

Tadalafil to improve cutaneous flap perfusion in smokers: A case series and literature review



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INTRODUCTION

The viability of cutaneous flaps and grafts is dependent on adequate circulation and perfusion. Smoking, excessive tension or pressure, arterial insufficiency, and venous congestion are factors that can contribute to flap failure due to poor perfusion. Early identification of tissue ischemia and its intervention can improve flap survival. Tadalafil is a phosphodiesterase-5 (PDE5) inhibitor that increases blood flow by vasodilation of the peripheral vasculature as well as inhibition of platelet aggregation. Although current indications for tadalafil by the US Food and Drug Administration are for erectile dysfunction and pulmonary hypertension,¹ its mechanism of action is theoretically beneficial in increasing blood perfusion in patients who are at risk of flap or graft ischemia due to poor circulation. The following case series presents the successful off-label use of tadalafil in preventing tissue ischemia in high-risk patients and treating patients with early signs of tissue necrosis.

CASE 1

An 83-year-old woman with a history of lymphoma and 1 pack per day tobacco use was treated for a basal cell carcinoma on the left nasal ala. The defect was repaired with a cartilage graft and melolabial interpolation flap. On postoperative day (POD) 3, there was evidence of tissue ischemia and early necrosis of the distal pedicle (Fig 1). After 3 days of tadalafil 5 mg daily, the interpolation flap demonstrated visible signs of improved perfusion and viability (Fig 2). Oral administration of tadalafil 5 mg was again started on the day of flap takedown and continued for 3 days. On POD 90, the patient had complete flap survival with excellent functional

Abbreviations used:

PDE5: phosphodiesterase-5
 POD: postoperative day

and cosmetic results and no medication side effects (Fig 3).

CASE 2

A 63-year-old woman with a history of 1 pack per day tobacco use and extensive sun exposure was treated for a nodular basal cell carcinoma on the distal part of nasal dorsum, resulting in a full-thickness defect. The defect was repaired with a combination of melolabial interpolation flap, cartilage graft, and paramedian forehead flap. On POD 3, there was a dusky pale discoloration of the distal paramedian flap and pedicle (Fig 4). The patient was prescribed tadalafil 5 mg once daily for 3 days. On POD 7, the pedicle coloration was improved, indicating an adequate perfusion (Fig 5). The patient presented for interpolation flap takedown on POD 30 with no signs of flap ischemia. Treatment with tadalafil 5 mg daily was started again on the day of flap takedown and continued for 3 days. The patient had complete flap survival with both satisfactory functional and cosmetic results and no medication side effects (Fig 6).

DISCUSSION

Tadalafil is a PDE5 inhibitor that prevents the breakdown of cyclic guanosine monophosphate and leads to sustained vasodilation of the peripheral vasculature and inhibition of platelet aggregation. Tadalafil has the longest half-life among the family of

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Fig 1. Case 1: Melolabial interpolation flap with the evidence of tissue ischemia and early necrosis on postoperative day 3.



Fig 2. Case 1: Melolabial interpolation flap with improved coloration and tissue viability on postoperative day 7 following 3 days of treatment with tadalafil 5 mg once daily.

phosphodiesterase inhibitors, including sildenafil, vardenafil, and udenafil. Given these properties, the use of tadalafil and similar PDE5 inhibitors has been investigated in conditions such as erectile dysfunction, pulmonary hypertension, Raynaud phenomenon, essential hypertension, and stroke.

The role of tadalafil and PDE5 inhibitors as pharmacologic agents in cutaneous flap repairs is



Fig 3. Case 1: Postoperative day 90 following melolabial interpolation flap takedown with excellent functional and cosmetic results.



Fig 4. Case 2: Paramedian forehead flap with dusky, violaceous coloration on postoperative day 3.



Fig 5. Case 2: Paramedian forehead flap with improved coloration on postoperative day 7 following the treatment with tadalafil 5 mg daily for 3 days.

in its initial stages with most of the data collected from laboratory studies. Oral, topical, and locally injected PDE5 inhibitors have been demonstrated to increase the perfusion and viability of ischemic flaps



Fig 6. Case 2: Satisfactory functional and cosmetic results at suture removal 1 week following paramedian forehead interpolation flap takedown.

in rat models.²⁻⁶ In 2014, Pfaff et al⁷ demonstrated that facial reconstruction with flaps in smokers may have improved clinical outcomes with sildenafil 20 to 50 mg, 1 to 3 times daily for 1 to 7 days, starting on POD 0 or 1.

The common side effects with the use of tadalafil include headaches, dyspepsia, myalgia, rhinitis, and flushing. The contraindications to PDE5 inhibitors include patients with a history of hypotension or heart failure and those taking nitrates or multiple antihypertensive medications. As tadalafil causes

vasodilation, theoretically, it may increase the risk of postoperative bleeding or hematoma.

This case series demonstrated 2 clinical scenarios in which flap perfusion in smokers was improved by the administration of tadalafil, resulting in satisfactory clinical outcomes. The suspected benefits of this medication must be weighed against the risk of postoperative bleeding and hematoma, among other side effects. The authors recommend and encourage further investigation into the use of tadalafil and other PDE5 inhibitors to improve flap perfusion and survival after Mohs micrographic surgery in both smokers and nonsmokers.

Conflicts of interest

None disclosed.

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