EJCRIM
European Journal
of Case Reports
in Internal Medicine

INHALED ILOPROST FOR DIGITAL NECROSIS IN SYSTEMIC SCLEROSIS – AN EFFECTIVE ALTERNATIVE

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Received: 23/09/2024
Accepted: 22/10/2024
Published: 19/03/2025

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: Signed patient consent was obtained.

How to cite this article: Yousfi J, Alami Idrissi S, Dakir F, Bott Z, Taouil C, Zahlane M, Essaadouni L. Inhaled iloprost for digital necrosis in systemic sclerosis – an effective alternative. *EJCRIM* 2025;**12**:doi:10.12890/2025_004913

ABSTRACT

Introduction: Vascular issues in systemic sclerosis (SSc), notably Raynaud's phenomenon, can lead to digital ulcers (DU) and necrosis, causing pain and infections. Intravenous prostacyclin (iloprost) is used for established DUs. We report a case where severe Raynaud's phenomenon revealed SSc sine scleroderma, which improved with inhaled iloprost.

Case description: A 52-year-old former smoker with protein C deficiency, on anticoagulation since 2016 for a previous deep vein thrombosis, presented with severe Raynaud's phenomenon and pulp necrosis of the third right finger. The capillaroscopy revealed megacapillaries suggestive of a connective tissue disease, and antinuclear antibodies were positive for centromere fluorescence. Doppler ultrasound and cardiopulmonary assessments were normal. The patient underwent necrosectomy but had ischemic pain and cyanosis post-surgery. Inhaled iloprost (2 ampoules of 10 mg/10 ml daily in 3 cycles of 5 days) led to significant clinical improvement.

Conclusion: Inhaled iloprost could be an effective and better-tolerated alternative to intravenous iloprost for treating SSc DUs. Further studies are needed to confirm this potential.

KEYWORDS

Systemic sclerosis, digital ulcers, necrosis, inhaled prostacyclin

LEARNING POINTS

- This case report shows the efficacy of inhaled prostacyclin in the treatment of digital ulcers in systemic sclerosis as an equally effective, better tolerated, and safer alternative to the usual intravenous route.

INTRODUCTION

Hand involvement in systemic sclerosis (SSc) is very common, often occurring early, and provides contributory elements for the diagnosis of the disease. Vascular involvement is prominent manifesting as Raynaud's phenomenon, which can lead to digital ulcers (DU) and digital necrosis causing pain and superinfections. Although no systemic treatment has proven efficacy in healing SSc DUs, intravenous prostacyclin (iloprost) is used in patients with established DUs. We report the case of a patient whose pulp necrosis secondary to severe

EFIM
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smc media srl

isolated Raynaud's phenomenon revealed systemic sclerosis sine scleroderma, which improved significantly with inhaled prostacyclin administration.

CASE DESCRIPTION

The patient was a 52-year-old ex-smoker who had been a chronic smoker for 25 years, with protein C deficiency (32%) revealed by deep vein thrombosis of the left lower limb, on anticoagulation therapy since 2016. He was admitted to the internal medicine department for severe Raynaud's phenomenon evolving since 2016, complicated by pulp necrosis of the third right finger. Clinical examination was unremarkable except for infected pulp necrosis of the third right finger *(Fig. 1)* and tenderness on palpation of the pulp of the fourth and fifth right fingers without obvious trophic signs. Peripheral pulses were present and symmetrical, and blood pressure was normal. Capillaroscopy revealed megacapillaries suggestive of a connective tissue disease. Antinuclear antibodies were positive at 1/640 with centromere fluorescence, and anti-centromere antibodies were >240 in the immunological workup. Doppler ultrasound of the right upper limb was normal. Transthoracic echocardiography and chest computed tomography (CT) angiography showed no signs of pulmonary hypertension.

The patient underwent surgical necrosectomy, followed by ischemic pain in the finger with cyanosis of the fingertip. Iloprost was administered via inhalation at a dose of 2 ampoules of 10 mg/10 ml per day in 3 cycles of 5 days each, with good clinical improvement *(Fig. 2)*.

DISCUSSION

Digital ulcers (DUs) in systemic sclerosis can be secondary to two main mechanisms: ischemic or traumatic, with the ischemic mechanism being more common due to occlusive intimal vasculopathy[1]. These DUs are painful and difficult to treat due to sclerosis and local hypoxia.

Treatment of DUs involves regular skin hydration, the use of healing creams, appropriate dressings, local and general analgesic treatments, and surgical interventions in severe cases. Iloprost, a vasodilator, is recommended for DUs in SSc and is administered intravenously at a minimum dose of 0.5 to 2 ng/kg per minute according to the recommendations of the European Scleroderma Trials and Research group (EUSTAR)[2]. It is often used as a first-line treatment to improve blood circulation and promote DU healing.

Inhaled iloprost is recommended for the treatment of pulmonary arterial hypertension in the context of SSc. A few studies in the literature have shown its efficacy in the treatment of DUs in SSc, with encouraging results. Pakozdi et al.[3] conducted a prospective study involving 20 patients with primary Raynaud's phenomenon and secondary Raynaud's phenomenon due to SSc. Each patient received two courses of iloprost treatment over 5 days, with a 5-week interval between courses, administered six times daily via nebulizer at a dose of 30-60 µg. There was significant improvement in patients with SSc after two courses of treatment, in whereas

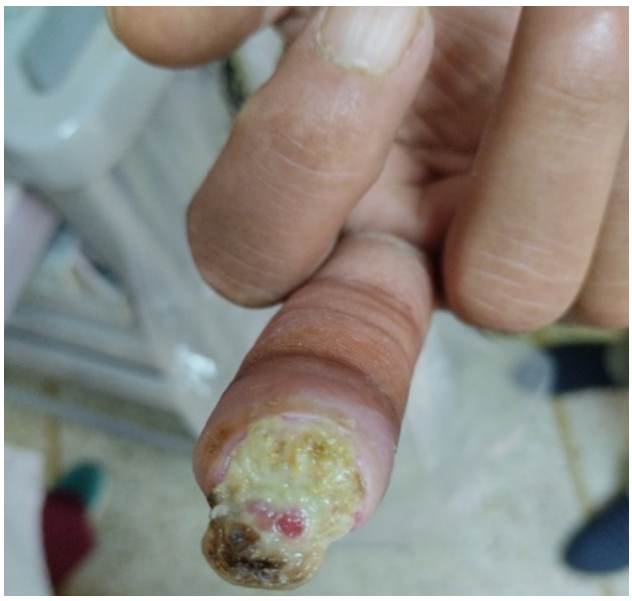

Figure 1. Pulp necrosis of the right third finger before treatment with inhaled iloprost.

patients with primary Raynaud's phenomenon there were no notable changes.

There is an ongoing trial by Chen et al.[4] to prove the efficacy of inhaled iloprost, comparing the plasma concentration of inhaled iloprost to that obtained via intravenous administration in rats. The rate of pulmonary absorption is assumed to be similar to the bioavailability of intravenous iloprost in both rats and humans. Thus, in this study, the plasma level of intravenously administered iloprost is achieved with two to three nebulisations of the molecule. This represents a good alternative for patients with Raynaud's phenomenon associated with SSc. Other vasodilator treatments such as calcium channel blockers and sildenafil can also be used[5], but iloprost remains a common choice in the treatment of SSc-associated DUs. Bosentan (endothelin receptor antagonist) is recommended for the prevention of DUs[6,7]. Preventive measures such as avoiding

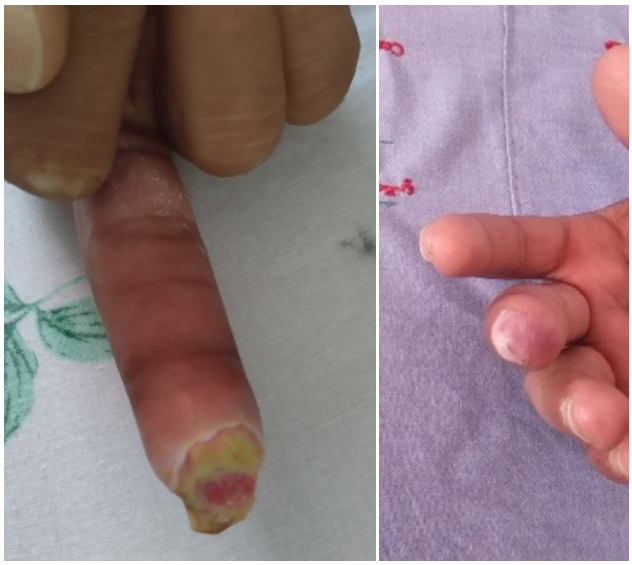

Figure 2. Progression of the pulp necrosis after the first course of inhaled iloprost (left) and after 3 courses of inhaled iloprost (right).

risk factors, rehabilitation, and managing superinfections are also essential in the overall treatment of SSc and its cutaneous complications.

CONCLUSION

Inhaled iloprost may be an effective and better-tolerated alternative to intravenous administration for the treatment of DUs in SSc. Further studies are needed to confirm or refute this hypothesis.

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