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Research Article

Influence of silver-ion-containing pharmacotherapeutic system for repair of anterior abdominal wall on connective tissue formation in experiment

Ekaterina S. Mishina[1], Marija A. Zatolokina[1], Anastasia V. Gureeva[1], Vladimir V. Gureev[1], Karina A. Elagina[1], Eugenia S. Zatolokina[1]

1 *Kursk State Medical University of the Ministry of Healthcare of the Russian Federation, 3 K. Marx St., Kursk 305041 Russia*

Corresponding author: *Ekaterina S. Mishina* (MishinaES@kursksmu.net)

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Abstract

Introduction: In modern medicine new pharmacotherapeutic systems significantly reducing the risk of complications are being actively searched for. The study undertaken was aimed at studying one of such systems consisting of a prosthesis coated with silver ions.

Materials and methods: The material for the study was standard endoprostheses produced by Lintex LLC (St.-Petersburg) for plastic repair of the anterior abdominal wall: Esfil and Uniflex, as well as Plasmofilter produced by Plasmofilter JSC (St.-Petersburg) and a pharmacotherapeutic system containing silver ions (FCS) applied to the experimental samples of endoprostheses – Esfil Ag and Unifleks Ag (patent RU 2473369C1), which were implanted into male Wistar rats. The results were evaluated using morphological, morphometric, immunohistochemical, ionometric, microbiological and statistical methods.

Results and discussion: As a result, it was found that the use of the FCS leads to a more rapid change in inflammation phases. The formation of a mature connective tissue capsule with a thickness of 4.5±0.01 mm was observed by Day 30. The study of the cellular component of the periprosthetic tissue revealed the prevalence of resident cells. The proliferative activity of fibroblastic cells when using FCS over 14 days was statistically significantly ($p \leq 0.05$) 3.5-time higher. Microbiological studies confirmed the antibacterial properties of FCS in vivo and in vitro.

Conclusion: The use of FCS contributes to the acceleration of reparative processes, earlier resolution of inflammation and stimulation of collagenesis both under sterile conditions and under microbial conditions.

Keywords

Silver nanoparticles, periprosthetic capsule, collagenogenesis, hernioplasty.

Introduction

One of the negative factors affecting the regeneration processes is infection overlay. The inflammatory phase of a wound process in the postoperative period may take a protracted course with different tissue development processes that is clinically shown in formation of seromas and hematomas with wound abscess (Omelyanenko et al. 2018, Vlasov and Kukosh 2013). In order to prevent the development of infectious processes, it is necessary to use complex pharmacotherapeutic systems (FCSs). In particular, to reduce infections processes, they apply an antibacterial therapy (Bukina and Sergeeva 2012, Dovnar et al. 2018, Larichev et al. 2018, Petritskaya et al. 2016, Shrivastava et al. 2007, Zatolokina et al. 2016), to reduce the hypoplastic reaction of connective tissue – allogeneic embryonic fibroblasts (Ivanov et al. 2017), to slow down tissue regeneration – ascorbic acid (Lazarenko et al. 2016, Singh et al. 2008), potassium orotate (Ivanov et al. 2017), and solcoseryl (Lazarenko et al. 2016). Despite this diversity of pharmacological methods, eliminating complications arising from the abdominal wall plasty seems to be impossible (Netyaga et al. 2013). Therefore, in modern medicine the development of new pharmacotherapeutic systems allowing to significantly reduce the risks of postoperative complications remains relevant. One of these existing approaches is applying ions, nanoparticles or other pharmacological means: protargol, silver, carbon coating, etc. onto the mesh endoprosthesis, which acts as a kind of matrix (Ivanov et al. 2016, Mishina et al. 2015, Yarmamedov et al. 2018).

Recently particular attention has been paid to silver ions, which have unique properties due to a high surface-to-volume ratio, which determines their great efficacy. The literature focuses on the functional activity of silver ions. It is proved that silver ions have various antimicrobial effect – from bactericidal to bacteriostatic. At the same time it is very important that silver ions are not cytotoxic for human cells, unlike microorganisms (Donahue et al. 2006, Janis et al. 2016, Si et al. 2002).

A promising direction in the use of the biocidal properties of silver nanoparticles is the production of textile and polymer products for medical purposes. Some of such materials are silver-ion-coated implants or pharmacological systems with silver ions, which are highly biocompatible, at the same time their silver coating makes it possible to use them to prevent wound complications (Bochek et al. 2015, Broderick et al. 2012, Melaiye and Youngs 2005, Wood et al. 2013).

So far, there has been no study of the influence of such a ”synergism” between a prosthesis and silver ions spread on it or between a pharmacotherapeutic system and silver ions, used for replacement of the abdominal wall, on inflammatory postoperative complications, which determined the purpose of this study.

Purpose of the study: Correction of inflammatory processes that occur when replacing the anterior abdominal wall, as well as, acceleration of regeneration and collagenesis when applying a pharmacotherapeutic system with silver ions (FCS).

Materials and methods

The experiment was conducted on 500 Wistar white male rats weighing 200–250 g each, 250 animals in each group. The animals for the experiment had been selected without any external signs of diseases after a two-week quarantine sequestration at the vivarium of Kursk State Medical University of the Ministry of Healthcare of the Russian Federation. The protocol of the experiments (sections on selecting, managing, operating and withdrawing animals) was conducted in complaince with bioethics principle, good laboratory practice (GLP), ethical norms, *The International Guidelines for Biomedical Research Using Animals (1985),* Order № 267 of 19.06.2003 of the The Ministry of Healthcare and Social Development of the Russian Federation “On Approval of Laboratory Practice Rules” and Order № 755 of 12.08.1977 of the Ministry of Public Health of the USSR ”On Measures to Further Improve the Organizational Forms of Work with Using Experimental Animals”. The ethical principles of treating laboratory animals were followed in compliance with the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, ETS № 170.

The material for the study were standard polypropylene endoprostheses produced by Lintex LLC (St.-Petersburg) for plasty of the anterior abdominal wall: a light polypropylene mesh endoprosthesis Esfil and an ultralight polypropylene and polyvinylidene mesh endoprosthesis Uniflex (control group 1), a mesh endoprosthesis Plazmofilter manufactured by Plazmofilter JSC (St.-Petersburg), with mixture of finely dispersed silver found in Poviargol and Polyvinylpyrrolidone applied on the mesh (control group 2) and a pharmacotherapeutic system containing silver ions (FCS) applied on experimental models of implants produced by Lintex LLC (St.-Petersburg) –

Esfil Ag and Uniflex Ag (patent RU 2473369C1) (experimental group).

The study was divided into 2 groups, depending on the conditions of endoprosthetics: using a PCS for plasty of the anterior abdominal wall under sterile conditions or under conditions of microbial contamination. There were 5 series in each group depending on the implant used: Uniflex, Uniflex Ag, Esfil, Esfil Ag, and Plazmofilter.

In all the series of the experimental part of the study, in order to learn which of the methods leads to better regeneration results of connective tissue after the implantation, the onlay plasty of the anterior abdominal wall was done. The surgical field was treated twice with 1% iodopyrone solution, once – with 95% ethyl alcohol solution and covered with sterile surgical drape. After intraperitoneal injection of 20% chloral hydrate solution at a dose of 200µl/100g per weight, skin and adipose tissue of the animals were incised along the abdominal midline in the upper third, 4.0cm long. The skin and the adipose tissue were separated from the aponeurosis of the rectus muscles, in which a 4.0×4.0 cm area was allocated. To that area, a mesh endoprosthesis of 2.0×2.0 cm was sutured interruptedly on all sides, using a 2/0 monofilament thread.

In the first experimental group, the surgical wound was sutured tightly layer-by-layer and treated with antiseptics.

In the second experimental group, in order to create microbial conditions, before suturing, the wound was injected with 1 ml of saline containing 1 bln microbial bodies of one-day culture of *Staphylococcus aureus* 592 and *E. coli*. After that, the skin and the adipose tissue were sutured. Surgical interventions were performed in evenings for 2 weeks. The animals were withdrawn from the experiment on Days 3, 7, 14, 21, and 30 by an overdose of general anesthetics.

To carry out a morphological study, an excision of 2.0×2.0 cm was made from the central part of the abdominal wall together with the implanted endoprosthesis samples and surrounding tissues. The biological sample was fixed in 10% neutral formalin. After the fixation, smaller slices, with fragments of implanted endoprosthesis, were cut out, embedded in paraffin according to standard procedures and microtomized to make slices of 5–7 µm thickness. The slices were stained with hematoxylin and eosin, by Van Gieson's and Mallory's methods.

Microscopy and microphotography were done with an optic system consisting of a Leica CME microscope and DCM 510 ocular camera, x40, x100, x200 and x400. The images were documented by means of the FUTURE WINJOE software, included into the ocular camera. In microphotographs, the cell inflammatory infiltrate area around threads of the implants, the thickness and structure of the connective-tissue capsule, presence of layers and their intensity, maturity of collagen fibers were assessed. In order to objectively compare the reaction of connective tissue to the studied materials, there was used a method for determining a cell index, calculated according to the following formula (1):

$$\frac{R.c.}{Nr.c.} = CI \quad (1)$$

where CI – cell index; R.c. – resident-cells (total number of macrophages, fibroblasts and fibrocytes); Nr.c. – non-resident cells (total numver of granulocytes, agranulocytes and mast cells in the cell layer of the capsule) for an objective comparison connective tissue reactions on elucidate materials. If the cell index was <1, the conclusion was that inflammatory changes prevailed, which is characteristic of phase I of the wound process, if CI was >1, it meant that repair processes prevailed, which is characteristic of phase II, according to M.I. Kuzin.

An immunohistochemical study was performed with use of monoclonal antibodies (to Ki67protein – a marker of proliferative cells) to rat's antigens (Santa Cruze, USA) (Dabbs 2019). For visualization of the products of the immune reaction, the streptavidin-biotin peroxidase method was applyied (DAKO, LSAB+Kit, HRP), with using diaminobenzidine (DAKO, Liquid DAB+) as a stain; nuclei were stained with hematoxylin. The Ki-67 index was calculated as a percentage ratio of specifically stained nuclei to the total number of nuclei in 10 fields of view.

The concentration of silver in the tissues of the rats' abdominal wall at various stages of the experiment after applying FCS containing silver ions was determined by means of the potentiometric method on an ionomer using an ion-selective electrode. Silver content was expressed in µg/g.

A microbiologic study was conducted by method by V.E.Radoman to estimate microbial content. The numbers of KOE St. aureus 592 and E. coli were calculated, their morphological and cultural properties were studied. The number of microbes in 1g of the tissue was calculated according to the formula (2):

$$N = n \times 10 \times 10\,K \quad (2)$$

where N – the number of microbes per 1g of biopsy tissue; n – the number of microbes grown in a plate, 10 – per 1 g of suspension, 10 – cultivation of material seeded on a Petri dish which is used for counting colonies; K – conversion rate of sub-sample per 1g of biopsy.

Descriptive statistics was used for all the date: they were checked for normality of the distribution. A type of distribution was determined by the Shapiro-Wilk criterion. In case of a normal distribution, the mean (M) and standard error of the mean (m) were calculated. Intergroup differences were analyzed using the non-parametric Mann-Whitney criterion. Taking into account low sensitivity of nonparametric methods to a type of distribution, and the level $p \leq 0.05$ allowable for experimental biomedical research, this significance level was chosen to confirm the statistical hypothesis. All the computations were done using analytical app package Microsoft Excel (Office 2010).

Results and discussion

The conducted morphological study revealed that aseptic inflammation develops in response to the implantation of the endoprosthesis in the surrounding tissue. In case of microbial contamination of the wound, the main signs of septic inflammation are expectedly seen. The speed of those reactions and the degree of their intensity depend on a sort of the material being implanted and the presence/absence of the coating on it.

At the initial stages of the experiment, the cell inflammatory infiltrate forms around implants, consisting primarily of such cellular elements such as: neutrophils, macrophages, and lymphocytes. On Day 3, in microbial conditions, the area of cell inflammatory infiltrate was significantly ($p \leq 0.05$) – 1.7 and 1.8 times – smaller when using Uniflex Ag and Esfil Ag, compared to using standard endoprostheses Esfil and Uniflex. By Day 14, in comparison with Day 3, when using FCS, the area reduced 1.8 and 1.5 times, respectively. In sterile conditions by Day 14, when using FCS based on Uniflex Ag, the area reduced 2.5 times, and using FCS based on Esfil Ag – 2.4 times.

By the end of the experiment (on Day 30), the minimum area was observed when using FCS containing silver ions,

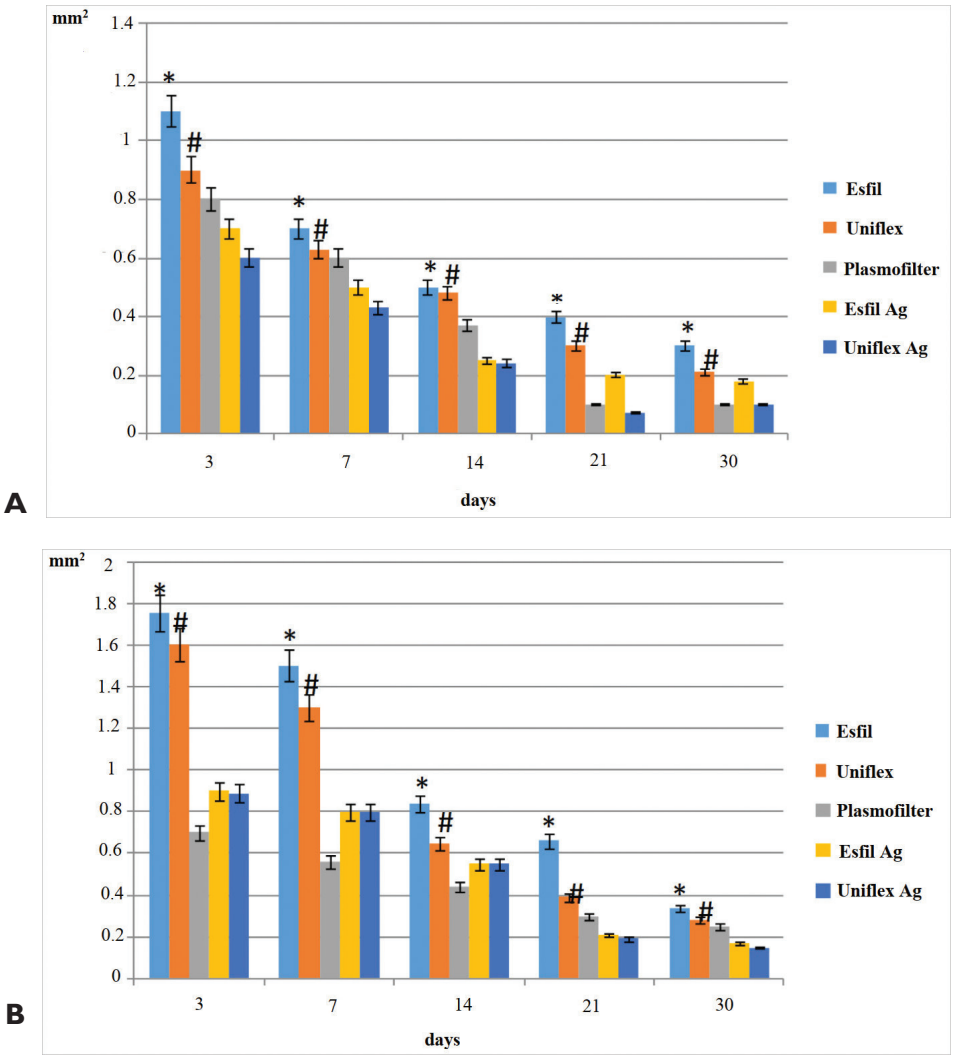

Figure 1. Influence of pharmacotherapeutic system containing silver ions on the infiltration area under sterile (**A**) and microbial contamination (**B**) conditions. **Note:** statistically significant differences at p≤0.05 FCS containing different types of endoprostheses: # – Uniflex Ag compared with Uniflex, * – Esfil Ag compared with Esfil.

the maximum area – when using standard prostheses , both in sterile conditions and in microbial contamination. Elucidating the general dynamics of the changes, the concludes can be made that the area decreases in direct ratio to the experiment duration (Fig. 1).

Comparison of the percentage of cells of different types in the infiltrate and calculation of the cell index showed a different ratio of resident and non-resident cells. From Fig. 2 it follows that by the end of the experiment under sterile conditions, there was a statistically significant (p≤0.05) increase in the cell index: a 2-time increase when using FCS with silver ions containing an Esfil Ag endoprosthesis and a 6-time increase when using FCS with silver ions containing a Uniflex Ag endoprotesis in comparison with standard endoprostheses.

Under the conditions of microbial contamination, by Day 30 of the experiment, the dynamics of the cell index was the same. At the same time, the use of FCS with silver ions containing an Esfil Ag endoprosthesis led to a double increase in the cell index, and using FCS with silver ions comprising a Uniflex endoprosthesis resulted in a 1.3-time increase. The fact that there was no cytotoxic effect towards the cellular component of tissues surrounding a FCS with silver ions for prosthetics of the anterior abdominal wall was confirmed by an increase in the proliferative activity index, using the cell proliferation marker Ki-67. When studying the cell proliferation index under sterile conditions, the maximum mitotic activity was observed on Day 14 of the experiment with use of FCS with silver ions for prosthetics of the anterior abdominal wall and was 41.26% and 44.89%, when using Esfil Ag and Uniflex Ag endoprostheses, respectively. When looking at the cell proliferation index under microbial contamination conditions, its value decreased in direct proportion to the duration of the experiment. On Day 3, when using the FCS FCSbased on Uniflex Ag and Esfil Ag, the number of Ki-67 positive cells was 54.97% and 51.36%, respectively (Fig. 3). By the end of the experiment, this index statistically (p≤0.05) decreased 2.3 and 2.2 times, respectively.

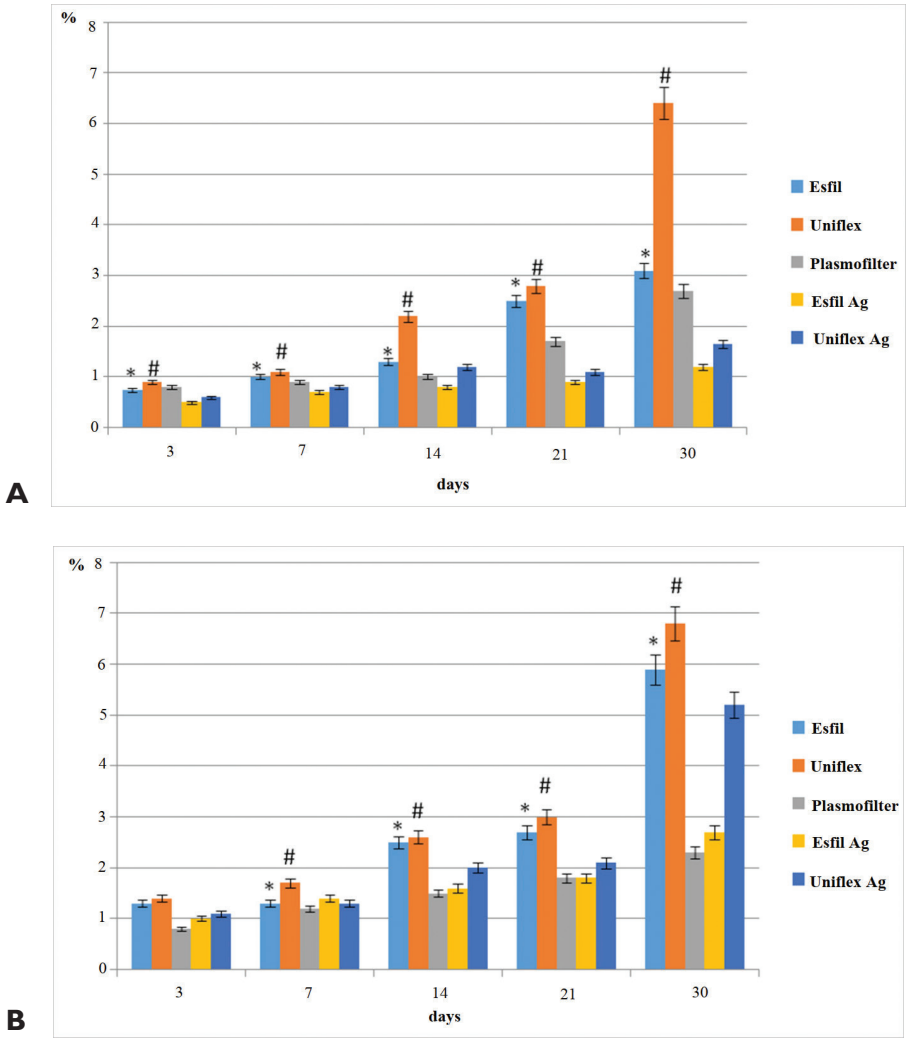

Figure 2. Effect of pharmacotherapeutic system containing silver ions on the cell index in endoprosthetics of anterior abdominal wall under sterile (**A**) and microbial contamination (**B**) conditions. **Note:** statistically significant differences at $p \leq 0.05$ FCS containing different types of endoprostheses: # – Uniflex Ag compared with Uniflex, * – Esfil Ag compared with Esfil.

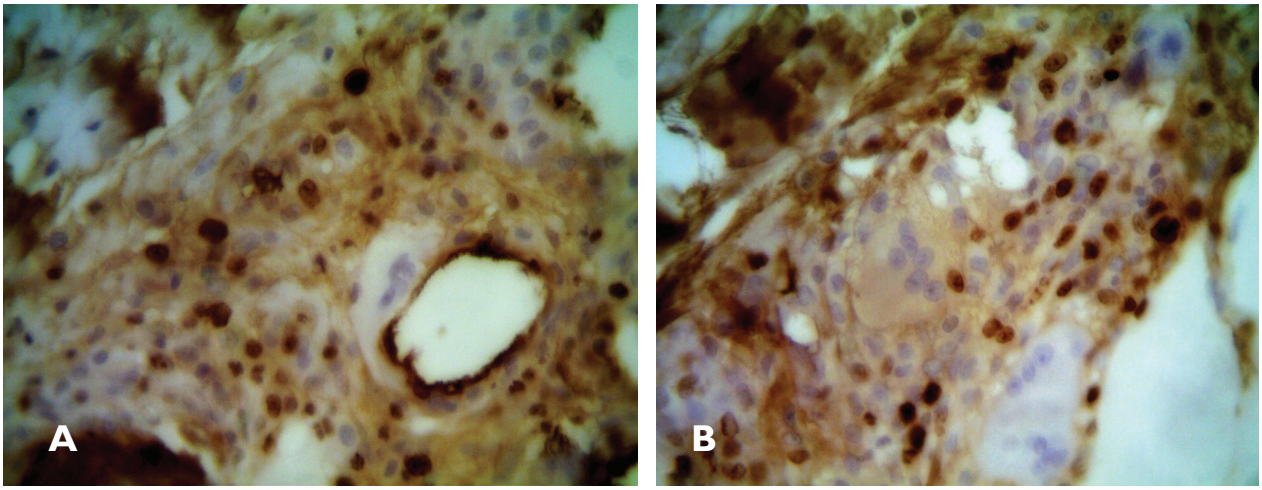

Figure 3. The expression of Ki-67 when using a pharmacotherapeutic system with silver ions for endoprosthetics of the anterior abdominal wall in a series of experiments using a Uniflex Ag endoprotesis for 3 days (**A**) and 30 days (**B**) after surgical intervention under sterile conditions. Immunohistochemical reaction, DAB. ×400.

Proliferative activity of fibroblastic cells under sterile conditions using FCS with silver ions beginning on the 14th day of experiment is reliably 3.5-time higher than when using standard endoprostheses.

The nature of this phenomenon is ”hyperstimulation” of the proliferative activity of fibroblastic cells by silver ions. Under the conditions of microbial contamination, the proliferative activity of fibroblastic cells whenusing endoprostheses with silver ions and standard endoprostheses decreases in direct proportion to the time of the experiment and on Day 30, it does not differ significantly.

At later stages, there was the second phase – proliferation resulting in the formation of a mature periprosthetic connective-tissue capsule, which consisted of two parts: an external fibrous part formed by collagen fibers and an internal cellular one containing cells of fibroblastic and lymphocyte differentiations and bordering directly on fibers of endoprostheses.

By the end of the experiment, quite a mature periprosthetic connective-tissue capsule was formed around the implanted endoprostheses, the thickness of the capsule depending on the kind of prosthesis and conditions of the experiment. The external fibrous layer of such a capsule contains mature collagen fibers which are located densely and in parallel to each other, stained bright with oxyphilic by Van Gieson’s method. In the internal cellular layer, fibroblasts and fibrocytes predominate.

When using FCS FCSwith silver ions under conditions of microbial contamination, the thickness of the newly formed capsule around fibers of the Uniflex Ag endoproteses was2.6 mm. Under sterile conditions, its thickness around fibers of the Uniflex Ag and Esfil Ag endoproteses was 6.1 mm and 5.4 mm, respectively (Fig. 4).

Thus, the mature periprosthetic connective-tissue capsule, consisting of bright oxyphilic collagen fibers, is formed by Day 30 of the experiment when using FCS with silver ions under sterile conditions.

When carrying out an ionometric study, there was observed the diffusion of silver ions and its particles from the surface of the fiber to the tissues surrounding the endoprosthesis (Figs. 5, 6). The maximum amount of silver

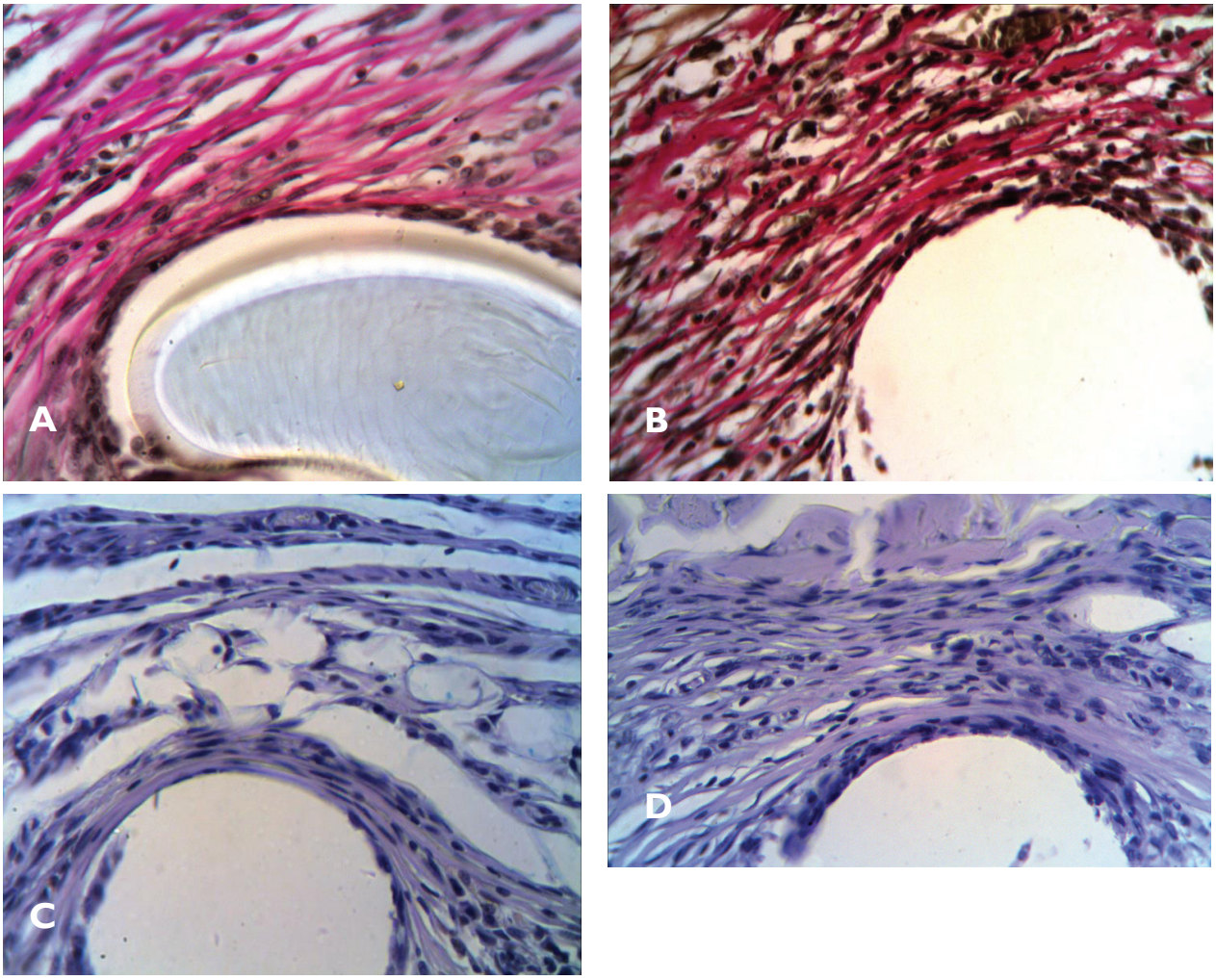

Figure 4. Microphotograph of tissue of anterior abdominal wall after usage of the pharmacotherapeutic system with silver ions for endoprosthetics in the series of the experiments using Uniflex Ag (**A, C**) and Esfil Ag (**B, D**) endoprostheses on Day 30 of the experiment under sterile conditions. Stained with hematoxylin and eosin (**B, D**) by Van Gieson’s method of (**A, C**). ×400.

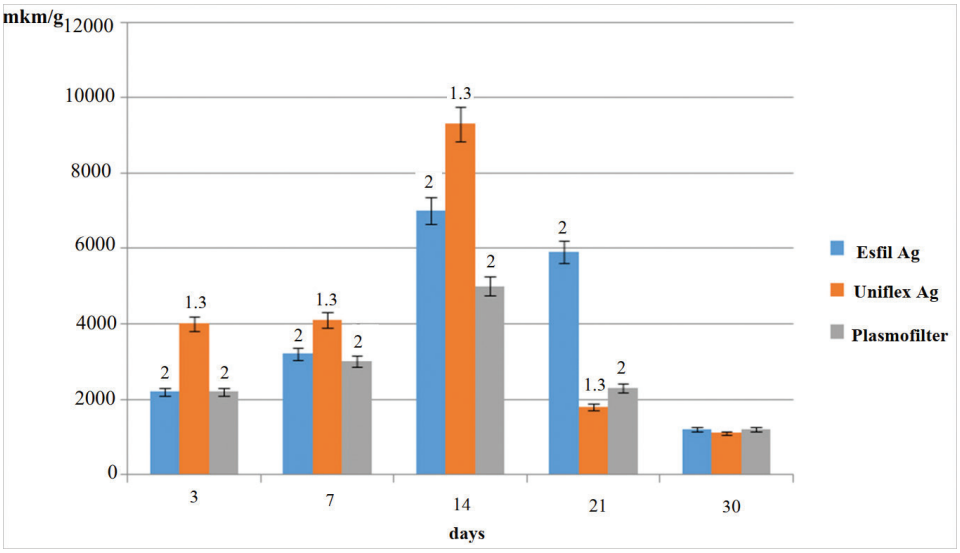

Figure 5. The dynamics of changes of the amount of silver in tissues when using the pharmacotherapeutic system with silver ions for endoprosthetics of the anterior abdominal wall under sterile conditions. **Note:** differences statistically significant at p≤0.05 when using FCSFCS, containing various types of endoparasites in comparison with EsfilAg (1), Uniflex Ag (2) and Plasmafilter (3).

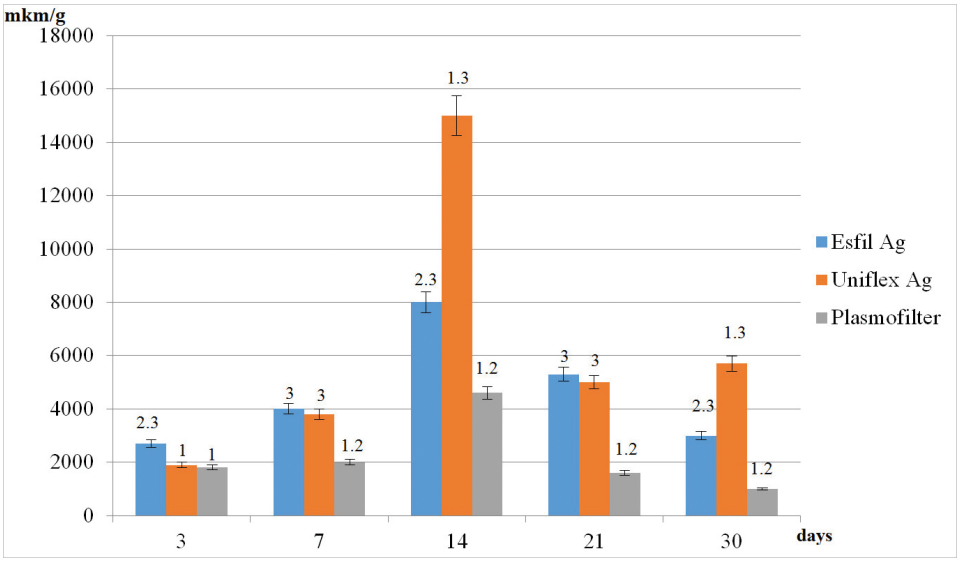

Figure 6. The dynamics of changes of the amount of silver in tissues when using the pharmacotherapeutic system with silver ions for endoprosthetics of the anterior abdominal wall under sterile conditions. **Note:** differences statistically significant at p≤0.05 when using FCSFCS, containing various types of endoparasites in comparison with EsfilAg (1), Uniflex Ag (2) and Plasmafilter (3).

ions in periprosthetic tissues was observed on Day 14 of the experiment, both under sterile conditions and microbial contamination conditions. Then silver ions were phagocyted, followed by a decrease ($p<0.05$) in their numbers in direct proportion to the terms of the experiment.

The correlation analysis revealed that by Day 14, maximum migration of silver particles to the surrounding tissue was observed when using a Plasmafilter endoprosthesis. That was proved by the presence of a correlation between the area of infiltrate and the amount of silver on the fibers of the prosthesis (Table 1).

When analyzing the correlation coefficients, it was assumed that when it was above 0.7, there was a strong connection between the two studied characteristics, which could be both direct (positive value) and indirect (negative value).

When carrying out a correlative analysis under conditions of microbial contamination, there was a decrease in the correlation to the medium and weak levels. The dominance of medium correlations was observed when using FCS with silver ions, containing UniflexAg, EsfilAg and Plasmofilter endoprostheses on Day 3 and EsfilAg and Plasofilter endoprosthethes on Day 30. Meanwhile, the direction of that correlation was reversed (Table 2).

The conducted microbiological study revealed that FCS with silver ions FCSfor endoprosthetics of the anterior abdominal wall had a bactericidal effect towards the studied

Table 1. Correlation Between the Amount of Silver in the Pharmacotherapeutic System for Endoprosthesics and the Area of Infiltrate (Thickness of Periprosthetic Capsule) Under Sterile Conditions.

Day	UniflexAg	EsfilAg	Plasmofilter
3	-0.19465***	0.747234*	-0.05006***
7	0.455407**	-0.40951**	-0.21646***
14	-0.04058***	-0.49102**	0.85885*
21	0.497807**	-0.21153***	0.098635***
30	-0.14848***	0.706889*	-0.32989**

Note: Spearman's rank correlation; * – strong connection, ** – medium connection, *** – weak connection.

Table 2. The Correlation Between the Amount of Silver in the Pharmacotherapeutic System for Endoprosthesics and the Area of Infiltrate (Thickness of Periprocthetic Capsule) Under Conditions of Microbial Contamination.

Day	UniflexAg	EsfilAg	Plasmofilter
3	-0.72237*	-0.77571*	-0.72216*
7	0.01170***	0.39658**	-0.00331***
14	0.07316***	-0.18522***	0.164573***
21	-0.30796**	-0.41086**	-0.314505**
30	-0.13265***	-0.76227*	-0.792594*

Note: Spearman's rank correlation; * – strong connection, ** – medium connection, *** – weak connection.

microorganisms. The major microbial contamination of a wound by *E. coli* microorganisms was observed after the implantation of an Uniflex endoprosthesis and amounted to 333.5±1.43x10^6 CFU, whereas the minor microbial contamination was observed when using UniflexAg and was 20.1±1.44x10^6 CFU. After the implantation of EsfilAg, the amount of CFU was 26.3±1.59x10^6, Esfil – 271.8±1.83x10^6, Plasmofilter – 4.6±0.87x10^6. The contamination of the wound by *Staphylococcus aureus* was significantly less than that by *E. coli*; however, when comparing, Esfil had the highest amount of CFU – 70.9±2.15x10^6. When using Uniflex Ag, CFU was 33.5±1.43 x10^6. The lowest amount of CFU was recorded when using endoprostheses with antibacterial coatings: Uniflex Ag – 9.4±1.6x10^6, Esfil Ag – 15.2±1.43x10^6, and Plasmofilter – 2.6±0.97 x10^6.

Conclusion

The hernia repair with mesh implants is currently considered the "golden standard" in the world practical treatment of abdominal hernias. However, during the hernioplasty with mesh implants, the risk of development of infectious postoperative complications increases. The standard problem solution in herniology is the regular usage of antimicrobial medications. Meanwhile, the resistance of microorganisms to many antimicrobial medications is becoming even more threatening. That is why the development of new pharmacotherapeutic systems, made as mesh polypropylene or polypropylene-polyvinylidene fluoride endoprostheses with silver ions on their surface, has considerable advantages over all existing antimicrobial medications, since silver compounds have a wide range of antibacterial activity and have no disadvantages in terms of the problem of resistance of pathogenic microorganisms to them.

As a result of the experiment, it was found that FCS in form of FCSEsfil Ag and Uniflex Ag endoprostheses coated with threads of silver ions leads to rapid completion of the exudative phase and the onset of the proliferative phase. The comparison of the proportion of cells of various types in the infiltrate (in the early stages) and in the internal layer of the connective-tissue capsule (in the later stages) showed an absolute predominance of resident cells as early as on Day 14 under sterile conditions and on Day 7 under conditions of microbial contamination. By the end of the experiment, under sterile conditions, there was a 2-fold (when using a polypropylene prosthesis with silver ions) and 6-fold (when using a polyvinylidene fluoride prosthesis with silver ions) increase in the cell index in comparison with the standard endoprostheses.

The microbiological study proved biocidal properties of a FCS with silver ions. Biocidal activity was established both towards tests strains of *E. coli* and *St. aureus*. On Day 14 (the peak of silver ions content in the tissues while using a PST with silver ions, containing an Esfil Ag endoprotesis and the considerable amount of them while using Uniflex Ag) the microbial contamination of wounds reached its minimum. By Day 21 of the experiment, when determining microbial contamination when using FCS with silver ions containing a Uniflex Ag endoprosthesis, the microbial growth was not detected. In the late postoperative period, the microbial contamination was completely absent while using all kinds of endoprostheses.

Thus, the fundamental issue in the process of integration of the prosthesis into the tissues is the response of tissues with less reactivity. It includes minimum inflammation caused by the implant and rapid formation of the connective-tissue capsule, formed by mature collagen fibers around the filbers of the endoprosthesis. The usage of FCS with silver ions for plasty of the abdominal wall contributes to the activation of the wound process, which leads to an earlier relief of the inflammatory response and stimulates processes of collagenogenesis under both sterile conditions and conditions of microbial contamination. The thickness of the capsule while using FCS with silver ions, containing polypropylene and polyvinylidene fluoride endoprostheses was 6.1 mm and 5.4 mm, respectively. Under conditions of microbial contamination, the thickness of the capsule was considerably smaller and amounted to 2.1 mm and 2.6 mm, respectively.

The conducted research showed that in response to implanting a foreign body, inflammation develops in the connective tissue notwithstanding the conditions (sterile or microbial contamination). The speed of these stages and their intensity depend on a kind of the prosthesis and the composition of its coating. According to the data of the conducted study, the morphological changes observed during the usage of FCS with silver ions for the abdominal wall plasty are the evidence of both the most optimal biocompatibility and the direct "effect" of their antibacterial properties under conditions of microbial contamination.

The usage of FCS with silver ions for the abdominal wall plasty facilitates the acceleration of reparative processes, which leads to an earlier relief of the inflammatory response and stimulation of collagenogenesis under both sterile conditions and conditions of microbial contamination.

Conflicts of interest

The authors have no conflict of interest to declare.

References

- Bochek AM, Vokhidova NR, Saprykina NN, Ashurov NSh, Yugai SM, Rashidova SSh (2015) The properties of chitosan-cobalt nanoparticle solutions and related composite films. Polymer Science Series A 57(4): 460–466. https://doi.org/10.1134/S0965545X15040033
- Broderick G, McIntyre J, Noury M, Strom HM, Psoinos C, Christakas A, Billiar K, Hurwitz ZM, Lalikos JF, Ignotz RA, Dunn RM (2012) Dermal collagen matrices for ventral Hernia repair: comparative analysis in a rat model. Hernia 16(3): 333–343. https://doi.org/10.1007/s10029-011-0891-0 [PubMed]
- Bukina YuA, Sergeeva EA (2012) Antibacterial properties and mechanism of bactericidal action of silver nanoparticles and ions. Bulletin of Kazan Technological University [Vestnik Kazanskogo Tekhnologicheskogo Universiteta] 15(14): 170–172. [in Russian]
- Donahue TR, Hiatt JR, Busuttil RW (2006) Collagenase and surgical disease. Hernia 10(6): 478–485. https://doi.org/10.1007/s10029-006-0146-7 [PubMed]
- Dovnar RI, Smotrin SM, Anufrik SS (2018) Hydrofiber non-woven silver-containing material in the treatment of aseptic wounds. Journal of Grodno State Medical University [Zhurnal Grodnenskogo Gosudarstvennogo Meditsinskogo Universiteta] 16(4): 408–413. https://doi.org/10.25298/2221-8785-2018-16-4-408-413 [in Russian]
- Dabbs DJ (2019) Diagnostic immunohistochemistry: theranostic and genomic applications. Fifth edition. Elsevier, Philadelphia, 944 pp.
- Janis JE, Khansa L, Khansa I (2016) Strategies for postoperative seroma prevention: a systematic review. Plastic and Reconstructive Surgery 138(1): 240–252. https://doi.org/10.1097/PRS.0000000000002245 [PubMed]
- Ivanov VS, Ivanov IS, Tsukanov AV, Gafarov GN, Obyedkov EG (2016) The effect of vitamin C on the ratio of collagen types I and III in the periprosthesis area in mice. Cell and Tissue Biology [Tsitologiya] 10(6): 453–457. https://doi.org/10.1134/S1990519X16060031 [PubMed]
- Ivanov SV, Lazarenko VA, Ivanov IS, Parfenov IP, Tsukanov AV, Tarabrin DV, Ob'edkov EG (2017) Influence of potassium orotate on neocollagenesis during implantation of polypropylene endoprosthesis and endoprosthesis made of polypropylene with lactic acid in the experiment. Surgery [Khirurgiya] 3: 50–54. https://doi.org/10.17116/hirurgia2017350-54 [in Russian]
- Lazarenko VA, Ivanov SV, Ivanov IS, Parfenov IP, Goryainova GN, Tsukanov AV, Ivanova IA, Ob'edkov EG (2016) Morphological changes in the field of implantation of Parietene and Progrip endoprostheses depending on the use of drug Solcoseryl. Kursk Scientific and Practical Bulletin "Man and Health" [Kurskiy Nauchno-Prakticheskiy Vestnik "Chelovek i Yego Zdorov'ye"] 4: 70–76. https://doi.org/10.21626/vestnik/2016-3/12 [in Russian]
- Larichev AB, Babadzhanyan AR, Fomin AN, Kryuchkov VB, Efremov KN, Smirnova AV (2018) The clinical pharmacokinetic parallels of peri-operational antibiotics prevention in abdominal surgery. Russian Medical Journal [Rossiyskiy Meditsinskiy Zhurnal] 24(2): 73–77. https://doi.org/10.18821/0869-2106-2018-24-2-73-77 [in Russian]
- Melaiye A, Youngs WJ (2005) Silver and its application as an antimicrobial agent. Expert Opinion on Therapeutic Patents 15(2): 125–130. https://doi.org/10.1517/13543776.15.2.125
- Mishina ES, Klimova LG, Zatolokina MA, Netyaga AA (2015) Study of the antimicrobial activity of new reticular endoprostheses coated with silver nanoparticles. Basic Research [Fundamental'nye Issledovaniya] 1(2): 307–310. [in Russian]
- Netyaga AA, Parfenov AO, Nutfullina GM, Zhukovsky VA (2013) Influence of various types of endoprostheses for hernioplasty on the state of muscles of different sections of the abdominal wall (experimental study). Kursk Scientific and Practical Bulletin "Man and Health" [Kurskiy Nauchno-Prakticheskiy Vestnik "Chelovek i Yego Zdorov'ye"] 4(1): 26–32. [in Russian]
- Omelyanenko NP, Mishina ES, Kovalev AV, Volkov AV (2018) Structural dynamics of the fibrous base of a reparative regenerate during spontaneous healing of a skin wound. Bulletin of Experimental Biology and Medicine [Byulleten' Eksperimental'noy Meditsiny i Biologii] 166(8): 236–240. https://doi.org/10.1007/s10517-018-4331-3 [in Russian]
- Petritskaya EN, Rogatkin DA, Rusanova EV (2016) Comparative characteristics of the antibacterial action of preparations of silver and nanosilver in vitro. Almanac of Clinical Medicine [Al'manakh Klinicheskoy Meditsiny] 44(2): 221–226. https://doi.org/10.18786/2072-0505-2016-44-2-221-226 [in Russian]
- Shrivastava T, Bera A, Roy G (2007) Characterization of enhanced antibacterial effects of novel silver nanoparticles. Nanotechnology 18(22): 115–122.
- Si Z, Bhardwaj R, Rosch R, Mertens PR, Klosterhalfen B, Klinge U (2002) Impaired balance of type I and type III procollagen mRNA in cultured fibroblasts of patients with incisional hernia. Surgery 131(3): 324–331. https://doi.org/10.1067/msy.2002.121376 [PubMed]
- Singh M, Singh S, Prasad S, Gambhir IS (2008) Nanotechnology in medicine and antibacterial effect of silver nanoparticles. Digest Journal of Nanomaterials and Biostructures 3(3): 115–122.
- Vlasov AV, Kukosh MV (2013) The problem of wound complications in endoprosthetics of the abdominal wall about ventral hernia. Modern Technologies in Medicine [Sovremennye Tekhnologii v Meditsine] 5(2): 116–124. [in Russian]
- Wood AJ, Cozad MJ, Grant DA, Ostdiek AM, Bachman SL, Grant SA (2013) Materials characterization and histological analysis of explanted polypropylene, PTFE, and PET hernia meshes from an individual patient. Journal of Materials Science Materials in Medicine 24(4): 1113–1122. https://doi.org/10.1007/s10856-013-4872-y [PubMed] [PMC]
- Zatolokina MA, Mishina ES, Netyaga AA, Yarmamedov DM (2016) The results of electron microscopic study of the composition of the threads of endoprostheses with silver coating and the dynamics of changes in the amount of silver in the tissues of the anterior abdominal wall during endoprotesis replacement of the anterior abdominal

wall. Modern Problems of Science and Education [Uspekhi Sovremennoy Nauki i Obrazovaniya] 2(2). https://science-education.ru/en/article/view?id=24222 [in Russian]

- Zhukovsky VA, Mukhina NI, Anushchenko TYu, Shkarupa DD (2013) Russian patent No. 2473369. The method of obtaining antimicrobial silver-containing mesh endoprostheses for reconstructive surgery (options). 2011146895/15, application 15/15/2011; publ. 01/27/2013, Bull. Number 3, 15 pp.
- Yarmamedov D, Lipatov V, Medvedeva M, Zaharova K (2018) Study of the pharmacological impact of polymeric membranes with antibacterial effect in traumatic lesions of cornea. Research Results in Pharmacology 4(4): 89–96. https://doi.org/10.3897/rrpharmacology.4.31006

Author contributors

- **Ekaterina S. Mishina**, Candidate of Medical Sciences, Assistant, Department of Histology, Embryology, Cytology; e-mail: MishinaES@kursksmu.net, **ORCID ID**: 0000-0003-3835-0594. The author played the main role in writing the article, planning the experiment and analyzing the data.

- **Marija A. Zatolokina**, Doctor of Medical Sciences, Assistant Professor, Professor of the Department of Histology, Embryology, Cytology; e-mail: ZatolokinaMA@kursksmu.net, **ORCID ID:** 0000-0002-9553-1597. The author played the main role in writing the article and analyzing the data.

- **Anastasia V. Gureeva, 2nd**-year student, Department of General Medicine; e-mail: produmen@yandex.ru, **ORCID ID:** 0000-0003-1719-7316. The author participated in the planning of the experiments, analysis of literature and interpretation of the data.

- **Vladimir V. Gureev,** Doctor of Medical Sciences, Professor of the Department of Pharmacology and Clinical Pharmacology; e-mail: produmen@yandex.ru, **ORCID ID:** 0000-0003-1433-1225 The author participated in planning the experiments, analyzed the literature and participated in interpreting the data.

- **Karina A. Elagina,** 6th-year student, Department of General Medicine; e-mail: karina.elagina@yandex.ru, **ORCID ID:** 0000-0002-6949-5430. The author participated in the planning of the experiments, analysis of literature, and interpretation of the data.

- **Eugenia S. Zatolokina,** 2nd-year student, Faculty of Pharmacy, Kursk State Medical University. 3 K. Marx St., Kursk 305041; e-mail: zatolokina_e.s@mail.ru, **ORCID ID:** 0000-0003-0169-7885. The author participated in the planning of the experiments, analysis of literature, and interpretation of the data.