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Treatment of flat warts with trifarotene

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Abstract

This retrospective study explores the off-label use of trifarotene, a topical retinoid currently approved only for acne in individuals aged 12 years and older for the treatment of verrucae planae (flat warts). Our study included patients aged 3 to 45 years, demonstrating a high safety and tolerability profile due to the minimal systemic absorption of trifarotene. The therapy allowed for the rapid resolution of warts, avoiding invasive and potentially scarring treatments, particularly crucial for pediatric patients and young adults. These findings suggest that trifarotene may provide a cosmetically favorable and effective alternative for managing flat warts, warranting further investigation.

Introduction

Flat warts, or verrucae planae, are benign lesions caused by human papillomavirus (HPV).[1] These lesions predominantly affect young adults or children and are particularly distressing when located on the face, where they can cause psychological and cosmetic concerns. Despite the availability of numerous treatments, including cryotherapy, salicylic acid, and tretinoin, many patients experience limited efficacy, significant irritation, or poor compliance. Trifarotene, a fourth-generation retinoid with selective activity on retinoic acid receptor gamma (RAR-γ), is currently approved for the topical treatment of acne vulgaris in patients aged 12 years and older.[2] Its pharmacologic profile and high selectivity for RAR-γ make it suitable for exploration in other keratinization disorders such as flat warts. Its mechanism of action promotes keratinocyte differentiation with a favorable safety profile, particularly for facial application. This retrospective observational case series explores the off-label use of trifarotene gel 0.005% in the management of facial verrucae planae in young adults or children in a real-world clinical setting.

Materials and Methods

Thirty-one patients (26 adults and 5 children aged 3-12 years) with facial verrucae planae were included. All patients had previously failed at least one conventional therapy such as cryotherapy, topical retinoids, CO_2 laser, and immunostimulants/nutraceuticals. Exclusion criteria included pregnancy, breastfeeding, or active inflammatory dermatoses. All patients were immunocompetent, and none had a history of immunosuppressive therapy or systemic diseases affecting immune function. HIV testing was not routinely performed, but no patients had known HIV infection or clinical suspicion thereof. None of the included patients received HPV vaccination during the study period. Although HPV vaccination is not currently recommended as a therapeutic intervention for established HPV infection, its possible role as an adjuvant measure in reducing viral persistence has been suggested in recent literature.[3]

Patients applied trifarotene gel 0.005% twice daily (morning and evening) for the first 10 days, followed by one-daily application in the evening for the next 45 days. A lentil-sized amount of gel was applied to each affected area, as instructed during the initial consultation.
Patients were encouraged to use a non-comedogenic moisturizer to mitigate dryness or irritation. Follow-up visits were conducted on days 10, 30, and 55.

Results

The detailed results for each patient are summarized in Table 1. Among the 26 adults, 2 discontinued treatments due to moderate irritation linked to over-application, leaving 24 evaluable patients. Between those who completed treatment, clinical improvement was observed in 13 patients (54.2%) at day 10. At day 55, 91.7% of patients achieved complete resolution. The pediatric group included 5 children, with 1 discontinuing treatment leaving 4 evaluable patients. By day 10 clinical improvement was noted in 1 patient (25.0%). By day 55, 4 patients (100.0%) achieved complete resolution. Three patients discontinued treatment due to moderate to severe side effects, including burning, itching, and peeling. These adverse effects were linked to excessive application of the gel, contrary to instructions. Mild and transient erythema, peeling, and dryness were reported in 10 patients, effectively managed with emollients. Patients reported high adherence to the treatment protocol, citing ease of use and rapid improvement.

Discussion

This study demonstrates the efficacy and safety of trifarotene gel 0.005% for treating facial verrucae planae (Figure 1 A-D). The high clearance rates and excellent tolerability, particularly with correct application, position trifarotene as a promising alternative to conventional therapies.[4] Trifarotene offers significant advantages over conventional treatments such as cryotherapy, salicylic acid, and tretinoin. Unlike cryotherapy and salicylic acid, which often cause discomfort and necessitate multiple treatment sessions, and tretinoin, which is known for causing considerable irritation, Trifarotene provides a more targeted approach. Its selective action on RAR-γ minimizes systemic absorption, thereby reducing the risk of irritation commonly associated with other retinoids.
Its rapid onset of action and patient-friendly dosing schedule further enhance its utility, particularly for facial lesions where cosmetic outcomes are critical. The discontinuation in 3 patients underscores the importance of patient education on proper application techniques. The rapid improvement seen with trifarotene suggests it may be particularly beneficial for patients requiring effective and cosmetically acceptable solutions for facial flat warts. The inclusion of moisturizers in the treatment protocol was crucial in mitigating side effects and improving patient adherence. While our study

focuses on topical retinoid therapy, it is worth noting that a potential therapeutic role for HPV vaccination in managing recalcitrant warts has recently been proposed, particularly in pediatric and immunocompetent populations.[3] This evolving evidence underscores the multifactorial nature of HPV persistence and the need for integrated management approaches.

Conclusions

This study lacks a control group and statistical analyses, limiting the ability to draw definitive conclusions. However, its findings provide valuable real-world evidence. Future randomized controlled trials should evaluate long-term efficacy, recurrence rates, and comparative outcomes with other therapies.[5,6]

References

1. Olguín-García MG, Peralta-Pedrero ML, Jurado-Santa Cruz F, et al. Low-dose oral isotretinoin in the treatment of recalcitrant facial flat warts: A clinical case and review of literature. Health Sci Rep 2023;6:e1633.
2. Cosio T, Di Prete M, Gaziano R, et al. Trifarotene: A Current Review and Perspectives in Dermatology. Biomedicines 2021;9:237.
3. Herzum A, Ciccarese G, Occella C, et al. Treatment of Pediatric Anogenital Warts in the Era of HPV-Vaccine: A Literature Review. J Clin Med 2023;12:4230.
4. Zhu P, Qi RQ, Yang Y, et al. Clinical guideline for the diagnosis and treatment of cutaneous warts (2022). J Evid Based Med 2022;15:284-301.
5. Olguin-García MG, Jurado-Santa Cruz F, Peralta-Pedrero ML, Morales-Sánchez MA. A double-blind, randomized, placebo-controlled trial of oral isotretinoin in the treatment of recalcitrant facial flat warts. J Dermatolog Treat 2015;26:78-82.
6. Yang YL, Sang J, Liao NX, et al. Off-label photodynamic therapy for recalcitrant facial flat warts using topical 5-aminolevulinic acid. Lasers Med Sci 2016;31:929-36.

Figure 1. A, **C**) Clinical images of a 26-year-old female and a 6-year-old boy with flat warts on the face. **B**, **D**) Complete disappearance of flat warts after application of trifarotene gel 0.05% for 45 consecutive days, with mild side effects such as transient erythema and dryness.

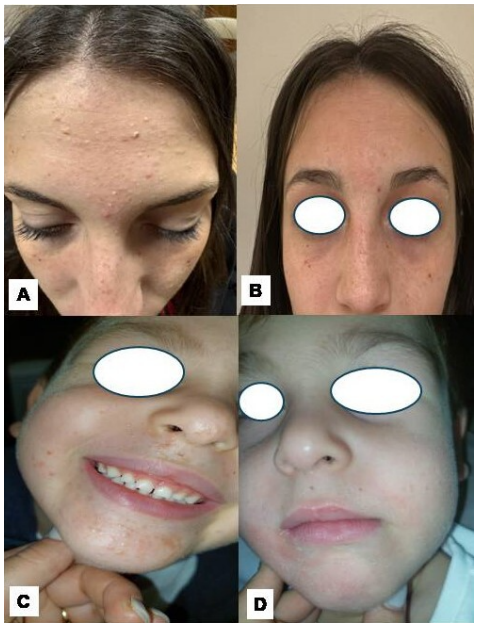

Table 1. Patients' demographics, treatment groups, and follow-up visits.

Among the adults (n=26), 2 discontinued treatment, leaving 24 for analysis. Day 10: clinical improvement observed in 54.2% (13/24) of patients; Day 30: significant clearance in 83.3% (20/24) of patients; Day 55: complete resolution achieved in 91.7% (22/24) of patients.

The pediatric group included 5 children, with 1 discontinuing treatment. Day 10: clinical improvement in 25.0% (1/4); Day 30: significant clearance in 75.0% (3/4); Day 55: complete resolution in 100.0% (4/4).

Patients	Sex	Age	Localization	Duration of warts	Previous treatments	Response at Day 10	Response at Day 30	Response at Day 55
P1	Male	25	Cheekbone, forehead	6 months	No treatment	Mild improvement	Moderate clearance	Complete resolution
P2	Female	30	Chin, nose	1 year	Imiquimod	No improvement	Significant clearance	Complete resolution
P3	Male	35	Cheeks	7 months	Cryotherapy	Significant improvement	Complete clearance	Complete resolution
P4	Female	28	Cheekbone, cheeks	8 months	No treatment	No improvement	Partial clearance	Complete resolution
P5	Male	40	Forehead, chin	1 year	Topical retinoids	Moderate improvement	Significant clearance	Complete resolution
P7	Female	26	Forehead, cheeks	9 months	CO_2 Laser	Moderate improvement	Significant clearance	Complete resolution
P8	Male	33	Nose, chin	1 year	Cryotherapy and retinoids	No improvement	Partial clearance	Moderate clearance

P9	Female	29	Cheeks, cheekbone	5 months	Imiquimod	Mild improvement	Moderate clearance	Complete resolution
P11	Female	32	Forehead	6 months	No treatment	Moderate improvement	Significant clearance	Complete resolution
P12	Male	27	Nose, forehead	1 year	CO_2 Laser	Mild Improvement	Moderate clearance	Complete resolution
P13	Female	31	Cheeks	8 months	Cryotherapy	No improvement	Partial clearance	Moderate clearance
P14	Male	23	Cheekbone	1 year	Imiquimod	Mild improvement	Significant clearance	Complete resolution
P15	Female	21	Chin	6 months	No treatment	Moderate improvement	Significant clearance	Complete resolution
P16	Male	38	Forehead, nose	9 months	Cryotherapy	No improvement	Partial clearance	Significant clearance
P17	Female	34	Cheeks	1 year	Topical retinoids	Mild improvement	Moderate clearance	Complete resolution
P18	Male	37	Cheeks, cheekbone	2 years	CO_2 Laser	Moderate improvement	Significant clearance	Complete resolution
P19	Female	29	Nose, forehead	1 year	Imiquimod	No improvement	Partial clearance	Complete resolution
P20	Male	36	Forehead, cheeks	7 months	Cryotherapy	Moderate improvement	Significant clearance	Complete resolution
P21	Female	28	Chin, nose	6 months	Topical retinoids	No improvement	Partial clearance	Significant clearance
P22	Male	32	Cheekbone	1 year	No treatment	Mild improvement	Moderate clearance	Complete resolution
P23	Female	30	Forehead, cheeks	6 months	CO_2 Laser	Moderate improvement	Significant clearance	Complete resolution
P24	Male	27	Cheeks	1 year	Cryotherapy and retinoids	No improvement	Partial clearance	Moderate clearance
P25	Female	26	Forehead, chin	8 months	Imiquimod	Mild improvement	Moderate clearance	Complete resolution
P26	Male	33	Chin, nose	1 year	No treatment	Moderate improvement	Significant clearance	Complete resolution
P28	Female	9	Cheeks, cheekbone	3 months	Topical retinoids	Mild improvement	Moderate clearance	Significant clearance
P29	Male	8	Forehead	6 months	Cryotherapy	No improvement	Partial clearance	Moderate clearance
P30	Female	4	Nose,ocularr egion	1 year	Cryotherapy	Moderate improvement	Significant clearance	Complete resolution
P31	Male	6	Forehead	1 year	Cryotherapy	No improvement	Partial clearance	Significant clearance
P29	Male	22	Cheeks, chin	8 months	No treatment	Treatment discontinued	Treatment discontinued	Treatment discontinued
P30	Female	24	Cheekbone	6 months	Cryotherapy	Treatment discontinued	Treatment discontinued	Treatment discontinued
P31	Male	10	Cheeks, nose	5 months	Topical retinoids	Treatment discontinued	Treatment discontinued	Treatment discontinued