**THERAPEUTIC EFFICACY AND ASSESSMENT OF THE DYNAMICS OF LOCAL HEALING OF THERMAL BURNS IN RATS TREATED WITH SYNTHETIC INHIBITOR OF MATRIX METALLOPROTEINASES**

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**Introduction.** Thermal burns currently occupy the first place in the structure of domestic and industrial injuries. The main task in the treatment of burns, along with the suppression of excessive inflammatory reaction, proteolytic activity, is the activation of the healing of the damaged area. The therapeutic efficacy of drugs acting on various links in the course of the wound process, as well as the dynamics of changes in the area of ​​the burn surface are one of the main criteria in choosing the tactics of treating patients. Despite the fact that doxycycline is a broad-spectrum antibiotic, it is also known as a synthetic inhibitor of matrix metalloproteinases, i.e. a drug that inhibits excessive proteolysis during the healing of injuries, therefore, it is relevant to study the therapeutic efficacy of this drug in the healing of burns.

**Aim.** To assess the therapeutic efficacy and dynamics of changes in the area of thermal burns during treatment with a synthetic inhibitor of matrix metalloproteinases doxycycline.

**Materials and methods.** Studies were performed on 96 rats of the WAG population weighing 200-250 g. Еxperiments were conducted in the laboratory of Department of Pharmacology and Prescription writing (Kharkiv National Medical University, Ukraine). On the shaved part of the back thigh under the thiopental anesthesia a thermal burn was caused. All experiments were conducted according to the European convention for the protection of vertebrate animals used for experimental and other scientific purposes (Strasbourg, 1986) and according to the guidelines of the State Expert Center Ministry of Health of Ukraine (Protocol № 9 meeting of the Commission on Ethics and Bioethics KhNMU, 03.12.2014).

The animals were divided into 4 groups of 24 individuals in each group. The first group - intact animals, the second (control) - rats with thermal burn without treatment, the third group - methyluracil at a dose of 0.126 mg / kg (reference drug), the fourth group - the synthetic inhibitor of matrix metalloproteinases (IMMP) - doxycycline at doses of 2.5 mg / kg. Preparations were administered orally in starch suspension immediately after thermal exposure and daily during the entire experiment period (28 days). Observations of the healing processes of burn wounds were carried out on the 7th, 14th, 21st and 28th days.

The dynamics of burn wound healing was assessed by visual observations, burn surface area, and therapeutic efficacy. The burn area was calculated using the formula:

S=πR2

 where: π – constant (=3.14);

R – circle radius.

The burn area as a percentage in relation to the total body surface was calculated using the Lee formula modified by the Mee - Rubner formula. The therapeutic efficacy was assessed by the dynamics of the area of the burn wound and the reduction in the time of its healing. Reduction of the wound healing time was determined by the formula (Andreev S.V., 1973; Sarkisov D.S., 1960).

**Results and discussion.** In the study of a group of animals with experimental thermal burns of the skin of the posterior surface of the thigh without treatment, severe hyperemia was noted, followed by the formation of a thin brown scab. Experiments have shown that from the third day, softening of the central part of the thick scab began, and when pressed, a serous-purulent exudate was released from under it. On the 7th day, the burn wound was a zone of deep necrosis and serous-purulent exudate. In the tissues of the bottom of the wound, edema persisted with the formation of granulation tissue at the border of the lesion. During the next two weeks of observation (14th - 21st days) in the center of the burn wound, a decrease in the zone of necrosis and epithelialization of the wound defect were noted. By the 28th day, the burn wound was partially epithelized with the formation of a thin delicate scar. When studying the dynamics of the area of ​​the burn wound, a decrease in the wound defect was noted by the 7th day - by 15.0%, by the 14th day - by 41.0%, by the 21st day - by 77.0% and by the 28th day - by 86.0% in comparison with the original area, which was 4 cm2. Complete healing of the burn wound in control animals is noted on the 31st day.

When animals were treated with methyluracil, severe hyperemia was observed with further formation of a thin brown crust. Starting from the 3rd day, softening of the central part of the thick scab also occurred, however, when pressed, serous exudate was released from under it. By the 7th day, the wound surface was covered with a dense scab, the exudate was serous. During the next two weeks of observation (up to 21 days) in the center of the burn wound, there was a decrease in the zone of necrosis, melting of the scab and epithelization of the wound defect. By the 28th day, the burn wound was completely epithelized with the formation of a delicate scar

The area of the wound defect decreased more intensively than in the previous group: by the 7th day - by 32.5%, by the 14th - by 45.0%, by the 21st - by 79.0% in comparison with the group without treatment, by the 28th day, complete healing of the wound defect was noted.

In animals using doxycycline at a dose of 2.5 mg / kg immediately after the application of the burn, hyperemia was noted, followed by the formation of a thin brown crust. The area of ​​necrosis in the wound area was filled with serous exudate. Starting from the third day, there was a softening of the central part of the thick scab, with the release of exclusively serous exudate. By the 7th day, the wound surface was covered with a dense scab, the exudate was serous. Over the next two weeks (up to 21 days), the zone of necrosis in the center of the burn wound decreased faster, epithelization of the wound defect was more intense, edema and hyperemia were less pronounced than in the group with a burn without treatment. By the 28th day, complete epidermisation of the regenerate zone is observed, with the formation of a scar.

The area of the wound defect decreased most actively in comparison with all previous groups: by the 7th day - by 34.0% and 21.0%, by the 14th - by 62.0% and 49.0%, in comparison with the group without treatment and with methyluracil, respectively, by the 21st day - complete healing of the wound defect is noted.

In terms of therapeutic efficacy, doxycycline was superior to the reference drug (on the 14th day - by 45.0%; on the 21st day - by 79.0%) (Table 1).

**Table 1**

**Therapeutic efficacy of doxycycline for burn wounds**

|  |  |  |
| --- | --- | --- |
| Drugs | Therapeutic efficacy, % | Reduction of the wound healing time, % |
| 7th day | 14th day | 21st day | 28th day |
| Doxycycline, 2,5 мг/кг | 34 | 62 | 100 | 100 | 32,3 |
| Methyluracil | 33 | 45 | 79 | 100 | 9,7 |

**Conclusion.** Thus, both investigated drugs had a positive effect on the healing of burn wounds. According to observations of the dynamics of local manifestations, as well as in determining the therapeutic efficacy of a synthetic inhibitor of matrix metalloproteinases, the most active healing occurred under the influence of doxycycline.