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# MORPHOLOGICAL CHANGES IN A FABRICS LUNGS UNDER INFLUENCE OF BIOLOGICALLY ACTIVE COMPONENTS OF VENOM MACROVIPERA LEBETINA OBTUSA

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# ფილტვის ქსოვილში გამოწვეული მორფოლოგიური ცვლილებები „MACROVIPERA LEBETINA OBTUSA"-ს შხამის აქტიური კომპონენტებით

[1]აზერბაიჯანის მეცნიერებათა ეროვნული აკადემია, ზოოლოგიის ინსტიტუტი, ბაქო, აზერბაიჯანი; [2]ტოკატ გაზიოსმაშას უნივერსიტეტი, ძირითადი სამედიცინო მეცნიერებების / ფიზიოლოგიის დეპარტამენტი, თურქეთი; [3]თბილისის სახელმწიფო სამედიცინო უნივერსიტეტი, სოციალური და კლინიკური ფარმაციის დეპარტამენტი

## რეზიუმე

წინამდებარე სამუშაოს მიზანი იყო Macrovipera lebetina obtuse-ს შხამის ბიოლოგიურად აქტიური კომპონენტების გავლენის შესწავლა, ფილტვის ქსოვილში მორფოლოგიური ცვლილებების გამოვლენა. ექსპერიმენტული კვლევები ჩავატარეთ 2-3 თვის ასაკის მქონე თეთრ არა სუფთა სისხლის მქონე ვირთხებზე. ექსპერიმენტის დროს შხამიანი გიურზას შხამი დოზით 4 მგ 100 გრამ ცოცხალ წონაზე შეგვყავდა ვირთხის სხეულის მასით 80-140 გ. ორგანიზმში.

ჩვენი გამოცდილებით, შხამის შეყვანის შემდეგ ფილტვის ქსოვილში ცვლილებები 3 საათის განმავლობაში მიმდინარეობს. აღინიშნება ლიმფოიდური სადინრების და სისხლძარღვების გაფართოება, სისხლძარღვებისა და ბრონქების გასწვრივ ლიმფოიდური ელემენტების დაგროვება შეერთებისა და კვანძების სახით; ინტერაალვეოლარული ძგიდის გასქელება. სუნთქვის შეწყვეტისთანავე იზრდება ფილტვის ქსოვილისა და სისხლძარღვების ცვლილება, რასაც თან ახლავს ბრონქული ეპითელიუმის შეშუპება, პერივასკულარული ლიმფური არხების და ლიმფური სადინრების გაფართოება.

ამრიგად, ჩვენს მიერ მიღებული ექსპერიმენტული კვლევების შედეგების გაანალიზებით, კავკასიური გიურზას შხამის ვირთხის ორგანიზმში შეყვანით გამოვლინდა აქტიური ბიოკომპონენტებით ფილტვის ქსოვილის სხვადასხვა ხასიათის დაზიანება დინამიკაში.

**INTRODUCTION.** Necessity studying patogenez to an intoxication snake venoms is not subject to doubt. In fact, on the data the CART annually on globe is exposed to stings of poisonous snakes about 500000 people. From them perishes about 30-40 thousand [2].

Experiments with rats have shown pathologic changes in lung tissue with ambient temperature increasing up to 50°C. These changes appear substantially less if toxins of cobra, bee, carpet viper and copperhead snake are applied under hyperthermic conditions [3,4,5].

Stings poisonous snakes fall to the spring and summer period of year, for the period of the greatest biological activity kowtowing more often. However, in separate warm days of winter months people connected from a various sort by field, forwarding and agricultural works, are not quite insured from stings of venomous snakes. Clinical physicians and experimentators in detail track the picture of an intoxication described extremely difficult it is a lot of symptoms, snakes

specific to everyone kind. Currently, it is generally accepted the point of view, according to which the main biological properties of animal poisons are determined by non-enzymatic polypeptides, along with them, poisons contain powerful enzyme systems, the nature and specificity of which in most cases determine the originality of the integral picture of poisoning [1,7].

Experiments with rats have shown pathologic changes in lung tissue with ambient temperature increasing up to 50°C. These changes appear substantially less if toxins of cobra, bee, carpet viper and copperhead snake are applied under hyperthermic conditions [6].

This study analyzed the pulmonary function in an experimental model of acute lung injury, induced by the Crotalus durissus cascavella venom (C. d. cascavella) (3.0 μg/kg - i.p), in pulmonary mechanic and histology at 1 h, 3 h, 6 h, 12 h and 24 h after inoculation. The C. d. cascavella venom led to an increase in Newtonian Resistance (RN), Tissue Resistance (G) and Tissue Elastance (H) in all groups when compared to the control, particularly at 12 h and 24 h. The Histeresivity (η) increased 6 h, 12 h and 24 h after inoculation. There was a decrease in Static Compliance (CST) at 6 h, 12 h and 24 h and inspiratory capacity (IC) at 3 h, 6 h, 12 h and 24 h. C. d. cascavella venom showed significant morphological changes such as atelectasis, emphysema, hemorrhage, polymorphonuclear inflammatory infiltrate, edema and congestion. After a challenge with methacholine (MCh), RN demonstrated significant changes at 6, 12 and 24 h. This venom caused mechanical and histopathological changes in the lung tissue; however, its mechanisms of action need further studies in order to better elucidate the morphofunctional lesions [8,10].

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Influence of venom on various functional systems of an organism is revealed. Nevertheless, till now there is no common opinion be relative pathogenesis a venoming at stings venomous snakes. A lot of questions now remains still poorly investigated or at all not found out.

Based on the above literature data the purpose of our research was to identify the degree of morphological changes in lung tissue under the influence of biologically active components of the venom of Macrovipera lebetina obtusa.

METHODS. Specification pathogenesis intoxications snake venoms can play the big role in the forecast of an intoxication and a choice of rational methods of treatment.

Proceeding from above stated the purpose of the present work was revealing a degree of morphological changes in lungs fabrics under influence of biologically active components of venom viper Macrovipera lebetina obtusa. For revealing morphological essence of amazing action of snake venom we have put experimental researches on white not purebred rats 2-3 monthly age with weight of a body 80-140g. Macrovipera lebetina obtusa was entered in a dose of 1, 2, 3, 4 mg on 100 grams of alive weight. Rats were injected intraperitoneally with 0.5 ml of saline (control). The lifespan of the rats corresponds to 42 ± 1.4 minutes; therefore, after 30 minutes, the animals were taken from the chamber and decapitated.

Microscopy in histological preparations of the lung prepared after 48–72 hours of fixation in a 10% buffered solution of aqueous neutral formalin. The material embedded in paraffin blocks was cut on a sled microtome. Sections were stained with iron hematoxylin. Microphotography of histological preparations was carried out using an MBI microscope.

RESULTS. It has been revealed by us, that from all internal bodies the greatest degree of change of permeability is marked in lungs. In our experiences after introduction of venom vipers within 3 hours infringements in lungs fabrics lymph manipulations were marked. Expansion lymphoid cracks and vessels, on a course of blood vessels and bronchial tubes with a congestion lymphoid element as mufts and noduls. Under action bioactivs components (biopolymers) of viperas venom first minutes of an intoxication in lungs fabrics are more expressed by a fatal dose of change, than at long action of a toxic doze. Reduction of the lightness was marked, many alveolus are filled with plasma. Some thickenings of interalveolar partitions are marked.

By the moment of respiratory standstill of change in lung fabrics and vessels accrues, accompanying with swelling epithelial bronchial tubes, expansion perivasculyars lymphatic cracks and lymphatic vessels.

In our experiences after introduction of venom vipers in a dose of 4 mg on 100 gramme of alive weight within 3 hours infringements in lungs fabrics lymph manipulations were marked.

Thus, analyzing the results of experimental researches received by us have revealed distinctions in character and dynamics of defeat lungs fabrics biologically active biocomponent – venom of Macrovipera lebetina obtusa.

CONCLUSIONS:

1. It was found that of all internal organs, the greatest degree of permeability is observed in the lungs.
2. Experimental use of Macrovipera lebetina obtusa venom at a dose of 1 mg per 100 grams of live weight under conditions of normothermia (20°C) showed that, in general, the histological organization of the lower respiratory tract and lung parenchyma was within normal limits.
3. With the introduction of Macrovipera lebetina obtusa venom at a dose of 4 mg per 100 grams of live animals at the microscopic level, it was possible to cause dystrophic and sometimes necrotic phenomena in parenchymal cells, as well as circulatory disorders.

REFERENCES:

1. Aliyev F.Sh., Nadirova G.T. Pathomorphological changes in lungs at rats at an intoxication venom Transcaucasian viper (Vipera lebetina obtusa) 11congress of Azerb. Physiologists and Pulmonologists and 60th Anniversary of Research Institute of Lung Diseases, Baku, 2004, 138-139 pp.
2. Berdiyeva A.T. To patogenez intoxications venoms of the Central Asian snakes viperas and cobras.Ashxabad, 1972, 142 p.
3. Khomutov A.E., Yagin V.V. Bulletin of the Nizhny Novgorod University. Biology series. N. Novgorod: UNN, 2005. Issue. 2 (10), pp152-156.
4. Khomutov A.E., Pursanov K.A., Danilova O.O. Actual problems of herpetology and toxicology. Issue 9. Togliatti, 2006, pp. 182–188.
5. Khomutov A.E., Pursanov K.A., Danilova O.O. Morphological changes in rat lungs affected by heparin and zootoxins under hyperthermic conditions. Bulletin of N.I. Lobachevsky University of Nizhny Novgorod. 2007, # 6, p. 112-115
6. Khomutov A.E., Yagin V.V. Bulletin of the Nizhny Novgorod University. Biology series. N. Novgorod: UNN, 2005. Issue. 2 (10), pp. 152-156.
7. Nadirova G.T., Aliyev F.Sh. Dynamics of morphological changes in lungs at action of venom Transcaucasian vipers Vipera lebetina obtusa in experiment. 11congress of Azerb. Phisiologists and Pulmonologists and 60th Anniversary of Research Institute of Lung Diseases, Baku, 2004, 138 p.
8. J.O., Silveira J.A., Serra D.S. Pulmonary mechanic and lung histology induced by Crotalus durissus cascavella snake venom. Toxicon. 2017,137, pp.144-149.
9. Neto J.O., Silveira J.A., Serra D.S.. Pulmonary mechanic and lung histology induced by Crotalus durissus cascavella snake venom. 2017, Toxicon, 8, p.137.
10. Sartim MA, Souza COS, Diniz CRAF Crotoxin-Induced Mice Lung Impairment: Role of Nicotinic Acetylcholine Receptors and COX-Derived Prostanoids. Biomolecules. 2020,10,5, p.794.

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## МОРФОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ В ТКАНЯХ ЛЕГКИХ ПОД ВОЗДЕЙСТВИЕМ БИОЛОГИЧЕСКИ АКТИВНЫХ КОМПОНЕНТОВ ЯДА ЗАКАВКАЗСКОЙ ГЮРЗЫ MACROVIPERA LEBETINA OBTUSA

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### РЕЗЮМЕ

Цель настоящей работы - выявление степени морфологических изменений тканей легких под воздействием биологически активных компонентов яда закавказской гюрзы Macrovipera lebetina obtusa. Нами экспериментальные исследования были проведены на белых беспородных крысах 2-3 месячного возраста с массой тела 80-140 г. Яд гюрзы вводили в дозе 4 мг на 100 грамм живой массы. В наших опытах после введения яда гюрзы в течение 3 часов были выявлены структурные изменения в тканях легких. Отмечены расширение лимфоидных трещин и сосудов по ходу кровеносных сосудов и бронхов со скоплением лимфоидных элементов в виде муфт и узлов. Отмечаются утолщения меж альвеолярных перегородок. К моменту остановки дыхания нарастает изменение в легочной ткани и сосудах, сопровождающееся набуханием эпителий бронхов, расширением периваскулярных лимфатических щелей и лимфатических сосудов.

Таким образом, анализируя полученные нами результаты экспериментальных исследований, были выявлены различия в характере и динамике поражения тканей легких под воздействием биологически активных компонентов яда закавказской гюрзы.

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## SUMMARY

The purpose of the present work was revealing a degree of morphological changes in lungs fabrics under influence of biologically active components of venom Macrovipera lebetina obtusa. We have put experimental researches on white not purebred rats 2-3 monthly age with weight of a body 80-140g. Venom vipers was entered in a dose of 4 mg on 100 grams of alive weight. In our experiences after introduction of venom vipers within 3 hours infringements in lungs. Expansion lymphoid cracks and vessels, on a course of blood vessels and bronchial tubes with a congestion limfoides elements as mufts and noduls. Some thickenings of interalveolar partitions are marked. By the moment of respiratory standstill of change in lung fabrics and vessels accrues, accompanying with swelling epithelium bronchial tubes, expansion perivasculyars lymphatic cracks and lymphatic vessels.

Thus, analyzing the results of experimental researches received by us have revealed distinctions in character and dynamics of defeat lungs fabrics biologically active biocomponent – venom Transcaucasian vipers.

**Key Words**: Lungs, morphological changes, venom Macrovipera lebetina.