



Microcirculation in rats with thermal trauma under the influence of Royal jelly

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ABSTRACT

Aim: The work was devoted to study the effect of Royal jelly (RJ) on the microcirculation during thermal injury in the experiment. **Materials and Methods:** The study was conducted on white Wistar rats weighing 180-220 g. Three groups of animals were formed: Intact group – Healthy animals ($n = 10$), control group – Animals with thermal injury ($n = 10$), and experimental group – Animals with thermal injury treated with RJ ($n = 8$). The method of laser Doppler flowmetry was used for the study of microcirculation. **Results:** The decrease of the intensity of microcirculation and the growth of bypass indicator was marked in animals with the burn. The results showed that the use of RJ in the treatment of thermal injury contributes to the stimulation of active factors (endothelial, neurogenic, and myogenic) of regulation of microcirculation, showing a potentiating effect in the healing of wounds. The analysis of passive factors of the microcirculation reflecting the blood flow out of the system of microcirculation revealed a statistically significant decrease in respiratory waves associated with a venular link on 24% in thermal injury in comparison to the intact group of animals. The tendency to increase of the amplitude of respiratory waves was marked by 13% in comparison to the control group of rats under the influence of RJ. **Conclusion:** The results showed that the use of RJ in the complex treatment of thermal injury contributes to the normalization of microcirculation. RJ stimulates active factors of the regulation of microcirculation, improves a blood circulation, accelerating the reparative processes in the area of the burn.

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INTRODUCTION

Burns are one of the most common traumatic lesions [1]. Burn injury is accompanied by increase of formation of reactive oxygen species, a sharp increase in the activity of lipid peroxidation and a decrease of content of antioxidants in the blood, which lead to oxidative stress and dramatic changes in vital functions of the body [2,3]. The accumulated information about changes of the circulatory system in thermal injury shows about violations of the central hemodynamics and microcirculation [4]. It is necessary to control these indicators and to search for ways of improvement of microcirculation of burn wounds and to restore health after injury [5].

The necessity of application of clinical nutrition to correct metabolic disorders in patients with severe burns in the form of dietary supplements has a theoretical substantiation. It is known that Royal jelly (RJ) has a therapeutic effect by activating the metabolism and stimulating tissue respiration. RJ is also used as an additional source of nutrients [6-11]. However, currently, there are no data about the effects of RJ on the body after burns,

and this is a limiting factor for the usage of RJ for the treatment of thermal injuries.

The aim of this work was to study the effect of RJ on microcirculation in rats with thermal injury.

MATERIALS AND METHODS

The experiment was conducted on 28 white rats of Wistar line weighing among 180-220 g. All animals were kept in standard vivarium conditions in cages with free access to food and water. Three groups of animals were formed:

1. Intact group: Healthy animals ($n = 10$);
2. Control group: Animals with thermal injury ($n = 10$);
3. Experimental group: Animals with thermal injury treated with RJ ($n = 8$).

The burn (III-IV degree) lesions were done to animals under anesthesia (Zoletil 100 (VIRBAC, France) + XylaVET (Pharmamagist Ltd., Hungary) on the 20% of the body surface of the back by contacting the isolated area of skin with the heating element, the exposure period was 5 s.

In the control group of animals during 10 days, the standard treatment was carried out by intraperitoneal injections with 1 ml of isotonic sodium chloride solution, and we used the ointment levomekol (STADA CIS, Russia).

Animals of the experimental group, similar to the control, had infusion (saline) and local treatment, in addition to which they received an RJ (100 mg/kg) every day. It was used the RJ by the production of Krasnopolyanskaya experimental station of beekeeping of Apiculture Research Institute of the Russian Academy of Sciences.

Animals were removed from the experiment by decapitation with pretransection of carotid artery under anesthesia (Zoletil 100 [60 mg/kg] + XylaVET [6 mg/kg]) on the 11th day. The study of microcirculation in area near the wound was performed by laser Doppler flowmetry [12] using a hardware-software complex LAKK-M before the application of the burn and for 10 days after injury. We evaluated the indicator of microcirculation (IM) illustrating the average level of perfusion (medium flow of erythrocytes) per unit volume of tissue per unit time. The wavelet analysis (amplitude-frequency spectrum) was conducted with the help of software tools. The wavelet analysis allows after the 3-min recording of laser Doppler flowgrams to make the calculation slow and high frequency oscillations of blood flow for to evaluate the role of passive (pulse wave and respiratory wave) and active factors (myogenic, neurogenic, and endothelial oscillations) of the regulation of microcirculation with the calculating of the indicator of bypass microcirculation (IB).

Statistical data processing was performed by the software (Statistica 6.0, StatSoft Inc., USA). The significance of

differences between groups was assessed using Student's *t*-test.

RESULTS AND DISCUSSION

In rats with thermal injury by laser Doppler flowmetry, the inhibition of microcirculation by 22% was revealed in comparison with healthy animals [Figure 1].

After using of RJ the IM was normalized, IM statistically did not differ from the indicator of the intact group ($P < 0.05$). The received results allow to speak about the positive influence of RJ on the IM in thermal injury. This is probably connected to the stimulation of the hemopoiesis by the action of RJ.

The analysis of the active factors of microcirculation control revealed the stimulation of endothelial and neurogenic mechanisms of regulation of the lumen and tone of blood vessels during the burn [Figure 2]. In the assessment of endothelial dysfunction, the increase of the oscillation amplitude was determined in animals with thermal injury by 19% in comparison to the intact group.

Neurogenic oscillations significantly increased in animals with thermal injury by 26% in comparison to healthy rats. This indicates a decrease in peripheral resistance of the arterioles and an increase of blood flow in arteriolar-venular shunt. In the experimental group under the influence of RJ, the indicator of neurogenic oscillations returned to normal and decreased by 30% in comparison with the control group.

There was a trend to inhibition of the myogenic mechanism of regulation of the lumen and tone of blood vessels in thermal injury. The analysis of the factor of control of regulation of microcirculation revealed a rise of myogenic oscillations in the treatment of RJ in comparison with the control group statistically significant by 47%. It is known that RJ causes the contraction of smooth muscles of the intestine and bronchi similar to acetylcholine. These effects may be associated with modification of the sensitivity of the receptors of smooth muscle and activation of presynaptic endings of neurons of intramural ganglions [7]. Therefore, the analysis of the mechanisms of vasomotor effect of RJ showed that the effect of RJ is probably mediated by its effect on vascular smooth muscles and may be the result of changes in the levels of

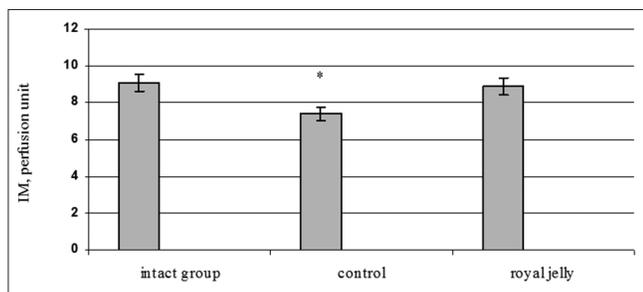


Figure 1: The indicator of microcirculation in the treatment of thermal injury by Royal jelly. *Differences were statistically significant compared with the intact group ($P < 0.05$)

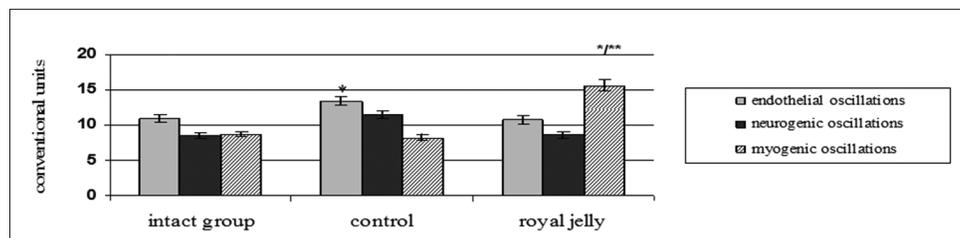


Figure 2: The active factors of microcirculation regulation in thermal injury after treatment of Royal jelly. *Differences were statistically significant compared with the intact group ($P < 0.05$); **Differences were statistically significant compared with the control ($P < 0.05$)

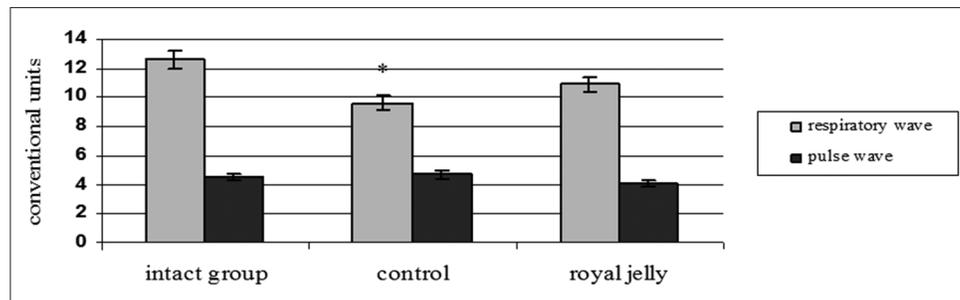


Figure 3: The passive factors of microcirculation regulation in thermal injury after treatment of Royal jelly. *Differences were statistically significant compared with the intact group ($P < 0.05$)

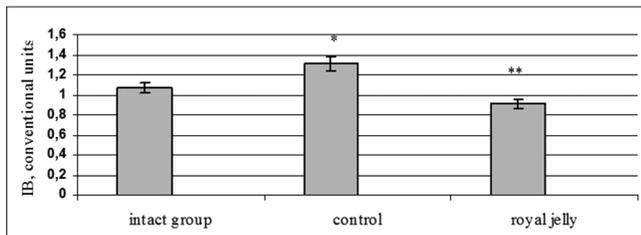


Figure 4: The indicator of bypass in the treatment of thermal injury by Royal jelly. *Differences were statistically significant compared with the intact group ($P < 0.05$); **Differences were statistically significant compared with the control ($P < 0.05$)

metabolites of carbohydrate metabolism (lactate, pyruvate, and citrate) in the walls of blood vessels. The increase of capillary permeability and reduction of blood pressure were shown under the influence of RJ.

The analysis of passive factors of the microcirculation reflecting the blood flow out of the system of microcirculation revealed statistically significant decrease respiratory waves associated with venular link on 24% in thermal injury in comparison to the intact group of animals [Figure 3]. The tendency to increase of the amplitude of respiratory waves was marked by 13% in comparison to the control group of rats under the influence of RJ.

The pulse wave reflecting the inflow of arterial blood in the microcirculatory channel increased 3% in thermal injury in comparison to the intact group. In the experimental group of rats, the amplitude of the pulse wave has decreased by 14% in comparison with the control group animals [Figure 3].

The IB increased significantly after application of burn injury by 22% in comparison to the intact group ($P < 0.05$) [Figure 4]. This is due to a violation of the permeability of capillaries, swelling of endothelium, and violation of the regulation of smooth muscle arteriolar. Therefore, the formation of additional quantities of shunt vessels has been required to move blood from the arterial to the venous channel.

The use of RJ contributed to the decrease of IB by 31% in comparison to the control group of animals. The reduction of IB in the application of RJ leads to an entry of significant amount of blood in the nutritional link of microcirculatory channel

amid a spasm of arteriolar-venular anastomoses [12] and the activation of the sympathetic vasomotor reflex.

CONCLUSION

Thus, experimental thermal injury in rats causes violations of microcirculation and increase in the number of shunting vessels in the field of burn wounds. The results showed that the use of RJ in the complex treatment of thermal injury contributes to the normalization of microcirculation by stimulating of its active factors (endothelial, neurogenic, and myogenic) and therefore changes the situation in relation to the circulatory system at a higher level, showing potentiating effect in the healing of burns. The improvement of microcirculation in thermal injury under the influence of RJ probably occurs under the influence of pteridine compounds and trace elements of RJ playing an important role in hematopoiesis and in metabolic processes [13].

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