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EXPERIMENTAL INVESTIGATION OF THE EFFECTIVENESS OF LOCAL APPLICATION OF A COMBINATION OF ANTISEPTIC AND ANESTHETIC ON THE MODEL OF CONTAMINATED WOUND

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Annotation. *A high risk of infections in surgery is associated with microbial contamination with opportunistic microorganisms Staphylococcus aureus. Objective: to study the antimicrobial and analgesic effect of decamethoxine combined with lidocaine applied locally to the model of a postoperative infectious wound. Fifty-two male rats weighing 250-300 grams were randomly divided into four groups. We modeled surgical wounds in the interscapular area, and then injected a suspension culture of S. aureus 47 (dose 108 CFU/ml) into the wounds. On the 2nd, 3rd, 7th and 10th day of the experiment, the wounds contaminated with staphylococcal culture were treated with 3 ml doses of the tested drugs: 0,9% saline in the control group (group A, n=13), 0,02% decamethoxine antiseptic (DCM) (group B, n=13), 10% lidocaine (group C, n=13) and their combination in the 1:1 ratio (group D, n=13). On days 3, 7 and 10, the wound area in each group was determined using contour planimetry by the L.N. Popova method and the average area (M±m) and the percentage of reduction in wound area from the initial size were calculated. The antimicrobial efficacy of the antiseptic and anesthetic was evaluated on days 3, 5, 7 and 10 using a standard microbiological study of the number of microorganisms in the wounds, the numerical values of which were expressed as the decimal logarithm of colony-forming units per ml (lg CFU / ml). To study the analgesic activity of DCM and 10% lidocaine in animals, the minimum threshold of pain sensitivity in the wound was determined using calibrated Von Frey monofilaments (VFMs). Statistical processing was performed using standard biometric methods. Differences at p<0.05 were considered significant. Results: As a result of microbiological examination of the wound surface, it was found that the number of S. aureus on the wound surface significantly decreased on the 5th day when using decamethoxine alone and in combination with lidocaine 10%. The use of antiseptic and its combination with lidocaine on the 10th day revealed almost complete eradication of S. aureus on the wound surface compared to the control group (p<0.01). When applying the combined antiseptic with lidocaine, it was found that the threshold of pain sensitivity increased by 12.2 times, which was practically no different from that of lidocaine monotherapy (11.9%). It was found that the healing and wound epithelization rate was the highest in group D (71.12% of the baseline). So, the combination of antiseptic with lidocaine 10% in the treatment of wounds has a high antimicrobial efficacy with a pronounced anesthetic effect. Thus, it opens the prospect of combined local use of antiseptic and anesthetic in the treatment of wounds.*
Keywords: *surgical wounds, antiseptics, local anesthetics, Staphylococcus aureus.*

Introduction

Despite significant progress in wound care, infectious complications and pain response to surgical stress and associated physiological changes can lead to postoperative complications and adversely affect wound healing and patient rehabilitation [4, 6]. Postoperative infectious complications remain the main cause of mortality, prolongation of treatment and worsening of the economic situation in millions of wounded patients worldwide [6, 7, 11]. According to international data, problems of treatment of infectious complications and pain syndrome remain even where antimicrobial and analgesic agents are available [3, 22].

Pain and infection are common links in the same pathological process. Until recently, it was believed that pain is secondary to inflammation caused by the penetration of pathogens. However, the discovery of the phenomenon of direct activation of nociceptor neurons by microbial pathogens has shown the important role of this interaction in the formation of pain in infection [4]. To prevent complications and improve the effectiveness of treatment of wound infections, antimicrobial agents of different groups are usually used [3, 7, 8, 11]. Highly effective bactericidal activity and the ability to reduce the effect of hyperalgesia are considered to be important requirements for such agents [19]. It is also known that the analgesic effect of local anesthetics helps to reduce nociceptive impulses from the wound and improves the course of the wound process [15]. Therefore, the study of the combined use of local anesthetics with antiseptics is relevant and promising. According to international studies, local anesthetics have antimicrobial properties against a wide range of human pathogens [12, 19, 20].

A thorough understanding of the phases of the wound process that are triggered in the patient's body after infection is crucial to developing new treatments. Experimental models are a standard approach to studying a wide range of external traumatic wound infections [5, 6].

The aim is to investigate the antimicrobial and analgesic effect of decamethoxine in combination with lidocaine at their local application on the model of a contaminated skin wound in rats.

Materials and methods

The study was conducted at National Pirogov Memorial Medical University, Vinnytsya. The antimicrobial and analgesic efficacy (AE) under conditions of hyperalgesia development on the model of primary contaminated skin wound was evaluated by using preparations based on 0.02% decamethoxine (Decasan, registration certificate № UA/ 5364/01/01 of 22.12.2016, manufactured by "Yuria-Pharm" LLC, Ukraine), 10% lidocaine (lidocaine 10 mg/ml, registration certificate No. UA/15384/01/01 of 19.08.2016, manufacturer JSC "Lekhim-Kharkiv", Ukraine) and their combination.

Experimental studies were conducted on 52 white nonlinear male rats (average weight - 253.2±3.401 g). The animals were previously kept in quarantine for 10 days. When handling animals, the requirements of the "European Convention for the Protection of Vertebrates" (Strasbourg, 1986) were observed. The experimental animals were kept in vivarium conditions with free access to food and water. Ethical approval for this study (Ethical Committee Protocol № 2, 02.03.2020) was provided by the Ethical Committee of the National Pirogov Memorial Medical University, Vinnytsya, Ukraine.

The animals were divided into 4 groups of 13 in each group (Table 1). Simulation of the experimental wound was performed under anesthesia (ketamine - 25 mg/kg, intraperitoneally). Wounds (1x1 cm in size) were applied in the interscapular area by dissection of the skin and subcutaneous fat layer after previous epilation, the operative field was treated with decamethoxine. On the first day of the experiment, 1 ml of S. aureus ATCC 25923 culture suspension (dose 108 CFU/ml) obtained from the museum of live cultures of the bacteriological laboratory of the Department of Microbiology of National Pirogov Memorial Medical University, Vinnytsya was injected to model a purulent wound. After that, 2 knot sutures were applied, an additional gauze napkin impregnated with staphylococcal culture was applied on top of the wound surface and the wound was closed for one day with a plastic film, which was fixed with adhesive tape [5].

On the 2nd, 3rd, 7th and 10th day of the experiment, the wounds contaminated with staphylococcal culture were treated with 3 ml doses of the test drugs: saline in the control group (group A, n=13), the wound was locally treated with the antiseptic decamethoxine (group B, n=13), in group C (n=13) the wounds were treated with the local anesthetic lidocaine 10%; and in group D (n=13) the wound was treated with a combination of 0.02% decamethoxine and 10% lidocaine in a ratio of 1:1. In all experimental animals, wound healing occurred by secondary tension, on days 3, 7 and 10, the wound area in each group was determined using contour planimetry by the method of L.N. Popova, the average area (M±m) and the percentage of reduction of the wound area from the initial size were calculated by the formula:

$V= ((S_0-S_t)/S_0) \times 100$,

where V - is the wound healing rate (%), S_0 - is the maximum wound area per group (mm^2), and S_t - the wound area on the day of measurement (mm^2) [25].

To avoid infection, swabs were taken from the wound surface before any procedure. The antimicrobial efficacy of the antiseptic and anesthetic was evaluated on days 3, 5, 7 and 10 using a standard microbiological study of the number of microorganisms in the wounds, the numerical values of which were expressed as the decimal logarithm of colony-forming units per ml (lg CFU/ml) [17, 18]. Animals were withdrawn from the experiment on day 10 by an overdose of ketamine anesthesia according to generally accepted principles.

To study the analgesic activity of DCM and 10% lidocaine in animals, the minimum threshold of pain sensitivity in the wound was determined using calibrated Von Frey monofilaments (VFMs). The pressure was applied to the skin with a force of 2 g (4.31) to 100 g (6.1) (Touch-Test Sensory Evaluator, North Coast Medical Inc., CA, USA), pressing the monofilaments in ascending order to the skin surface at an angle of 90°, between the studies an adaptation interval of 10 s was maintained. The "vocalization of pain" in rats, when pressed, was recorded as the smallest pressure force that caused a painful reaction of the rat on day 1 of the experiment before the procedure on a healthy skin area (in the interscapular area of the back); immediately after wounding; 15 minutes after the start of local treatment; on days 2, 3, 7 and 10.

Statistical data processing was performed using computer programs Microsoft Excel 2013, Statistica 6.0, and the reliability of differences was assessed at the level of significance $p \leq 0.05$ [24].

This study is part of a scientific projects Department of Microbiology, National Pirogov Memorial Medical University, Vinnytsya, Ukraine "Experimental clinical study of the multi-vector properties of antimicrobial agents using their directed transport" (№ 0110U006916) and "Research of the biological properties of pathogens of healthcare-associated infections and the development of combating them" (№ 0123U101070).

Table 1. Distribution of experimental animals by groups, depending on local therapy.

Groups	The test drugs	Microbial strains	Number of experimental animals
A (control)	0.9% saline	*S. aureus ATCC 25923*	13
B (test)	0.02 % decamethoxine	*S. aureus ATCC 25923*	13
C (test)	10 % lidocaine	*S. aureus ATCC 25923*	13
D (test)	0.02 % decamethoxine + 10 % lidocaine (1:1)	*S. aureus ATCC 25923*	13

Results

As a result of the microbiological investigation of the wound surface on the 3rd day after infection, no significant

differences in the colonization of wounds with Staphylococcus aureus were observed in the experimental groups of animals, and on average were determined within 106 CFU/ml. For convenience, the data were expressed according to the well-known method through the decimal logarithm of the number of colony-forming units (lg CFU/ml) (Table 2).

On the fifth day, the decrease in the number of CFU/ml of S. aureus on the surface of wounds treated with DCM and a combination of DCM with 10% lidocaine (1:1 ratio) was determined. It was found that the microbial colonization of wounds in groups B and D was 2.815±0.116 lgCFU/ml and 4.43±0.21 lgCFU/ml, respectively, which was significantly less than in the control group (A) 6.52±0.18 CFU/ml and in group C (10% lidocaine) 5.36±0.23 lgCFU/ml ($p<0.05$) (Table 2).

A significant advantage in reducing microbial colonization with Staphylococcus aureus was on the 7th day of observation in group B, where almost complete eradication of S. aureus was established. In group D, there was a 2 times decrease in the level of microbial contamination, and in experimental groups A and C there was a 1.3-1.4-times decrease in microbial contamination with Staphylococcus aureus, less than the critically acceptable level of 106 CFU / ml, an average of 3.55±0.23 lgCFU / ml in these groups of the study ($p<0.01$) (Table 2).

On the tenth day, with the local use of dressings impregnated with decamethoxine and its combination with lidocaine 10%, the growth of microorganisms was not determined, and in the control group and group C a decrease in microbial contamination of S. aureus to 3.280±0.190 and 2.09±0.08 lgCfu/ml, respectively ($p<0,01$) (Table 2).

In the investigation of the threshold of pain sensitivity, before the experiment threshold of pain sensitivity was measured for control on a healthy area of the body in all groups of animals and found almost the same, which was 90.74±3.760 g/mm2. After wounding, the threshold of pain sensitivity was also almost the same in all experimental animals and was 3.95±5.48 g/mm^2. After the start of wound treatment, it was found that in control group A and in group B, where the treatment was carried out only with decamethoxine solution immediately after treatment and after 72 hours of the experiment, the threshold of pain sensitivity remained the lowest, compared to the first day of the experiment, the indicators increased only 1.7 and 2.1 times, respectively ($p<0.05$) (Table 3).

The use of 10% lidocaine in the wound (group C) after the start of treatment led to a pronounced analgesic effect, which was confirmed by an increase in the threshold of pain sensitivity by 15.48 times compared to the data before treatment ($p<0.05$). But after 72 hours, the analgesic effect persisted and was 8.19 times greater compared to groups A and B ($p<0.05$). The use of 10% lidocaine in combination with 0.02% decamethoxine led to a similar effect and an increase in the mechanical threshold of pain sensitivity by 13.9 times on the first day of treatment compared to groups A and B ($p<0.05$). In the first 72 days, the analgesic effect in groups C and D was almost the same, on the third day in group D the analgesic effect was 1.1 times higher compared to group C ($p>0.05$) (Table 3).

On the seventh day in the control group the threshold of pain sensitivity remained low and increased compared to the third day by only 1.7 times ($p<0.05$), in group B the threshold was higher compared to the control group by 3.28 times and compared to the third day by 4.23 times ($p<0.001$). The best analgesic effect was in group D, where the threshold of pain sensitivity increased by 6.6 times compared to the control group and in group C, where the analgesic effect was 6.18 times greater than in the control group

Table 2. Dynamics of microbial colonization of the wound with S. aureus (lg CFU/ml; M±m).

Groups	3rd day	5th day	7th day	10th day
A (control)	6.106±0.091	6.520±0.180	3.709±0.120	3.280±0.190
B (test)	5.782±0.096*	2.815 ±0.116 **	0.636±0.083 ***	0***
C (test)	6.186±0.124*	5.368±0.239**	3.357±0.933 ***	2.098±0.082***
Д (test)	5.653±0.122*	4.435±0.211**	2.475±0.218***	0***

Notes: M - mean value of CFU/ml in the wound; m - standard deviation of the mean; *p>0.05; **p<0.05; ***p<0.01 - compared to the control group (A).

Table 3. Mechanical threshold of pain sensitivity in rats during local wound treatment with antiseptics and local anesthetics.

Groups	Mechanical threshold of pain sensitivity. g/mm^2 (M±m)						
№	intact skin area	first day (after the incision)	1st day (15 min. after the start of treatment)	2nd day	3rd day	3rd day	10th day
A (control)	90.67±8.801	4.003±2.402	4.901±3.120	6.902±4.562	7.384±8.221	12.69±3.541	36.46±6.344
B	87.69±4.541	4.307±1.040	4.674±1.411	79.25±2.404	9.846±1.285	41.69±5.644	84.61±7.105
C	93.84±1.843	3.692±3.442	58.48±4.802	75.38±4.620	67.69±6.670	81.48±5.860	90.76±4.411
D	90.76±6.540	3.846±4.363	60.07±4.452	67.07±1.471	76.30±7.290	84.61±4.791	93.84±2.542

Notes: M - mean value of skin pressure of Von Frey monofilaments, in g/mm^2; m - standard deviation of the mean p>0.05 - compared to the control group (A).

Table 4. Changes in the area of contaminated wounds in rats after local wound treatment.

The day of research	Wound area. mm² (M±m)			
	Group A (Control)	Group B	Group C	Group D
Initial data (1st day)	78.5	78.5	78.5	78.5
3rd day	71.14±8.701	59.45±4.311	60.19±5.810	53.65±8.812
7th day	62.61±6.810	39.65±2.449	44.02±3.704	39.70±3.710
10th day	48.48±4.650	32.21±3.481	26.00±2.341	22.67±2.830

Notes: M - mean change in wound area in mm²; m - standard deviation of the mean p>0.05 - compared to the initial data.

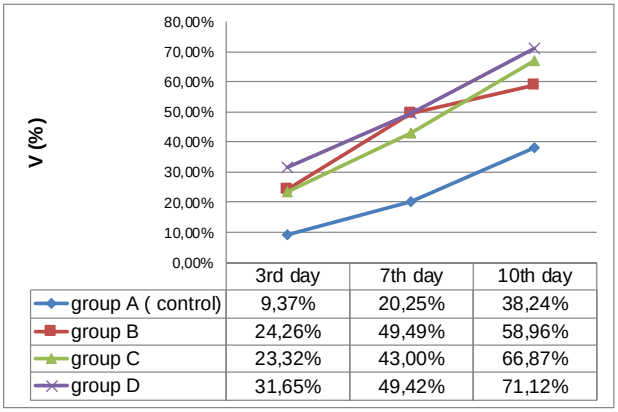

Fig. 1. The rate of healing of contaminated wounds in rats on the background of local treatment (V(%) - wound healing rate).

(p>0.05).On the tenth day of the experiment in groups C and D the threshold of mechanical pain sensitivity was comparable to the data collected before the experiment, group B also had a high threshold of pain sensitivity, only 0.9 times lower than in the healthy area in the same group, the control group had the lowest index, the level of mechanical pain sensitivity was 2.4 times lower than before the experiment (p<0.05) (Table 3).

According to the above terms, we determined the wound area and the dynamics of its change in each group of animals. Observations showed that in each group of animals on the third day there was an active inflammatory process, the edges of the wound were roller-shaped, swollen, the wound was covered with hemorrhagic crusts, the bottom was hyperemic. These signs were the most pronounced in animals of the control group (A).

In the following periods of observation, significant changes in the condition of wounds and the course of healing were determined. On the seventh day, the wound area in animals treated locally with decamethoxine (group B) and a combination of decamethoxine with 10% lidocaine (group D) significantly decreased by 49.49% and 49.42% of the initial data, respectively, the wound edges were tightly adjacent to the bottom of the wound, where the granulation process began. Further wound healing in all groups was characterized by the formation of granulation tissue and the beginning of wound epithelialization from the edges. The processes of epithelization were much more active in the groups where decamethoxine was used locally (groups B and D). On the 10th day, the wound condition was characterized by further epithelialization from the edges and, accordingly, a decrease in the wound area.

In the control group, wound healing processes were slower by 38.24% of the initial data. The expressed positive changes were found in the wound area in animals of experimental groups B and D, in the treatment of which decamethoxine solution was used, consisted in the fact that they had a small clean oval-extended wound in the middle of the modeling area of the primary wound. On the 10th day, the wounds in the control group were much larger, and in group C they slightly decreased compared to the control by 46.36%. The best result of healing and the process of wound epithelization was found in group D (71.12% of the initial indicators). The reduction in wound size and the final healing time indicated the speed of regeneration processes (Table 4, Fig. 1).

Discussion

To date, there are no clear recommendations for the local use of antimicrobial drugs in the wound, which don't belong to antibiotics [1]. Treatment protocols and recommendations are mainly focused on reducing the use of antibiotics for the treatment of infections, to reduce antibiotic resistance and mandatory identification of infectious agents by culture of wound materials and tissue biopsy of infected tissues [9, 14]. Therefore, short-term topical antimicrobial antiseptic therapy for an uncertain infectious status of wounds is currently being widely studied, as well as the search for possible ways to optimize antimicrobial tactics in infected wounds to reduce the routine use of antibiotics.

In our investigation, we simulated a purulent wound by introducing 1 ml of S. aureus ATCC 25923 suspension. The wound was treated with the antiseptic decamethoxine 0.02%, the anesthetic 10% lidocaine, and their combination before suturing and dressing the wounds with the application of antiseptic dressings impregnated with these solutions. According to the results, the best indicator of perioperative pathogen eradication was when using decamethoxine antiseptic. Thus, on the 5th day of the study, the number of CFU/ml was two times less compared to the control group, and on the 10th day, complete eradication of the pathogen was noted. The obtained data correlate with the data of the literature, which showed a high antimicrobial effect of decamethoxine on gram-positive opportunistic microorganisms [9, 21].

As for the local anesthetic lidocaine, there is evidence that in addition to analgesic and anti-inflammatory effects, the drug has antimicrobial properties [16]. Thus, according to scientific sources of literature, in the study of in vitro bactericidal and bacteriostatic properties of lidocaine by adding a suspension containing 105 colony-forming units of bacteria to different concentrations of lidocaine (1%, 2%

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and 4%, 10%), it was studied that the drug has bactericidal and moderate bacteriostatic properties against common pathogens of intraoperative infectious complications, such as S. aureus, E. faecalis, and even P. aeruginosa [2, 13, 23, 26].

It was found that the antibacterial effect was evident during the first two hours, but the maximum effect was achieved up to eight hours. Therefore, scientists recommend using lidocaine in high concentrations to achieve maximum antibacterial effect [22, 23, 25]. According to our study, when using 10% lidocaine for wound irrigation in the first days of observation, the number of CFU / ml was practically the same as in the control group, but the level of microbial contamination with Staphylococcus aureus decreased below the critical level of 106 CFU / ml. The best effect from the use of 10% lidocaine was on the 7th day of observation, when microbial contamination decreased by 1.3 times, in contrast to the control group ($p>0.05$). When 0.02% DCM solution (1:1 ratio) was added to the anesthetic, the level of microbial contamination was 2 times lower than in the control group.

In addition to the treatment of the infectious process in the perioperative period, the treatment and prevention of pain is important. Today there is no ideal analgesic or method of treatment for acute postoperative pain [15]. Therefore, all over the world, in the search for ways to solve the problem of adequate analgesia, the concept of multimodal analgesia is used, which involves the simultaneous administration of two or more analgesics and/or analgesia methods with different mechanisms of action, which allows to achieve adequate analgesia and reduce the risk of side effects [8].

The investigation showed that the use of local anesthetic for wound rehabilitation significantly reduced the level of pain sensitivity in animals in the study of the minimum threshold of pain by Von Frey monofilaments. And the combination of anesthetic with antiseptic decamethoxine had both analgesic effect and accelerated the eradication of the pathogen in the wound.

Indicators of wound healing rate were relative and made it possible to characterize the dynamics of the wound process regardless of the difference in the size of the wound areas. Observations of the wound healing process showed that starting from the 3rd day of the experiment, the wound area in all groups decreased, but the best result was achieved using 0.02% decamethoxine and its combination with 10% lidocaine.

Thus, against the background of the treatment, the wounds in the experimental animals were cleared and epithelialized faster, on the 10th day of the study a significant decrease in wound area (58.96% and 71.12%) was found in groups B and D. In rats that did not receive treatment, healing was slower. The data of the study are confirmed by a number of scientific papers, which indicate that the treatment of infected wounds with the antiseptic decamethoxine reduces the time to healing of surgical wounds by secondary tension and the drug has no cytotoxic properties on host cells compared to other antiseptics [19, 20, 21].

Local anesthesia intraoperatively can significantly reduce the need for opioids, and their combination with antiseptics can improve the antimicrobial effect and reduce the use of antibiotics [23]. Different mechanisms of action of these drugs allow them to be prescribed in combination and in low doses to achieve a significant analgesic and antimicrobial effect [11], which makes it possible to propose the use of a combination of antiseptics with anesthetics in clinical practice.

Conclusions and prospects for further development

1. The use of antiseptic decamethoxine and dressings impregnated with antiseptic reliably provide early eradication of S. aureus in pre-contaminated wounds, which creates favorable conditions for accelerating wound healing ($p<0.05$). Simultaneous use of decamethoxine with local anesthetic provides an additional analgesic effect.

2. A distinct wound healing efficacy was found, 11.6% higher than the control group in the local treatment of contaminated wounds in rats with the antiseptic decamethoxine in combination with the local anesthetic lidocaine.

3. Based on the total indicators of our investigation, the combination of anesthetic and antiseptic in their local application in the perioperative period best provides prevention of pain and infectious complications, which requires further detailed study.

Prospects for further research - the development of complex drugs for certain phases of the wound process, which will simultaneously affect several factors of pathogenesis.

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ЕКСПЕРИМЕНТАЛЬНЕ ДОСЛІДЖЕННЯ ЕФЕКТИВНОСТІ МІСЦЕВОГО ЗАСТОСУВАННЯ КОМБІНАЦІЇ АНТИСЕПТИКА З АНЕСТЕТИКОМ НА МОДЕЛІ КОНТАМІНОВАНОЇ РАНИ

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Анотація. *Високий ризик розвитку інфекцій в хірургії пов'язаний з мікробною контамінацією умовно-патогенними мікроорганізмами Staphylococcus aureus. Мета дослідження - дослідити антимікробну та знеболювальну дію декаметоксину в комбінації з лідокаїном при їх місцевому застосуванні на моделі контамінованої рани шкіри у щурів. П'ятдесят два щури-самці масою 250-300 грамів були рандомізовано розподілені на чотири групи. У міжлопатковій ділянці були змодельовані хірургічні рани та внесений завис культури S. aureus 47 (доза 108 КУО/мл). На 2, 3, 7 та 10 добу експерименту контаміновані культурою стафілокока рани обробляли дозами досліджуваних препаратів по 3 мл: фізіологічного розчину в контрольній групі (група А, n=13), антисептика декаметоксину (ДКМ) 0,02% (група В, n=13), 10% лідокаїну (група С, n=13) та їх комбінації у співвідношенні 1:1 (група D, n=13). На 3, 7 та 10 добу визначали площу рани в кожній групі за допомогою контурної планіметрії за методом Л.Н. Пономарьової, вираховували середню площу (M±m) та відсоток зменшення площі рани від початкового розміру. Оцінку протимікробної ефективності антисептика та анестетика проводили на 3, 5, 7 та 10 добу за допомогою стандартного мікробіологічного дослідження кількості мікроорганізмів у ранах, числові значення яких виражали через десятковий логарифм колонієутворюючих одиниць у мл (lg КУО/мл). Для вивчення аналгетичної активності ДКМ та*

10% лідокаїну у тварин визначали мінімальний поріг больової чутливості в рані за допомогою каліброваних монофіламентів Вон-Фрея (VFMs). Статистичну обробку проводили за допомогою стандартних біометричних методів. Вірогідними вважали відмінності при p<0,05. У результаті мікробіологічного дослідження ранової поверхні встановлено, що кількість S. aureus на поверхні ран достовірно зменшувалась на 5 добу при застосуванні декаметоксину та його комбінації з 10% лідокаїном. Застосування антисептика та його комбінації з лідокаїном на 10-ту добу виявило практично повну ерадикацію S. aureus на поверхні рани порівняно з контрольною групою (p<0,01). При застосуванні комбінованого антисептика з лідокаїном встановлено, що поріг больової чутливості підвищився у 12,2 рази, що практично не відрізнялося від такого при монотерапії лідокаїном (11,9%). Отже, встановлено, що швидкість загоєння та процесу епітелізації ран були найкращими в групі D (71,12% від вихідних показників). Поєднання антисептика з лідокаїном 10% при лікуванні ран супроводжується однаково високою антимікробною ефективністю з вираженим анестезуючим ефектом, що відкриває перспективу їх комбінованого місцевого застосування.

Ключові слова: *хірургічні рани, антисептики, місцеві анестетики, золотистий стафілокок.*