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Oral isotretinoin for the treatment of dermatologic conditions other than acne: a case series

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Abstract

Dermatophyte infections, also known as tinea, along with viral warts, are common skin conditions that can be difficult to treat, especially when they recur or resist standard therapies. Isotretinoin, a medication traditionally used for acne, has recently shown promise as an adjuvant therapy for these conditions.

This retrospective case-series study included four adult patients with persistent or recurrent tinea infections (tinea cruris and tinea corporis) or viral warts (genital and facial) who were treated with oral isotretinoin in addition to standard therapies. The patients' demographics, clinical presentations, treatment regimens, and responses were analyzed.

All four patients showed significant clinical improvement after starting isotretinoin. Two patients with viral warts achieved complete clearance, and two patients with tinea infections experienced notable improvement. No severe side effects were reported.

This case series suggests that isotretinoin may be a promising adjunctive therapy for patients with persistent or recurrent tinea infections and viral warts. However, further quantitative controlled studies are needed to confirm these findings and establish optimal treatment protocols.

This study provides preliminary evidence for the potential benefit of using isotretinoin as an adjunctive therapy for recalcitrant tinea infections and viral warts. Further research is warranted to explore its efficacy and safety in larger populations.

Introduction

Dermatophyte infections, also known as tinea, are among the most common skin infections.¹ Based on their locations, they are clinically classified into tinea capitis (scalp), tinea faciei (face), tinea barbae (beard), tinea corporis (body), tinea manuum (hands), tinea cruris (groin), and onychomycosis or tinea unguium (nails).² The rise of tinea infections could be attributed to a complex intersection between the environment, *e.g.*, humidity and geographical region, as well as the host factors such as genetic proneness to infections, pets, mechanical skin lesions, in addition to the dermatophytic virulence, species of fungus, and adaptation.³ The mainstay of treatment of tinea is with antifungals. However, unusual presentations, *i.e.*, chronic recurrent infections, resistance to conventional therapy, and severe itching, are not uncommon in daily clinical practice.⁴ The use of oral isotretinoin as an adjunctive therapy with antifungals was recently suggested. This is because it has a keratolytic effect on the skin, which supposedly leads to rapid sloughing of the epidermis and removal of fungal spores, thereby decreasing the fungal load.⁵ Based on a study by Alhamdi *et al.*, 97.5% of patients who receive isotretinoin and itraconazole show earlier and complete clearance with a lower recurrence rate of 12.8% compared to a

lower cure rate of 53.7% and a higher recurrence rate of 68.1% in patients who were on itraconazole alone.⁶ Warts are cutaneous and mucous membrane lesions caused by Human Papillomavirus (HPV) commonly manifest as warts including flat warts (*verruca plana*, on hands and face), common warts (*verruca vulgaris*), planta warts (*verruca plantaris*, on soles of feet), and condyloma acuminatum (anogenital warts, on genitalia, anus, or perianal area).⁷ Recalcitrant warts are verruca lesions that were resistant to an initial treatment method, necessitating the need for an alternative therapy.⁸ Isotretinoin inhibits the replication of the HPV-infected cells due to its role in growth and cell differentiation. Retinoids have been used alone or as an adjunctive therapy to treat HPV skin infections, especially the recurrent or recalcitrant warts.⁹ According to Olguin-García *et al.* in a study on patients with refractory facial warts, those who received oral isotretinoin showed complete clearance of all flat warts, while none of the patients in the placebo group showed any improvement.¹⁰

In this case series, we aim to evaluate whether isotretinoin has a synergistic effect with antifungals in the treatment of recurrent dermatophytosis and to determine its effectiveness in the treatment of recalcitrant cutaneous and genital warts.

Case Series

This retrospective case-series study included patients with either fungal or viral infection, specifically tinea cruris, tinea corporis, and viral warts, who were treated with oral isotretinoin at the dermatology clinic in Salmaniya Medical Complex, Bahrain. Those who were eligible for the inclusion criteria were adults aged 18 or older, regardless of their gender or ethnic group. In both conditions, namely dermatophytes and warts, the included patients were diagnosed by a consultant in dermatology, based on the corresponding diagnostic criteria and supported with laboratory investigations as required. Moreover, their conditions were decided to be persistent or recurrent despite being compliant and receiving single or multiple courses of standard anti-fungal and/or several cryotherapy sessions over a sufficient amount of time. Patients who missed follow-ups, appointments, or were non-compliant with prescribed oral and topical therapy were excluded from the study. Since isotretinoin is contraindicated for pregnant and breastfeeding females, they were also excluded. All the patients were prescribed oral isotretinoin with scheduled follow-up visits. The I-SEHA national medical database was utilized to collect data from patients' electronic hospital records, including patient demographics and clinical details such as prior unsuccessful treatment approaches, isotretinoin dosage and frequency, additional adjuvant therapies, treatment duration and response, as determined by the consultant based on patient history, physical examination, and previous photographs of the lesion. The dose of isotretinoin prescribed was 20 mg to

30 mg according to weight and response, which was established as an appropriate and efficient dose.¹⁰ The study was approved by the Research Ethics Committee of Government Hospitals, and informed consent was signed by all four participating patients.

In total, four patients were included in the study, among whom three were males. The clinical diagnoses, duration of complaint and the date of first visit are mentioned in Table 1. The dose of isotretinoin prescribed was 20 to 30 mg per day. All laboratory investigations needed were done before and during treatment. No abnormalities necessitating the discontinuation of the treatment were detected.

Case 1

Patient 1 is a 27-year-old male who was diagnosed with extensive genital warts. His first visit was on February 16, 2023, during which he underwent his first session of cryotherapy. One week later, on the second visit, the patient was started on isotretinoin 20 mg by mouth (PO) once a day (OD) along with a second session of cryotherapy. Due to work commitments, the patient was not able to come for regular cryotherapy sessions and continued to administer the same dose of isotretinoin. Starting from April 6, 2023, after approximately six weeks of isotretinoin, the patient showed significant clinical improvement in every follow-up visit.

Case 2

Patient 2 is a 65-year-old male who was diagnosed with numerous and extensive perioral warts. The patient was started on isotretinoin 20 mg PO OD for two months, with one session of cryotherapy done. Two months later, he showed mild improvement. Accordingly, the dosage of isotretinoin was increased to 30 mg for a period of three months, and a second session of cryotherapy was administered during this timeframe. After three months of isotretinoin dose escalation and a total of two sessions of cryotherapy, warts were cleared, and isotretinoin was discontinued as shown in Figure 1.

Case 3

Patient 3, who is a 63-year-old male, has been complaining of tinea cruris for 10 weeks. Neither 4 weeks of terbinafine 250 mg PO OD nor four weeks of itraconazole 200 mg PO OD alleviated the patient's condition. In March 2023, in addition to topical anti-fungal and ketoconazole shampoo, he was started on dual oral antifungal medications: griseofulvin 500 mg PO twice daily (BID) along with itraconazole 200 mg PO BID. In the following visit, which was 3 weeks later, the patient complained of nausea, abdominal pain, and headache; hence, itraconazole was discontinued and switched to terbinafine 250 mg

PO BID along with the previously prescribed dose of griseofulvin. Despite being on two antifungal agents, the patient showed no improvement three weeks later. On April 17, 2023, the patient was started on isotretinoin 30 mg PO OD along with the dual oral antifungal. Two months after the isotretinoin had been started, the patient showed an obvious clinical improvement as shown in Figure 2.

Case 4

Patient 4 is a 28-year-old female who was diagnosed in 2018 with resistant tinea cruris and corporis. Prior to presenting at our clinic, the patient underwent multiple courses of terbinafine and voriconazole treatment administered by the infectious disease team between September 2018 and September 2021. The patient showed mild improvement of the lesions, but never cleared. When we visited the patient in September 2021, the lesions were still active; a KOH skin scraping test was performed, which revealed numerous hyphae. Accordingly, the patient was started on itraconazole 200 mg PO BID along with topical anti-fungal and ketoconazole shampoo. Ten weeks later, the lesions cleared, and therefore oral itraconazole was discontinued. The patient attended the clinic three months later, in February 2022, complaining of a relapse. She was restarted on itraconazole for one month with the same previously given dose; however, the lesions failed to respond and showed no improvement. Griseofulvin 500 mg PO BID was started in March 2022 for one month as an add-on therapy along with itraconazole, but it showed only minimal improvement, and the lesion remained active. In April 2022, the patient was started on isotretinoin 20 mg PO OD in addition to the dual oral anti-fungal therapy. Two months later, the lesions were cleared, as shown in Figure 3, and isotretinoin was discontinued.

Discussion

In this study, the clinical information of four adult patients suffering from viral warts and tinea infections was included. All patients have been treated with isotretinoin as an adjunct to the standard treatment of their conditions, which failed to achieve a cure of their diseases. In our case series, two out of four patients suffered from viral warts, one in the genital area and the other in the perioral area.

Viral warts are considered common dermatologic and cosmetic problems that are caused by HPV infection. Some challenging cases failed to improve with conventional methods such as cryotherapy, topical salicylic acid, and topical immunotherapy. Both patient 1 and patient 2 were started on the standard treatment; in their cases, it was cryotherapy, which resulted in a suboptimal response or clearance; hence, isotretinoin was used. Moreover, viral warts are often interrelated with poor cosmetic outcome since they cause disfiguring, pain, bleeding, and high recurrence rates, thus requiring a systemic

agent to avoid recurrence.^{11,12} Since isotretinoin, as mentioned previously, is thought to have a mechanism of inhibiting the replication of HPV infected cells, it has been used in patients who fail the standard treatments of viral warts, *e.g.*, imiquimod, 5-fluorouracil, and cryosurgery.¹³ In one study, using low-dose isotretinoin (30 mg/day) for two months on 31 patients with recalcitrant facial plane warts showed that 73.07% of the patients involved in the study had complete clearance, which concluded that oral isotretinoin was effective in the management of difficult cases. Researchers in this study mentioned the possible advantages of increasing the dose to 60 mg/day to decrease the relapse rate and speed up the response.¹² Compared to this study population and our case reports, patient 2 received what is considered a low dose of isotretinoin, 20 mg per day for two months, then increased to 30 mg per day for three months until the lesions cleared. A systematic review on the use of oral isotretinoin found that treating condyloma acuminata with isotretinoin monotherapy resulted in a response ranging between 2.5 and 4.1 months. It demonstrated that integrating it with other modalities was more effective than monotherapy. In fact, there was a significant reduction in the duration of therapy when using isotretinoin in combination therapy, as well as a reduction in the recurrence rates.¹⁴ This was the case with patient 1.

In our case series, patient 3 and patient 4 suffered from tinea infections, treated with the standard treatment, with no or trivial improvement. Over the last years, incomplete clearance of dermatophytic infections has been a primary concern. Despite patients being managed with the same gold standard medications, namely griseofulvin, terbinafine, and azoles such as itraconazole, whether used topically or systemically, cases of recurrent and chronic dermatophyte infections are notably increasing.¹⁵⁻¹⁷ All these agents have been used in both patients with no complete clearance. This increased incidence of tinea infections, particularly recurrent and chronic cases, significantly impacts patients' quality of life and creates economic burdens due to longer treatment courses.^{3,18} Based on these factors, we opted to try isotretinoin for our patients with tinea infections. To achieve higher cure rates for these infections, various approaches have been explored, including lengthening the course of antifungals, increasing the doses of such medications, or using combinations of drugs.¹⁹ In the current case series, this has been the strategy for patient 3 and patient 4. They both received courses of combined topical and systemic antifungals, as well as different antifungal agent combinations.

There have been limited studies investigating the treatment of recalcitrant tinea infections with isotretinoin. A case study was published concerning a 23-year-old man with a history of recurrent tinea infections spanning two years, during which he received multiple courses of topical and systemic antifungal treatments without achieving complete remission. His lesions were completely eradicated once low-dose isotretinoin (20 mg/day) was added to dual antifungals.²⁰ Another study concluded that

combining low-dose isotretinoin with itraconazole resulted in earlier and complete clearance of lesions compared to treatment with the sole ordinary anti-fungal treatment.⁶ This was the management plan for patients 3 and 4; isotretinoin was prescribed in addition to dual antifungal, and collectively they achieved clearance of the lesions. Although there is limited information on the use of isotretinoin in treating viral warts or tinea infections, based on our case studies and the studies published on the use of isotretinoin in addition to the conventional treatment, it could be promising in the treatment of these recurrent infections. Indeed, more studies are essential, especially clinical trials, to highlight the pharmacokinetics, determine the doses with minimization of side-effects, and assess the efficacy of isotretinoin in treating recurrent fungal infections and viral warts, especially with the increased endemicity of these conditions. To our knowledge, this is the first case series to be published about the use of isotretinoin in the treatment of viral warts and dermatophytic infections in our region. These case reports open new horizons for more research on this topic. One of the limitations of our study was the small number of patients; some cases were not reportable as they lost follow-up in our institution during the COVID-19 pandemic.

Conclusions

The findings of the current study show an apparent synergetic effect of isotretinoin as an add-on treatment line with the conventional treatments in patients with persistent or recurrent tinea infections and HPV warts. These findings should be supported by quantitative studies on a larger number of patients with a solid methodology to inform recommendations for isotretinoin as part of treatment guidelines.

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Table 1. General characteristics of the patients.

	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	27	65	63	28
Gender	Male	Male	Male	Female
Clinical diagnosis	Extensive genital warts	Severe perioral warts	Tinea cruris	Tinea cruris and tinea corporis
Date of first visit	16/02/2023	27/10/2021	27/02/2023	25/09/2018

Figure 1. Extensive perioral warts: **A)** after failure of conventional wart therapy; **B)** after administration of oral isotretinoin along with cryotherapy.

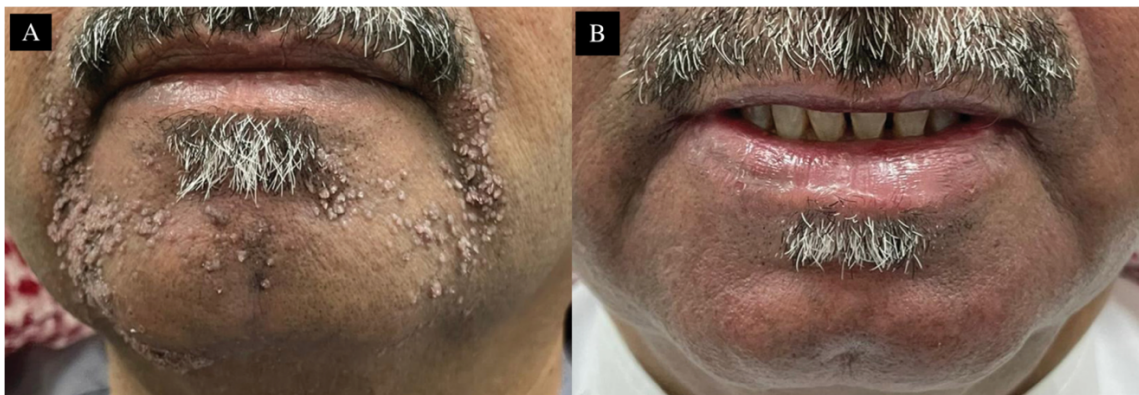


Figure 2. Resistant tinea cruris: **A)** after failure of conventional tinea therapy; **B)** after administration of oral isotretinoin along with dual oral anti-fungal therapy.



Figure 3. Resistant tinea corporis: **A)** after failure of conventional tinea therapy; **B)** after administration of oral isotretinoin along with dual oral anti-fungal therapy.

