To the Editor:

In systemic sclerosis, the collagen deposition, vasculopathy, and Raynaud phenomenon produce abnormalities in microcirculation that lead to ischemia, distal ulceration (DU) and, occasionally, necrosis of one or more phalanges. We report 2 cases in which sildenafil was used as a treatment option.

The first case was a 46-year-old woman with a history of diffuse cutaneous systemic sclerosis diagnosed 4 years previously, who was receiving antiplatelet therapy and nifedipine. Four months earlier she presented DU with necrosis of the distal phalanx of the fifth finger on the right-hand, requiring amputation. The patient recently attended presenting new DU on the third finger of the right-hand, with periungual hemorrhagic lesions but no signs of necrosis of the finger. On the fifth finger of the same hand, partial closure of the surgical scar could be observed on the amputation stump (Figure 1). The patient tested positive for antinuclear antibodies with a titer of 1:640 but negative for antiglomerular basement membrane (anti-GBM) antibodies. Periungual capillaroscopy revealed enlarged capillaries, avascular areas and hemorrhages in the proximal nailfold. Given this situation, treatment was initiated with oral sildenafil 50 mg/d (in a single dose at night). A subjective improvement (reduction in number and intensity) of episodes of Raynaud phenomenon was
achieved with complete recovery of the finger pad on
the affected finger, disappearance of the ischemic and
hemorrhagic lesions, and complete closure of the surgical
wound 60 days after treatment was started (Figure 1).
A year later the patient presented serious renal insufficiency,
and was admitted to the intensive care unit where she later
died.

The second case was a 63-year-old woman diagnosed
2 years ago with limited cutaneous systemic sclerosis and
a recent history of gastroesophageal reflux. Treatment
was initiated with antiplatelet drugs, ranitidine, and
calcium channel blockers, which exacerbated the digestive
symptoms and were therefore replaced with pentoxyfilline.
A year previously she had developed necrosis of the
distal phalanx of the ring finger, requiring amputation.
The patient consulted for DU on the finger pad of the
third finger of the right-hand, with signs of ischemia and
necrosis, associated with subungual hemorrhage, edema,
and erythema on the distal phalanx of the same finger
(Figure 2).

She tested positive for antinuclear antibodies with a
titer of 1:320 with positive anticentromere antibodies.
Periungual capillaroscopy revealed megacapillaries and
avascular areas. Treatment was initiated with oral sildenafil
50 mg/d (in a single dose at night), obtaining subjective
improvement in the episodes of Raynaud phenomenon
and complete healing of the lesion in 60 days (Figure 2).
Twenty months later she began to experience dyspnea, and
an echocardiograph showed indirect signs of moderate
pulmonary hypertension.

Raynaud phenomenon and DU are common in
patients with systemic sclerosis. Treatment includes local and general measures: the application of antiseptics
and debridement of wounds; and avoidance of exposure to
cold and drugs that induce vasospasm, giving up smoking,
and adequate use of analgesia, respectively. Where there
are serious lesions, vasodilator treatment should be started
with calcium channel blockers, associated with antiplatelet
treatment and heparin at anticoagulant doses. In serious
and persistent digital ischemia, benefits have been seen
in the use of prostacycline analogs such as intravenous
alprostadil, iloprost, or epoprostenol. Bosentan (an
endothelin-receptor antagonist) has proven effective in
the prevention of further DU.

Recently improvements in DU have been reported
when using sildenafil in patients with primary and
secondary Raynaud syndrome. As drugs such as iloprost
and epoprostenol are not available in our hospital, we
used sildenafil in both cases. We followed the therapeutic
regimen first outlined by Lichtenstein for the treatment
of Raynaud syndrome and DU. In both cases the DU
resolved rapidly, with good tolerance and no adverse
effects. An increase of oxidative stress associated with
a deficit in nitric oxide is one of the factors involved in
the pathogenesis of microvascular abnormalities and
in wound-healing mechanisms. The inhibition of
5-phosphodiesterase mediated by sildenafil results in
the accumulation of cyclic guanosine monophosphate
(cGMP), leading to a reduction in intracellular calcium
that produces relaxation of the vascular smooth muscle
and therefore vasodilation. This type of inhibition
prevents the breakdown of cGMP, increasing the effects
of nitric oxide on the endothelium—a phenomenon
that constitutes an attractive proposal in the treatment
of DU in systemic sclerosis. Early intervention of this
type could provide benefits without producing major
adverse effects when used with caution in patients with
arterial hypertension; it is contraindicated in patients on
treatment with nitrates. In terms of dosage, the duration
of treatment with sildenafil has varied, though it is usually
given for at least 4 weeks, and doses of 50 mg/d or every
12 hours are used.
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Conflicts of Interest
The authors declare no conflicts of interest.

References