by 0.2 to 0.5 ml of vitamin D3 (600000 IU/15 ml) at the base of each wart. In Group B, a mixture of 2 units (0.5 ml) of 2% lidocaine with adrenaline (1:200000) and 10 units of 5-fluorouracil (250 mg/5 ml) was administered via an insulin syringe at the wart base. Injections were given weekly for up to five injections in both groups. Efficacy, defined as a greater than 50% reduction in lesion size and number assessed through visual inspection, was evaluated five weeks post-treatment by a dermatologist with at least five years of post-fellowship experience.

Data analysis was performed using SPSS 27. Age, weight, height, and body mass index were calculated using mean and standard deviation. Frequencies and percentages were evaluated for gender, efficacy, wart types, education, occupation, residence, and socioeconomic status. Efficacy between groups was compared using the chi-square test, with a p-value of less than or equal to 0.05 considered statistically notable. The types of warts and demographics were stratified with efficacy in both groups using the chi-square test with a P value notable at ≤ 0.05 .

In Group A (vitamin D3), the mean age of participants was 33.04 ± 11.895 years, while Group B (5-fluorouracil) had a mean age of 33.30 ± 11.319 years. The mean BMI was comparable between the groups, with Group A at 24.9498 ± 1.39270 and Group B at 24.8345 ± 1.51776 . Both groups consisted of 96 participants, ensuring balanced sample sizes.

Gender distribution showed slight variations, with Group A comprising 40 (41.7%) males and 56 (58.3%) females, whereas Group B had 45 (46.9%) males and 51 (53.1%) females. The distribution of wart types was comparable, with common warts being the most frequent in both groups, 43 (44.8%) in Group A and 46 (47.9%) in Group B (Table 1).

The primary outcome efficacy demonstrated a substantial difference between the groups. In Group A, 57 (59.4%) participants achieved efficacy, whereas in Group B, 78 (81.2%) participants achieved efficacy after five weeks of treatment ($p = 0.001$) (Table 2). Stratification of efficacy between both groups, categorized by demographics and type of warts, is presented in Table 3.

RESULTS

Table 1: Demographics and type of warts

Demographics and type of warts		Groups			
		Group A (Vitamin D3)		Group B (5 Fluorouracil)	
		n	%	n	%
Gender	Male	40	41.7%	45	46.9%
	Female	56	58.3%	51	53.1%
Education	Educated	37	38.5%	47	49.0%
	Uneducated	59	61.5%	49	51.0%
Occupation status	Employed	43	44.8%	46	47.9%
	Unemployed	53	55.2%	50	52.1%
Residence	Urban	53	55.2%	40	41.7%
	Rural	43	44.8%	56	58.3%
Socioeconomic status	Lower class	25	26.0%	24	25.0%
	Middle class	47	49.0%	54	56.2%
	Upper class	24	25.0%	18	18.8%
Type of wart	Common	43	44.8%	46	47.9%
	Mosaic	5	5.2%	2	2.1%
	Palmoplantar	43	44.8%	40	41.7%
	Periungual	5	5.2%	8	8.3%

Table 2: Comparison of efficacy between both groups

		Groups				P value
		Group A (Vitamin D3)		Group B (5 Fluorouracil)		
		n	%	n	%	
Efficacy	Yes	57	59.4%	78	81.2%	0.001
	No	39	40.6%	18	18.8%	

Table 3: Stratification of Comparison of efficacy between both groups with demographics and type of warts

		Groups				P value
		Group A (Vitamin D3)		Group B (5 Fluorouracil)		
		n	%	n	%	
Gender	Male	40	41.7%	45	46.9%	P > 0.05
	Female	56	58.3%	51	53.1%	
Education	Educated	37	38.5%	47	49.0%	P > 0.05
	Uneducated	59	61.5%	49	51.0%	
Occupation status	Employed	43	44.8%	46	47.9%	P > 0.05
	Unemployed	53	55.2%	50	52.1%	
Residence	Urban	53	55.2%	40	41.7%	P > 0.05
	Rural	43	44.8%	56	58.3%	
	Lower class	25	26.0%	24	25.0%	P > 0.05

Socioeconomic status	Middle class	47	49.0%	54	56.2%	P > 0.05
	Upper class	24	25.0%	18	18.8%	
Type of wart	Common	43	44.8%	46	47.9%	
	Mosaic	5	5.2%	2	2.1%	
	Palmoplantar	43	44.8%	40	41.7%	
	Periungual	5	5.2%	8	8.3%	

DISCUSSION

We compared the efficacy of intralesional vitamin D3 and 5-fluorouracil (5-FU) in treating cutaneous warts. The study observed the reduction in lesion and wart numbers, with a visual assessment of patients showing more than 50% improvement after several weeks. In Group A (5-FU), 81.8% of patients achieved complete clearance, while Group B (vitamin D3) showed a lower complete clearance rate of 63.6%. These findings align with Gupta et al., who documented notably higher efficacy rates for 5-FU as compared to vitamin D3 in treating cutaneous warts (14). Kamal et al. observed a 75% excellent response rate with intralesional 5-FU, further supporting its effectiveness.(15)

Fatima K et al. in their study assessed the efficacy of 5-FU for the treatment of warts; they reported that over 70% of their patients had an excellent response in terms of more than 75% clearance of warts (12). Bdaiwi et al. documented a complete response to the treatment of intralesional 5-FU in 80% of patients with cutaneous warts (16). Shaikh RB et al. also documented that 5-FU is a safe and effective therapy for treating cutaneous warts (17).

Yazdanfar et al., who reported a 64.7% complete response rate for 5-FU, though their study used a combination of 5-FU, lidocaine, and epinephrine, which may account for the slightly lower efficacy compared to our results (18). Similarly, the higher efficacy in our study could be attributed to the standardized dosing regimen and the inclusion of a broader range of wart types.

In contrast, Aktas et al. (2016) reported an 80% complete clearance rate with intralesional vitamin D3 (19). Raghukumar et al. (2017) noted a 90% clearance rate with vitamin D3, but their study primarily included palmoplantar warts, which might respond better to immunotherapy due to their thicker keratin layer (20). Our findings suggest that while vitamin D3 is a viable option, its efficacy is more inconsistent compared to 5-FU, particularly for warts in anatomically challenging locations like periungual areas.

Based on these findings, intralesional 5-FU emerges as the more effective and reliable treatment for cutaneous warts, particularly for recalcitrant or anatomically challenging cases. Its higher complete clearance rates and consistent performance across studies make it a first-line option, especially in resource-limited settings where cost and accessibility are critical. Vitamin D3, while safer and capable of inducing systemic immune responses, may be better suited as an adjunctive therapy or for patients with contraindications to 5-FU. Future research should explore combination therapies such as 5-FU with vitamin D3 to leverage the strengths of both treatments while minimizing drawbacks.

CONCLUSION

In conclusion, the efficacy of intralesional 5-fluorouracil in terms of reductions in both size and number of lesions was significantly better than intralesional vitamin D3 in the treatment of cutaneous warts.

DECLARATIONS

Data Availability Statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned. (IRB-549/DME/KMC)

Consent for publication

Approved

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

HAMEED ULLAH (Trainee Medical Officer)

Contributed to study design, data collection, data analysis, and initial drafting of the manuscript.

MEHRAN KHAN (Associate Professor)

Supervised the overall study, provided critical guidance in study, and reviewed the final manuscript.

IMDAD ULLAH KHAN (Trainee Medical Officer)

Critical input, and review of literature.

HAJIRA AMIN (Trainee Medical Officer)

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