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Issues of experimental development and prospects of using wound coatings based on chitosan for wound treatment

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Introduction: Optimizing methods of stimulating reparative processes in the treatment of soft tissue wounds is an urgent task in modern medicine. One such area is currently the use of biopolymer wound coatings with polyfunctional properties. This is prolonged action, wound healing, detoxification and antiseptic effects, and in addition, the ability to manage biodegradation and more, the ability to act as a depot or biomatrix for various pharmacological agents immobilized in their structure.

We conducted studies of the natural chitin polysaccharide and its deacetylated derivative - chitosan, having the above properties, and of interest in promising wound coating development in such indicators as: controlled biodegradability, high wound healing activity, biocompatibility, bioadhesiveness, hypoallergy, apirogenicity and sorption activity. In this work, two experimental samples of biodegradable wound coatings synthesized on the basis of chitosan in the treatment of soft tissue wounds were compared. The aim of the study is to compare the effectiveness of wound coatings developed on the basis of chitosan with different physicochemical characteristics in the treatment of soft tissue wounds in the experiment.

Materials and methods: The object of the study was two types of experimental wound coatings based on chitosan, with technological parameters calculated by the Department of Surgical Diseases of the FSBOU VO KubMU of the Ministry of Health of Russia, synthesized by the Kurchatov Institute Research Center (Moscow). Chitosan sample No. 1 had a molecular weight of 600 kDa, a porosity of 98%, isotropic pores of diameter 20-45 μm, a wall thickness range of 350-1000 nm, a modulus of elasticity of 0.749 MPa, compression deformation of 44.32% and vertical orientation of the fibers. Chitosan sample No. 2 had a molecular weight of 600 kDa, a porosity of 98%, isotropic pores with a diameter of 70-200 μm, a wall thickness range of 600-2000 nm, a modulus of elasticity of 0.369 MPa, compression deformation of 50.43% and vertical orientation of the fibers. Sample No. 1 also had a pronounced sorption effect.

The study was carried out on 18 male rabbits of the Sovetskaya Shinshilla breed with a body weight of 3000-3700 gr., In which a soft tissue wound model was formed. The method for forming an experimental wound was based on the method developed by the department team (patent for the invention RU No. 2703709 C1 "Method for modeling an experimental soft tissue wound in rats for developing treatment tactics"). All stages of the experiment were carried out in accordance with regulatory documents: GOST 33215-2014 "Guidelines for the maintenance and care of laboratory animals. Rules for equipment of premises and organization of procedures, "GOST 33216-2014" Manual for maintenance and care of laboratory animals. Regulations for the Maintenance and Care of Laboratory Rodents and Rabbits, "Directive of the 2010/63/EU of the European Parliament and the Council of the European Union on Animal Welfare, etc. The anesthesiological manual was carried out using veterinary preparations Telazol, Zoletil, Antisedan, in dosages calculated according to conventional methods. Humane euthanasia of laboratory animals was carried out by overdose of an anesthetic and met the requirements of regulatory acts of the Russian Federation and international standards.

In accordance with the goals and objectives of the study, two experimental, and one control group, 6 animals each, were formed. The wound healing properties of the wound coating samples were studied by immersing them in a simulated soft tissue wound in laboratory animals. In the control group, traditional wound treatment was carried out: administration of 10% methyluracil ointment and treatment of the wound with a solution of chlorhexidine bigluconate 0.5%.

On the 7th, 14th, 21st day to study the histomorphological picture of wound tissue samples, two animals in each experimental and control groups were deduced from the experiment. When evaluating the results of the study, morphometric, histological, bacteriological methods were used.

The level of bacterial insemination was determined using the developed computer image analysis method. To **o**bjectify the results of the study, as well as to minimize the number

of experimental animals, we used ultrasound diagnostics of the operation zone. Ultrasound was performed immediately before and after the operative intervention in each reference period and on the 3rd day after it. Used the portable device Mindray M7 with the linear L12-4s sensor in the frequency range of 6.0-11.0 MHz and the digital medical Sony Hybrid Graphic Printer UP-X898MD printer.

When studying chitosan samples, physicochemical properties, speed and degree of biodegradation, the possibility of providing framework and drainage functions, as well as the ability to form a biomatrix-depot drug were studied.

Statistical analysis and processing of the obtained data was carried out on a personal computer with a windows operating system (Microsoft) installed, using a set of application software using the method of variation statistics.

Results and discussion: Both studied samples No. 1 and No. 2 of homogeneous wound coatings based on chitosan showed in the experiment high wound healing activity, biocompatibility, biodegradability, bioadhesiveness, hypoallergy, pyrogenicity and sorption activity. The samples had sufficient strength, density, elasticity, the ability to maintain a given shape and initial dimensions but had different periods of complete biodegradation: 6 ± 1.1 days for sample No. 2, and 12 ± 1.7 days for sample No. 1. By having a more "loose" structure with a high degree of porosity, sample No. 2 had a higher adhesion to surrounding tissues and the ability in the wound during exudate sorption to be transformed into a gel with a highly ordered internal micellar-type nanostructure, which makes it possible to use it as a biomatrix depot for drugs introduced into its structure in order to prolong the local medicament. Sample No. 1, due to the tighter structure with unidirectional pore orientation, effectively performed the framework functions, preventing contact of the wound walls and thereby ensuring adequate drainage of the pathological focus and gradual filling of the tissue defect, preventing the possibility of formation of residual cavities.

Conclusions:

1. The examined samples of wound coatings based on chitosan have a number of positive properties (high wound healing activity, biocompatibility, biodegradability, bioadhesiveness, hypoallergy, pyrogenicity and sorption activity), which allows determining promising directions for the development of new types of wound coatings for the treatment of soft tissue wounds of various genesis.

2. Changes in the technology of synthesis of chitosan-based biopolymers make it possible to create wound coatings that differ in 3-dimensional spatial structure, pore characteristics, stiffness and rate of biodegradation, which ensures the performance of various wound coating functions. More porous materials ("loose" types) provide adhesion and are most promising as a carrier for pharmacological agents. High density samples undergo biodegradation at a later time (up to 14 days) and can act as a framework, providing a draining effect in the wound.

3. The introduction of the ultrasound diagnostic method significantly complements the traditional methods used in experimental surgery, the method is very informative, allows for continuous monitoring of the dynamics of the wound process *in vivo* in experimental animals throughout the study.

Recent publications

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Speaker Biography

D I Ushmarov graduated from the Kuban State Medical Institute with a degree in medicine, internship in surgery; The Institute of Economics and Management in Medicine and Social Affairs, specializing in economics and management at the enterprise. Medical experience since 1994, worked as a surgeon in medical institutions of the mountains. Krasnodar (Russian Federation). The main areas of work were urgent surgery, abdominal surgery, oncology, vascular surgery, military field surgery. I have been working at FSBOU VO KubMU MZ of the Russian Federation since 2010. I combine the main position of the head of the educational and production department with teaching at the department of surgical diseases. Since 2013, a member of the Russian Society for Simulation Training in Medicine (ROSOMED). I have more than 25 scientific papers, 4 patents for inventions. I have the honorary title "Honored Worker of Health of the Kuban.

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