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L-ARGINİNLƏ MODİFİKASIYA EDİLMİŞ POLİQLAKTİN-910-DAN VƏ POLİKAPROLAKTONDAN EKSPERİMENTLƏ İSTİFADƏ ZAMANI KOR BAĞIRSAĞIN STRUKTUR ELEMENTLƏRİNİN MORFOMETRİK PARAMETRLƏRİNİN MÜQAYİSƏLİ QIYMƏTLƏNDİRİLMƏSİ

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Xülasə. Məqalədə toxumalardan sorula bilən sintetik poliqlaktin-910 sapının və yeni tikiş materialı olan polikaprolaktonun L-argininlə modifikasiya edilmiş növünün eksperimentul şəraitdə korbəğirsəğin selikli qışası бүкüşlərinin morфометрик параметrlərinə təsirini müqayisəli şəkildə öyrənmək məqsədilə aparılmış tədqiqat işi haqqında məlumat verilmişdir.

Cinsi yetişkənliyə çatmış, kütləsi $2,62 \pm 0,21$ kq olan 65 dovşana cərrahi müdaxilə edilmişdir. Heyvanlar kontrol və 2 eksperimental olmaqla 3 qrupa bölünmüşdür: birinci eksperimental qrupda poliqlaktin-910 cərrahi sapından, ikincidə isə polikaprolaktonun L-argininlə modifikasiya edilmiş növündən istifadə edilmişdir. Operasiyadan sonrakı 3,7,14,21,30 və 60-cı günlərdə yaranın və əmələ gələn çapığın vəziyyəti öyrənilmişdir. Ekspirementin gedişində düz bağırsəğin perivulnar nahiyyəsinin selikli qışasında olan бүкüşlərin morфометрик tədqiqi aparılmışdır.

Tədqiqat nəticəsində müəyyən edilmişdir ki, sapdan kor bağırsəğin perivulnar nahiyyəsindəki operasiya yaralarının tikilməsi üçün L-argininlə modifikasiya edilmiş polikaprolakton cərrahi sapından istifadə edildikdə бүкüşlərin struktur komponentlərinin fəaliyyəti poliqlaktin-910 istifadəsindəkinə nisbətən 7 günə qədər tez bərpa olunur.

Açar sözlər: morфометриya, L-arginin bağırsaq бүкüşləri, selikli qışa, bağırsaq divarı, cərrahi sap

Ключевые слова: кишечник, морфометрия, L-аргинин, крипты, слизистая оболочка, кишечная стенка, хирургическая нить

Key words: intestine, morphometry, L-arginine, crypts, mucosa, intestinal wall, surgical thread

COMPARATIVE ASSESSMENT OF MORPHOMETRIC PARAMETERS OF STRUCTURAL ELEMENTS OF CRYPTS OF THE CECUM USING SURGICAL THREADS POLYGLACTIN-910 AND POLYCAPROLACTONE MODIFIED WITH L- ARGININE IN THE EXPERIMENT

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The article presents a research study conducted to comparatively examine the effects of synthetic absorbable polyglactin-910 sutures and a novel suture material, polycaprolactone modified with L-arginine (PCL-MA), on the morphometric parameters of the crypts in the mucosa of the cecum under experimental conditions.

Surgical interventions were performed on 65 sexually mature outbred domestic rabbits aged 9-10 months and weighing (2.62 ± 0.21) kg, which were divided into three groups: control and two experimental groups (the first one using PG-910 surgical thread and the second one using surgical thread PCL-MA). After the surgical intervention, the condition of the wound and the formed scar were studied on days 3, 7, 14, 21, 30, and 60. The morphometric method was used to analyze quantitative changes in the structural components of

crypts in the cecum's perivulnar area in the experiment's dynamics. Statistically, the reliability of these quantitative changes was established.

As a result of the study, it was found that when PCL-MA is used for suturing a wound defect, the functioning of the structural components of the crypts in the mucosa of the perivulnar area of the cecum is faster on average by 7 days than when using PG-910.

Introduction. An important and controversial issue in the surgical treatment of various nosological forms of large intestine diseases is the problem facing the surgeon in choosing a surgical suture material for surgical intervention directly on the intestine [1, 2]. Modern suture material should be bioinert. Its degradation should not cause a general toxic effect on the body, be resistant to infection, not cause an allergic reaction, be reliable, atraumatic, or not cause an absorbing or adhesive effect [3]. Most importantly, it should stimulate the healing process and not cause the formation of an excessive scar in the area of the wound defect caused by surgery. In addition, the suture material should have optimal manipulation and technical characteristics [4].

Absorbable sutures, such as polyglactin-910 (PG-910), meet these requirements and are widely used in surgical practice [5]. The newest Ukrainian suture material, polycaprolactone modified with L-arginine (PCL-MA) is a surgical suture bioabsorbable material intended for surgical operations in clinics, hospitals, ambulance services, and field conditions, which is very important today in the context of military operations in Ukraine. The addition of L-arginine or other substances with antihypoxic, reparative, and antioxidant properties plays an important role in reducing the systemic inflammatory response and oxidative-nitrosative stress and shortening the healing time of a postoperative wound [6, 7, 8].

PG-910 and PCL-MA are very similar in terms of their characteristics and resorption time, even though PG-910 is a polyfilament thread and PCL-MA is a monofilament thread [9, 10, 11]. Surgical thread polycaprolactone modified with L-arginine is a new stage in improving surgical suture material.

The aim of the study. To conduct a comparative analysis of the morphometric parameters of the structural elements of the crypts of the mucosa of the cecum in the experiment using synthetic absorbable threads polyglactin-910 and a new thread

polycaprolactone modified with L-arginine.

Material and methods. The experiment was conducted on 65 sexually mature outbred domestic rabbits (of different sexes) aged 9-10 months and weighing (2.62 ± 0.21) kg. The rabbits were kept in the vivarium of Poltava State Medical University, following sanitary and hygienic standards and rules. All stages were carried out in compliance with the principles of bioethics by the provisions of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986), Council of Europe Directive 2010/63/EU, Law of Ukraine No. 3447-IV "On Protection of Animals from Cruelty". According to the decision of the Biomedical Ethics Committee of Poltava State Medical University (Protocol No. 220 of 25.10.2023), no violations in handling laboratory animals were found.

Surgical interventions on animals were performed in the operating room of the Department of Anatomy with Clinical Anatomy and Operative Surgery of Poltava State Medical University.

The experimental animals were divided into three groups. The first was a control group (5 animals), the second was an experimental group (30 animals) in which the wound defect was sutured with synthetic polyfilament absorbable thread PG-910, the third experimental group (30 animals) was sutured with monofilament absorbable thread PCL-MA. The thread was used with an atraumatic needle, metric size - 3. The operation was performed according to our patented method of surgical intervention on the large intestine.

The cecum was dissected between the omental taenia and free taeniae of the intestine parallel to them and perpendicular to the haustrae, 3-4 cm long.

A two-row suture was applied to the cecum using different suture surgical materials. The first row of sutures was a continuous Schmidts suture. The second row was a Lambert serous nodular suture. This ensured the wound tightness, and during the subsequent collection of intestinal tissue for examination in due time, it allowed the obtainment of high-quality histological material with a research thread. The material was taken on days 3, 7, 14, 21, 30, and 60. Adequate methods were used in the experimental study: experimental – for surgical interventions on the large intestine (colotomy); histological - to determine the general morphology

of the wall of the cecum in the normal and perivulnar areas in the dynamics of the experiment; the method of semi-thin serial sections – to detail the histological structures of the intestinal wall; morphometric method – to analyze quantitative changes in the histocytotopography of the structural components of the crypts at different stages of the experiment; statistical method - to establish the reliability of quantitative changes in the structural components of the crypts in the dynamics of the experimental study.

To determine the main morphometric parameters, cecal biopsies were removed and embedded in paraffin and epoxy resin according to generally accepted methods. Thin sections of 4-5 μm were obtained from paraffin blocks stained with hematoxylin and eosin, according to van Gieson's method with Hart's poststaining. Semi-thin sections 1-2 μm thick were made from epoxy blocks and stained with methylene blue and toluidine blue. The sections were examined under a light microscope with a digital camera Olympus C 3040-ADU with programs adapted for these studies (Olympus DP-Soft, license No. VJ285302, VT310403, 1AV4U13B26802) and Vorex 3 (serial number 5604).

Morphometric parameters such as the depth of crypts and dynamic changes in the structural components of crypts of the large intestine mucosa, namely columnar enterocytes with a border, goblet cells, endocrinocytes and intraepithelial lymphocytes, were determined.

Statistical data processing was performed using Statistica 10, BiostatPro 6, and Microsoft Excel 2016. The reliability of the calculations and indicators of the samples was checked using the Shapiro-Wilk test. The arithmetic mean of the variation series (M) and its standard error (m) were determined to evaluate quantitative data. Student's t-test was used to compare quantitative values in paired series. The difference was considered significant at a value of $p < 0.05$.

Research results and their discussion. The studies found that the crypts of the rabbit cecum are a structural and functional unit of the cecum's mucosa and are represented by finger-like outgrowths. The crypts consist of the following main components: columnar enterocytes with a border, goblet cells, single endocrinocytes, and intraepithelial lymphocytes.

Changes in the histotopography of these components in relation to the surface layer of the mucosa begin to occur from day 3 of the experimental study. Thus, in the area of the wound defect, they were visualised deeper relative to the submucosa. When using PCL-

MA surgical thread, the mean crypt depth was $87.48 \pm 2.28 \mu\text{m}$, which is 5.35% less than PG-910 ($92.42 \pm 1.64 \mu\text{m}$).

After 7 days of experimental study, the depth of crypts using PCL-MA surgical thread was $89.34 \pm 2.32 \mu\text{m}$, which was 14.49% less compared to PG-910 ($104.48 \pm 3.12 \mu\text{m}$), after 14 days - significantly by 19, 62% (with $79.27 \pm 3.02 \mu\text{m}$ for PCL-MA and $98.62 \pm 3.26 \mu\text{m}$ for PG-910), after 21 days by 11.14% ($72.34 \pm 2.46 \mu\text{m}$ for PCL-MA and $81.41 \pm 2.26 \mu\text{m}$ for PG-910) and after 30 days by 3.71% ($78.68 \pm 2.26 \mu\text{m}$ to $81.71 \pm 2.84 \mu\text{m}$, respectively). This indicator was statistically significant, at $p < 0.05$, and reached control values after 30 days of the experiment when using PCL-MA surgical thread. When using the PG-910 thread, this trend was determined after 60 days of observation (**Figure 1**).

Thus, it can be argued that the functioning of the crypts of the mucosa of the perivulnar area of the cecum is faster on average by 7 days when using PCL-MA than when using PG-910 suture.

It was found that the histotopography of crypts directly depends on quantitative changes in the population of its cellular components. Thus, the average number of absorptive enterocytes decreased sharply after 3 days of the experimental study. However, when PCL-MA surgical thread was used, this indicator was 3.12 ± 0.24 , which was 16.57% less than that of PG-910 (3.74 ± 0.24).

On the 7th day of the experiment, the mean number of these cells was 13.57% lower with PCL-MA surgical thread (3.44 ± 0.32) compared to PG-910 (3.98 ± 0.32), after 14 days - significantly by 21.93% (with 4.52 ± 0.26 for PCL-MA and 5.79 ± 0.36 for PG-910), after 21 days – by 21.11% (6.28 ± 0.28 for PCL-MA vs. 7.96 ± 0.42 for PG-910) and after 30 days – by 11.35% (10.62 ± 0.46 and 11.98 ± 0.31 , respectively). The control value of the number of absorptive enterocytes was statistically significant at $p < 0.05$ when using PCL-MA suture on day 30 of the experiment. When using PG-910 suture, it was determined after 60 days of observation (**Figure 2**). The obtained results of the experimental study demonstrate the positive effect of L-arginine on the processes of destruction of absorptive enterocytes in the crypts.

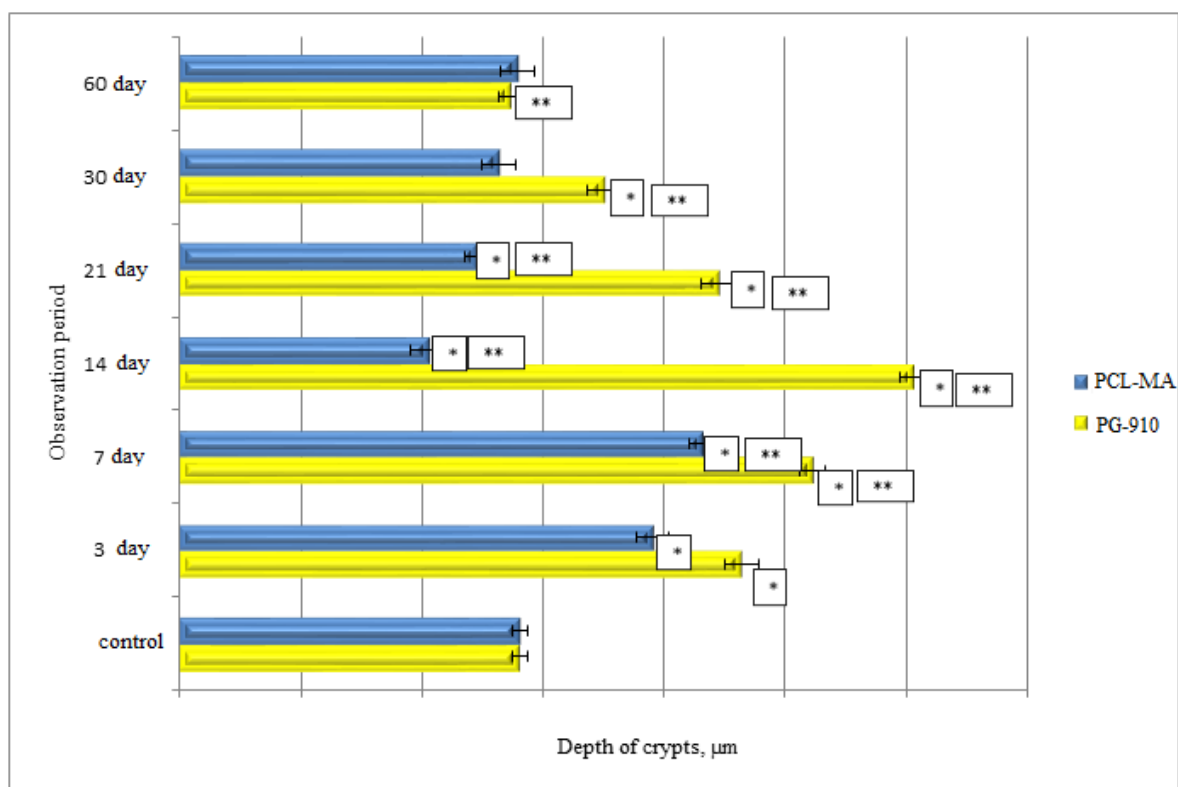


Figure 1. Morphometric characteristics of changes in the mean depth of crypts in the perivulnar area of the mucosa of the rabbit cecum during suturing of the wound defect with surgical threads PG-910 and PCL-MA in the dynamics of the experimental study. Notes: * – $p < 0.05$ compared to the control group, ** – $p < 0.05$ compared to the previous term of the experimental study.

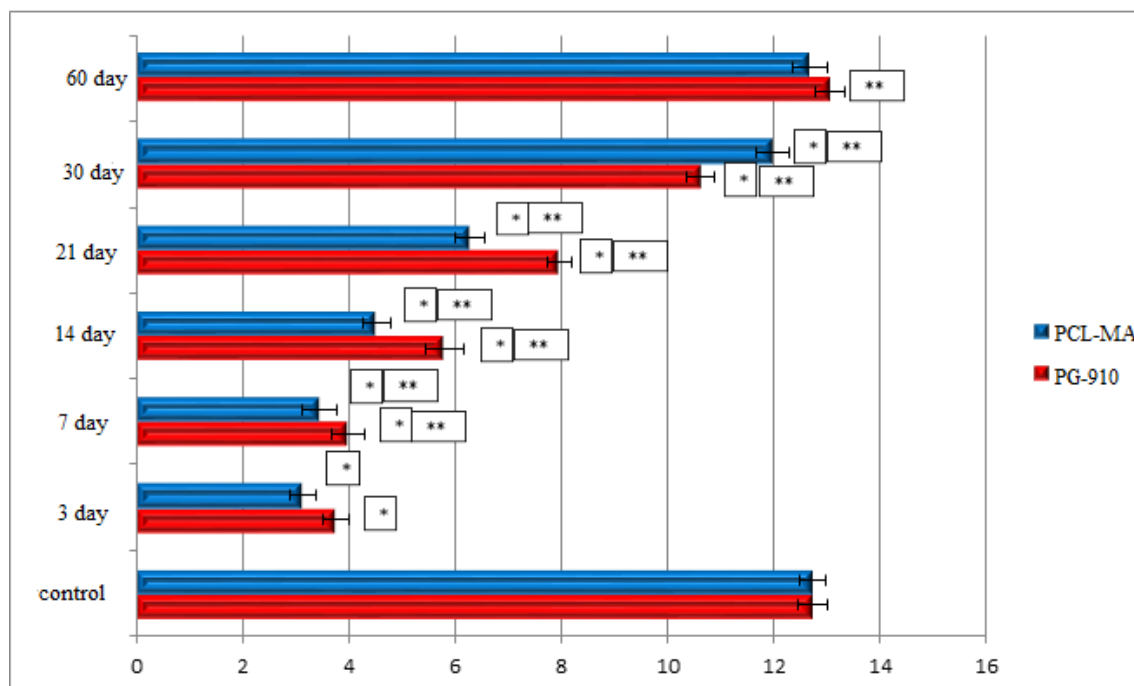


Figure 2. Morphometric characteristics of changes in the mean number of absorptive enterocytes in the crypts of the perivulnar area of the mucosa of the rabbit cecum during suturing of the wound defect with surgical threads PG-910 and PCL-MA in the dynamics of the experimental study (mean number in 10 fields of view). Notes: * – $p < 0.05$ compared to the control group, ** – $p < 0.05$ compared to the previous term of the experimental study.

The study of changes in the mean number of goblet cells in the crypts of the perivulnar area of the mucosa of the cecum showed that after 3 days, their mean number decreased sharply. But when using PCL-MA surgical thread, this indicator became $72,62 \pm 4,12$ and was 17,71% less than when using PG-910, which was equal to $88,24 \pm 4,12$. After 7 days, the mean number of goblet cells when using PCL-MA surgical thread became $86,24 \pm 4,41$, which is 14,48% less in comparison with PG-910 ($100,84 \pm 4,41$); after 14 days – significantly by 9.61% (68.36 ± 3.12 vs 75.63 ± 3.12), after 21 days - by 15.75% (56.64 ± 3.41 vs 67.23 ± 3.41) and after 30 days - by 15.95% (42.38 ± 3.68 vs 50.42 ± 3.68). This indicator reached control values on day 30 when using the PCL-MA suture and after 60 days when using the PG-910 suture (**Figure 3**).

As a result of the study, it was found that enteroendocrine cells in the crypts of the

mucosa of the cecum are of great importance in the reparative processes of the wound area. It was found that after 3 days of the experiment, their mean number decreased sharply, but when using PCL-MA surgical thread, this indicator was equal to 1.86 ± 0.08 , which is 23.46% less than when using PG-910 (2.43 ± 0.08). After 7 days, the mean number of enteroendocrine cells was 21.4% less with PCL-MA surgical thread (2.24 ± 0.06) compared to PG-910 (2.85 ± 0.06); after 14 days - by 12.5% (3.08 ± 0.08 vs 3.52 ± 0.08), after 21 days - by 21.19% (2.12 ± 0.09 vs 2.69 ± 0.09) and after 30 days - by 6.52% (0.86 ± 0.08 vs 0.92 ± 0.06). This indicator statistically significantly (at $p < 0.05$) reached the control values when using PCL-MA surgical thread after 30 days of the experiment and PG-910 one after 60 days of observation (**Figure 4**).

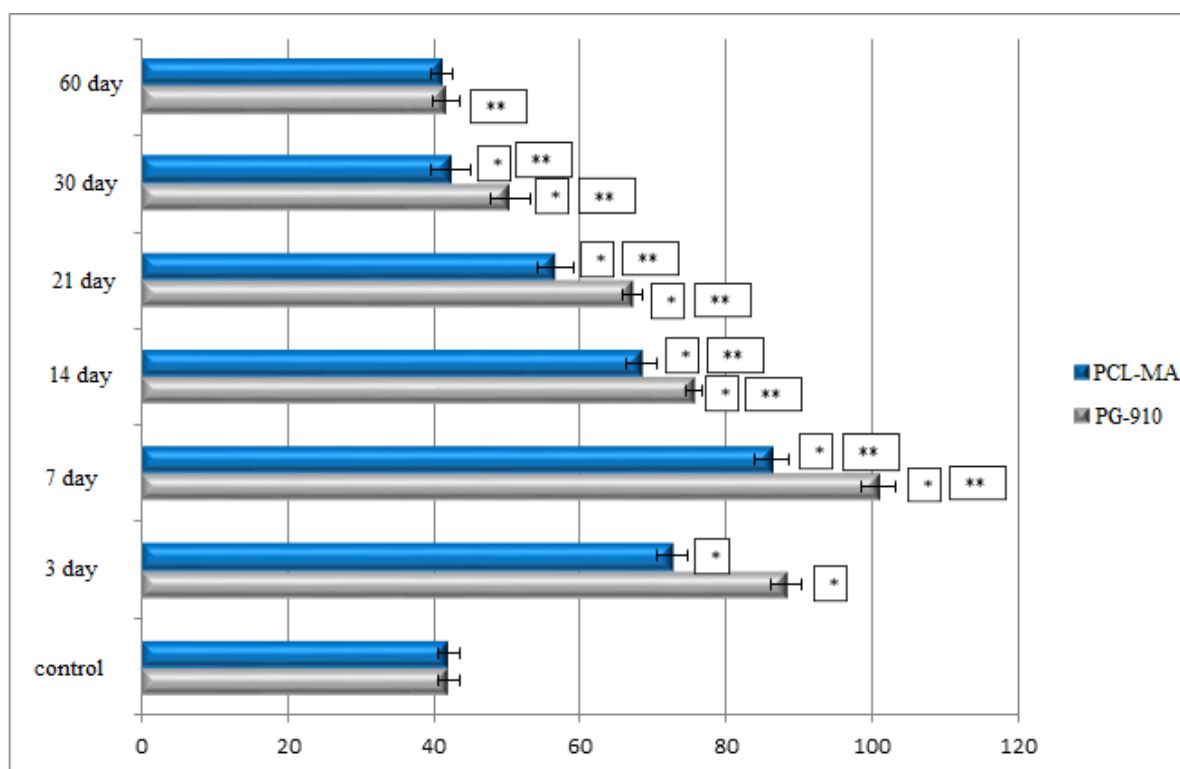


Figure 3. Morphometric characteristics of changes in the mean number of goblet cells in the crypts of the perivulnar area of the mucosa of the rabbit cecum during suturing of the wound defect with surgical threads PG-910 and PCL-MA in the dynamics of the experimental study (mean number in 10 fields of view). Notes: * – $p < 0.05$ compared to the control group, ** – $p < 0.05$ compared to the previous term of the experimental study.

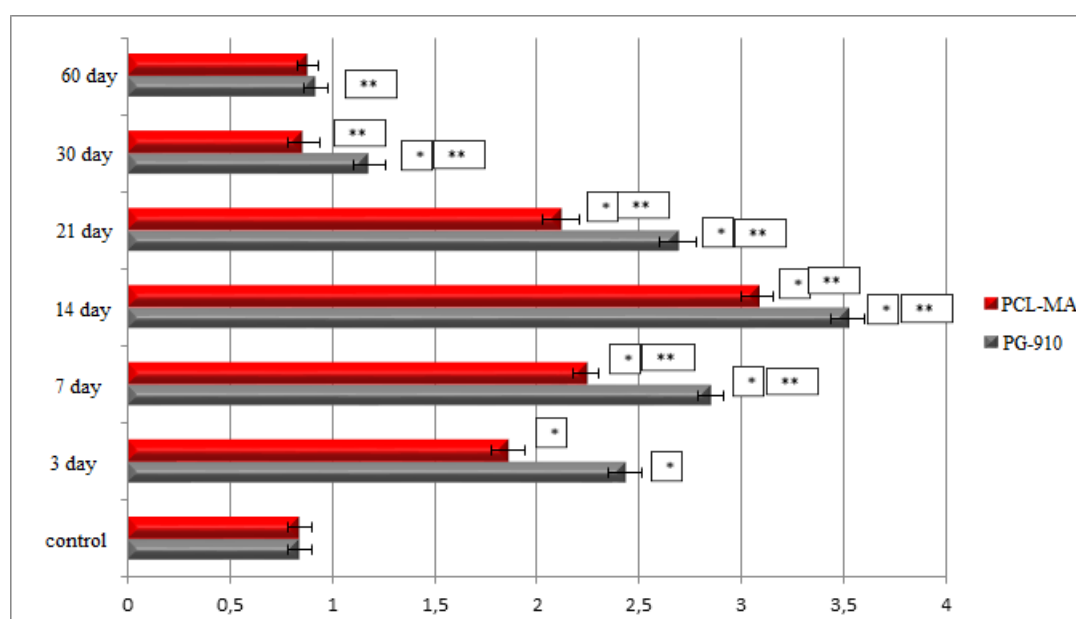


Figure 4. Morphometric characteristics of changes in the mean number of enteroendocrine cells in the crypts of the perivulnar area of the mucosa of the rabbit cecum during suturing of the wound defect with surgical threads PG-910 and PCL-MA in the dynamics of the experimental study (mean number in 10 fields of view). Notes: * – $p < 0.05$ compared to the control group, ** – $p < 0.05$ compared to the previous term of the experimental study.

Conclusions. Thus, the morphometric analysis of the processes of remodelling the structural components of the crypts of the mucosa of the cecum in the perivulnar area using PG-910 surgical thread and PCL-MA

surgical thread proved the positive effect of PCL-MA one on the reparative processes in the area of the wound defect, accelerating them by an average of 7 days.

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СРАВНИТЕЛЬНАЯ ОЦЕНКА МОРФОМЕТРИЧЕСКИХ ПАРАМЕТРОВ СТРУКТУРНЫХ ЭЛЕМЕНТОВ СЛЕПОЙ КИШКИ ПРИ ИСПОЛЬЗОВАНИИ ХИРУРГИЧЕСКИХ НИТЕЙ ПОЛИГЛАКТИН-910 И ПОЛИКАПРОЛАКТОН, МОДИФИЦИРОВАННЫЙ L-АРГИНИНОМ В ЭКСПЕРИМЕНТЕ

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Резюме. В статье представлены результаты исследования, проведенного с целью проведения сравнительного анализа морфометрических параметров структурных элементов крипт слизистой оболочки слепой кишки в эксперименте с использованием синтетических рассасывающихся нитей полиглактин-910 и нового шовного материала поликапролактон, модифицированный L-аргинином (PCL-MA).

Хирургические вмешательства выполнены 65 половозрелым беспородным домашним кроликам в возрасте 9-10 месяцев и массой $2,62 \pm 0,21$ кг, которые были разделены на три группы: контрольную и две экспериментальные (первая из них – с использованием хирургической нити полиглактин-910 и вторая – с использованием хирургической нити поликапролактон, модифицированный L-аргинином). После операции изучалось состояние раны и образовавшегося рубца на 3, 7, 14, 21, 30 и 60 суток. Морфометрический метод был использован для анализа количественных изменений структурных компонентов крипт в перивульнарной области слепой кишки в динамике эксперимента. Достоверность этих количественных изменений была статистически подтверждена.

В результате проведенных исследований установлено, что при использовании модифицированной L-аргинином хирургической нити для ушивания раневого дефекта функционирование структурных компонентов крипт в слизистой оболочке перивульнарной области слепой кишки происходит раньше в среднем на 7 дней, чем при использовании хирургической нити полиглактин-910.

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