Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/burns

An effective antioxidant drug on prevention of the necrosis of zone of stasis: N-acetylcysteine

Murat Deniz [a,*], Huseyin Borman [b], Tamer Seyhan [b], Mehmet Haberal [c]

[a] Igdır Public Hospital, Department of Plastic and Reconstructive Surgery, Igdır, Turkey
[b] Baskent University, Faculty of Medicine, Department of Plastic and Reconstructive Surgery, Ankara, Turkey
[c] Baskent University, Faculty of Medicine, Department of General Surgery, Ankara, Turkey

ARTICLE INFO

Article history:
Accepted 28 June 2012

Keywords:
Burn
Zone of stasis
N-acetylcysteine

ABSTRACT

The zone of stasis, the encircling area of the zone of coagulation, is a critical area which determines the depth and width of the necrosis in burns. Many agents were proposed to salvage the zone of stasis. Due to the known preventive and therapeutic effects of N-acetylcysteine on hepatotoxicity, nephrotoxicity, pulmonary injury, and multiple organ failure in humans, the effect of N-acetylcysteine on saving the zone of stasis was investigated in this experimental study. The effects of N-acetylcysteine administration via oral or intraperitoneal route was compared in a rat comb-burn model. The extent of burn wounds was evaluated by photography and planimetry in the groups. Additionally, skin samples were obtained to analyze malondialdehyde levels to see the antioxidant effect of N-acetylcysteine. In control group (no treatment), the burn areas went to near total necrosis. In intraperitoneal and oral treatment groups, skin survival occurred in the interspace area of the comb. There was no difference between the groups in terms of MDA concentrations. In conclusion, this study showed us the possible saving effect of N-acetylcysteine on the zone of stasis. N-acetylcysteine may be used in the cases of severe burns, not only for its effects on wound healing but also the systemic effects of the drug.

1. Introduction

These are three zones of burn that were described by Jackson in 1947 [1]. The zone of stasis surrounds the zone of coagulation where tissue loss is irreversible. The injury in this zone is progressive after the first 24 h following the trauma due to continuous release of mediators from burned tissues and oxidative stress that leads to ischemia-induced cell death [2–4]. Progressive tissue loss in this zone is potentially salvagable, but may progress to necrosis if not treated properly. In addition to adequate fluid resuscitation, a variety of treatment modalities were used save the zone of stasis.

In this study we planned an experiment to investigate the effects of N-acetylcysteine (NAC), which is a precursor of the endogenous antioxidant glutathione and a direct antioxidant, on the zone of stasis.

2. Materials and methods

This study was approved by The Institutional Review Board of our university and supported by our university Research Fund Committee, and all the investigations complied with the 1996 National Academy of Science's Guide for Care and Use of Laboratory Animals.

* *Corresponding author at*: Igdır Public Hospital, 76000 Igdir, Turkey. Tel.: +90 476 226 03 01; fax: +90 476 227 63 58.
E-mail address: lmuratdeniz@yahoo.com (M. Deniz).
0305-4179/$36.00
http://dx.doi.org/10.1016/j.burns.2012.06.015

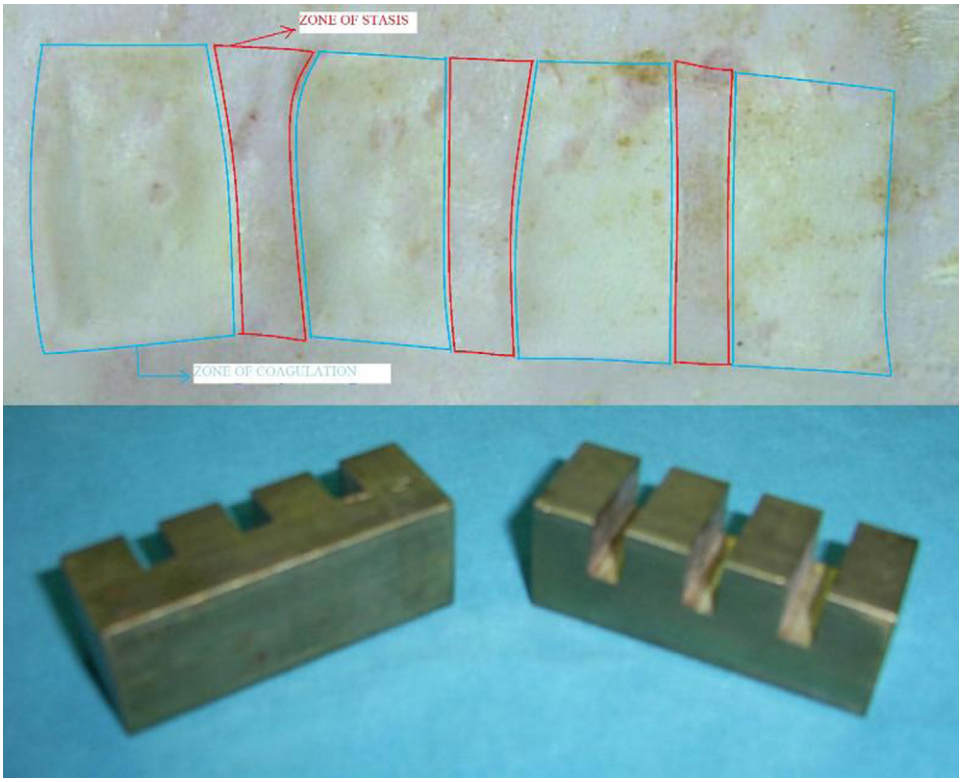

Fig. 1 – The probe that was used in the comb model and the dorsum of a rat after burn.

Thirty adult male Sprague-Dawley rats (350–450 g) were used in this study. They were caged in a controlled environment of 22 °C with 12 h of light and dark cycles. Standard rat feed and water were provided ad libitum. Thirty rats were randomly divided into three groups ($n = 10$ in each group). In Group 1 (control group), no treatment was accomplished. One hour after the burn, 100 mg/kg/day NAC was started and administered intraperitoneally for 10 days in Group 2. Similarly, 490 mg/kg/day NAC was started and administered orally for 10 days in Group 3. All the rats were anesthetized with an i.p. administration of 50 mg/kg ketamine hydrochloric acid and 10 mg/kg xylazine hydrochloric acid. The burn wounds were created on the shaved rat dorsum using "the comb model" [5]. In this model, a brass probe, consisting of four rows (10 mm × 20 mm) and three interspaces (5 mm × 20 mm), was immersed in the boiling water for 5 min and was held for 20 s without applying pressure (Fig. 1).

In each of the groups, the total burn wound area and surviving areas were calculated with a translucent millimetric graphic paper, 10 days after the burn. Survived skin area ratio to the burn injured area was calculated.

Tissue malondialdehyde (MDA) concentration, as a marker of lipid peroxidation, was measured in the skin homogenates [6]. MDA was measured from samples of non-burned areas and viable to necrotic transition skin in each animal from three groups at the end of the 10th day. Tissue MDA sampling results and percentage of surviving areas of three groups were compared statistically by Mann–Whitney *U* test.

3. Results

In Group 1, the burn areas went to near total necrosis on the 10th day (the mean ratio of living area was 4%) (Fig. 2). In Group 2 (the mean ratio of living area was 27%) and 3 (the mean ratio of living area was 20%), the skin survival occurred in the interspace area of the comb (Figs. 3 and 4). The surviving area of skin in Group 1 was different than those Group 2 ($p = 0$) and Group 3 ($p = 0.003$), but there was no difference between the Groups 2 and 3 ($p = 0.513$) (Table 1).

There was no difference between neither the groups nor sampling areas in terms of MDA concentrations in non-burned areas and transition skin samples ($p > 0.5$).

4. Discussion

Progressive tissue necrosis in a burn can be prevented by saving the zone of stasis. Singer et al reported the role of

Table 1 – .

	Surviving area (%)	MDA in normal skin (nmol/g)	MDA in transition (nmol/g)
Group 1	4	12.2	12.6
Group 2	27	11.125	18.75
Group 3	20	12.3	11.8