

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Viability of randomized skin flaps—an experimental study in rats

Nsingi N. António, MD,^{a,*} Andréa Monte Alto Costa, PhD,^b
and Ruy G. Marques, MD, PhD^c

^a Post-Graduation Program in Physiopathology and Surgical Sciences, Department of General Surgery, Rio de Janeiro State University, Rio de Janeiro, Brazil

^b Laboratory of Tissue Repair, Institute of Biology Roberto Alcantara Gomes, Rio de Janeiro State University, Rio de Janeiro, Brazil

^c Laboratory of Experimental Surgery, Department of General Surgery, Rio de Janeiro State University, Rio de Janeiro, Brazil

ARTICLE INFO

Article history:

Received 28 January 2016

Received in revised form

13 July 2016

Accepted 18 August 2016

Available online 31 August 2016

Keywords:

Randomized skin flap

Viability

Necrosis

Pentoxifylline

Hyaluronidase

ABSTRACT

Background: Randomized skin flaps are extensively used in plastic surgery, but the possibility of necrosis has challenged their use. Several studies have been conducted aiming to find ways to reduce the occurrence of necrosis. We evaluated the effects of pentoxifylline (PTX) and hyaluronidase (HLD), each alone or combined, on randomized rat skin flaps.

Materials and methods: Fifty male Wistar rats were divided into five groups of 10 animals each: control I, control II, PTX, HLD, PTX-HLD. Substances were administered from the first to the 14th postoperative day. The necrotic area was measured on the seventh and 14th postoperative day; the animals were killed on the 14th day, when samples were collected for histologic and immunohistochemical examination.

Results: On the seventh day, percentage of the necrotic area was significantly reduced in PTX, HLD, and PTX-HLD animals compared with control groups. On 14th day, percentage of the necrotic area in PTX, HDL, and PTX-HLD groups was also significantly reduced compared with control groups. PTX and PTX-HLD showed a significant reduction in dermis cellularity, V_V of macrophages, and myofibroblasts compared with control groups; PTX showed a significant enhancement of L_V of blood vessels compared with all other groups. **Conclusions:** The use of each substance alone or combined increased flap viability compared with control groups. On the seventh day, PTX exhibited lower viability than HLD, whereas on the 14th day there was no difference between treated groups. PTX alone enhanced the L_V of blood vessels, whereas PTX-HLD did not. However, PTX-HLD was more effective in decreasing the dermis cellularity and macrophage V_V than HLD alone.

© 2016 Elsevier Inc. All rights reserved.

Introduction

Randomized skin flaps are extensively used in plastic surgery, mainly for tissue reconstruction.^{1–4} However, the possible occurrence of necrosis appears to be the greatest

challenge regarding their use.^{1,3} Several factors are involved in the partial or total necrosis of randomized skin flaps, possibly related to the patient, such as metabolic alterations, tonus changes, vascular obstruction,⁴ or the flap confection itself.

* Corresponding author. Rua Cadete Ulisses Veiga 56/201, São Cristóvão, 20940-240 Rio de Janeiro, Brazil. Tel.: +55 21 30210053.

E-mail address: nsingiantnio@yahoo.com.br (N.N. António).

0022-4804/\$ – see front matter © 2016 Elsevier Inc. All rights reserved.

<http://dx.doi.org/10.1016/j.jss.2016.08.065>

The search for strategies to ensure greater viability of randomized skin flaps has driven investigations aiming not only to reduce harmful effects but also to expand mediators that promote wound healing.⁵⁻⁷ To this end, the action of various substances such as vasodilators, antioxidants, corticosteroids, and some enzymes has been studied.^{5,8,9}

Pentoxifylline (PTX) is a nonselective phosphodiesterase inhibitor, a methylxanthine derivative¹⁰⁻¹³ whose molecular formula is C₁₃H₁₈N₄O₃, with a molecular weight of 278.31 Da. PTX is a drug with multiple pharmacologic properties,¹⁴ promotes relaxation of vascular smooth muscle, causing vasodilatation and preventing vascular spasm,^{15,16} enhances blood cell flexibility, including erythrocytes, favoring blood flow in peripheral vessels,^{9,14,17,18} promotes platelet disaggregation, and increases fibrinolysis, contributing to reduced blood viscosity.^{10,14,18-20}

PTX modulates the immunologic activity by acting on cytokines, suppresses leukocyte hyperactivity by reducing superoxide release and neutrophil adhesion,¹⁷ inhibits the action of integrin and interleukin 2 (IL-2), preventing lymphocyte adhesion to endothelial cells,²¹ and reduces the synthesis of IL-1 and tumor necrosis factor α .^{14,18,20,22} It is used clinically to treat diseases of peripheral vessels.^{15,21,23,24}

Hyaluronidase (HLD) is an enzyme of approximately 60,000 Da that acts on hyaluronic acid (HA) by temporarily depolarizing it and consequently reducing the viscosity of the intercellular medium, which in turn increases tissue permeability to other substances, whereas promoting the absorption of excess fluids, mobilizing edemas, and infiltrations.^{11,25} It is believed that this action increases the flow of interstitial fluid to the flap base, thus enhancing the drainage of metabolites from the flap extremity to more distant areas with normal vascularity.^{12,13}

Considering the beneficial effect of both of these drugs on the rheological properties of organic fluids and on the wound healing process, based on different mechanisms of action, it has been hypothesized that the combined use of these drugs could increase the viability of randomized skin flaps. Thus, the aim of the present study was to evaluate the randomized skin flaps of rats treated with the combined use of these drugs compared with the separate use of each one.

Materials and methods

The study was approved by the Ethics Committee on Animal Research of the Biology Institute Roberto Alcântara Gomes (University of Rio de Janeiro), under the CEUA/014/2015 protocol. All procedures strictly followed the care recommended by Brazilian law for the use of animals in research.²⁶

Animals and groups

The study was conducted on 50 male Wistar rats weighing 250-300 g from the vivarium of the Experimental Surgery Laboratory, Medical Science School, State University of Rio de Janeiro. The rats were housed in individual cages in a temperature-controlled room (22°C) on a 12-h light and 12-h dark cycle, with free access to food and water.

The animals were randomly divided into five groups of 10 animals each:

- (1) Control I (CTL-I): no treatment before or after the surgical procedure.
- (2) Control II (CTL-II): 0.25 mL of physiological saline solution (PSS) administered intraperitoneally (IP) twice a day, and 0.5 mL of the same solution administered intralesionally (Int.L) once a day.
- (3) PTX: 20 mg/kg PTX IP twice a day, and 0.5 mL PSS Int.L once a day.
- (4) HLD: 75 IU/d of HLD Int.L once a day, and 0.25 mL of PSS IP twice a day
- (5) PTX-HLD: same doses and routes of administration as described previously.

Anesthesia and trichotomy

The animals were anesthetized with a combination of ketamine hydrochloride (150 mg/kg) and xylazine hydrochloride (15 mg/kg) at a 2:1 ratio, injected intramuscularly in the amount of 0.1 mL/100 g body weight. After anesthesia, the animals were submitted to trichotomy of the dorsal region.

Preparation of the skin flap

The dorsal area was submitted to antisepsis with an alcoholic chlorhexidine solution, and a 3-cm wide and 10-cm long skin flap with a caudal base was drawn with a marking pen according to a modification of the McFarlane model,^{10,27,28} at the level of a horizontal line connecting the two iliac crests.

A flap consisting of skin, subcutaneous tissue, fleshy panicle, and superficial fascia was lifted and then repositioned in its original bed with the use of separate 4-0 nylon monofilament sutures.

Administration of the substances

After the surgical procedure, the animals received PSS, PTX (PTX injectable solution; Vascer), and HLD (3000 UTR HLD; Biometil) at the same dose and by the same route of administration as described previously. Int.L administration was performed at the two cephalic thirds of the flap in the dermal and subdermal planes, and IP administration was carried out with introduction of the needle into the abdominal cavity. The substances were administered until the 14th day of the experiment, with each session being preceded by sedation of the animals with inhaled anesthetic sevoflurane (Sevocris; Cristália Produtos Químicos Farmacêuticos Ltda, Itapira, Sao Paulo).

Sample collection

The animals were killed with anesthetic overdoses on the 14th day of the experiment, and a tissue fragment was collected from the boundary area between necrotic and viable tissue for histology and immunohistochemistry examinations (Fig. 1).

Download English Version:

<https://daneshyari.com/en/article/5733924>

Download Persian Version:

<https://daneshyari.com/article/5733924>

[Daneshyari.com](https://daneshyari.com)