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PROSPECTS FOR THE USE OF SILVER PREPARATIONS FOR THE LOCAL TREATMENT OF WOUND INFECTION

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Abstract
Cytomorphological studies have revealed that a differentiated approach with the use of a two-component ointment based on silver ions combined with Povidone-iodine, taking into account the phase of the wound process in the treatment of wound infection, in contrast to traditional methods of treatment, has a number of positive aspects. In particular , the wound is cleared of infection by 2,0-2,5 days faster, the process of transition of the wound process from phase I to phase II is accelerated by 2,5-3,0 days, already on the 4-5 day of treatment, the cytological picture is replaced by an inflammatory-regenerative type of cytogram, which is characteristic of the uncomplicated course of the inflammatory process, and the number of purulent-necrotic, dysregenerative complications in the wound, which contributes to rapid scarring and epithelization of its surface.

Keywords: Wound infection, Povidone-iodine, two-component silver preparations.

Introduction

Treatment of wound infection still remains one of the pressing problems of modern surgery. In recent decades, the number of patients with purulent surgical pathology has not shown a tendency to decrease [1, 3, 4, 10, 15, 18]. With the generalization of the pathological process, signs of a systemic inflammatory response (SIR) with organ dysfunctions develop, leading patients to disability and mortality of up to 10-25% [11, 13, 14, 18, 23]. The basis of wound infection treatment is local sanitization and dressings depending on the stage of the wound process. To date, an incalculable number of methods of local wound infection treatment have been proposed, which are constantly updated, and a search is underway for highly effective, safe methods of correcting the pathological process [2, 6, 10, 16, 19, 21, 25]. The outcome of the entire treatment process largely depends on the correct determination of the stage of the wound process, the severity of endogenous intoxication, and the choice of drugs and substances for the treatment of wound infection [7, 12, 17, 20, 24]. A possible way to overcome antibiotic resistance and increase the effectiveness of treatment of wound infection may be the use of local medicinal substances based on iodine and silver compounds. At the same time, preparations containing other classes of antimicrobial substances at the same time are attractive [5, 8, 9, 15, 19, 21]. In terms of their antimicrobial action, local silver preparations in most cases surpass routine methods of exposure to the wound, and their combination with a solution of Povidone iodine can lead to the desired effect in the treatment of wound infection.

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All of the above indicates the advisability of the combined use of Povidone-iodine solution and preparations based on silver compounds in the complex treatment of wound infection.

Purpose of the study: study of the cytomorphological picture under the influence of two-component silver preparations in combination with Povidone-iodine on wound infection.

Material and Methods:

Experimental studies were conducted in vivo on laboratory animals (white non-pedigree rats) with a model of a suppurating wound obtained by infecting it with 1 ml of a daily suspension containing 0.5 ml of E. coli 10^9 CFU/ml and 0.5 ml of P. aeruginoza 10^9 CFU/ml according to the method proposed by Lepekhova S.A. 2013. The proposed model, in its characteristics, corresponded to the clinical course of the wound process.

Depending on the method of treatment of wound infection, laboratory animals were divided into 4 groups of 10 rats. The laboratory rats of the first control group were not treated. The laboratory rats of the first control group were not treated. Animals of the third group underwent local sanitation of the wound surface with a two-component ointment Sulfargin, which contains silver ions Ag+ and sulfadiazine (Sulfanilamide). In animals of group IV, local treatment varied depending on the phase of the wound healing process and was carried out by the combined use of a solution of Povidone-iodine and Sulfargin in the first phase of inflammation; in the second phase of the wound healing process, only Sulfargin ointment was used once a day. In all studied groups of animals, local treatment began with primary surgical treatment of the wound, followed by the above-mentioned treatment measures for the groups of laboratory animals. Cytomorphological studies of wounds were carried out from the first day of treatment and continued dynamically on days 3, 5, 7, 9-10.

Results and Discussions:

Experimental studies conducted in vivo revealed that microscopic examination of samples taken from a suppurating wound and surrounding tissue revealed the absence of epidermis from the first day. The edges were loosened with necrobiotic changes, and were also covered with detritus consisting of keratin and blood clots. A bloody-necrotic mass with an admixture of leukocytes covered the surface of the wound. The wound defect penetrated to the muscle layer. The dermis was edematous, loosened, with foci of necrosis and hemorrhage. Hyperemic vessels were visible, which were surrounded by neutrophilic-leukocyte infiltration. It even covered the skin appendages. On the 5th-7th day of experimental studies, a purulent-necrotic mass was detected on the surface of the wound and surrounding tissue, which in places around the wound destroyed the epidermis and formed foci of leukocyte accumulation, especially around the hair follicles. Also, in the dermis around the wound, massive areas consisting of inflammatory granulation tissue were identified. A characteristic feature of this infiltrate was the predominance of neutrophilic-leukocyte infiltration with the formation of microabscesses and foci of necrosis. The epidermis was subjected to various destructive and dysregenerative changes. In particular, abscesses formed in the thickness of the epidermis and new (secondary) foci of necrosis appeared closer to the wound defect. With hyperplasia and destruction of hair follicles in the wound area, the dermis was transformed into a polymorphic inflammatory granulation tissue infiltrate. On the superficial layers there were many microabscesses, necrosis and keloid. Inflammatory infiltrates were

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oriented towards the vessel and consisted predominantly of neutrophilic leukocytes. In the lumen of individual vessels, thrombi were determined. At the same time, in places in the infiltrate, foci consisting of mature fibrous tissue were determined. However, they also had a chaotic structure with edema and perivascular inflammatory infiltrate.

The cytological picture on days 1-3 of the study was characterized by the predominance of detritus, fragments of destroyed neutrophils, and the absence of cellular reactions and phagocytosis. Pathogenic microorganisms were isolated from the wounds of all animals, with their association predominating. The average concentration of microbes in the wound was 10^9 mg/g. On the 5th-7th and 9th-10th days, incomplete phagocytosis was detected and a large number of neutrophils in a state of destruction were determined. The microbial landscape of the wound during these periods was characterized by an increase in the number of the above-mentioned associations in 8 observations, and the average geometric concentration of microbes in the wound was $10^{9\text{-}10}$ mt/g, which indicated the progression of the purulent process in the wound.

The results of studies using a 10% Povidone-iodine solution as a local solution indicated a significant decrease in the purulent-necrotic process over time.

Thus, by the 3rd-5th day, small layers of necrosis and leukocyte mass were detected in the wound surface. There was less inflammatory granulation tissue at the bottom and around the wound, and it occupied a smaller area. There was less inflammatory granulation tissue at the bottom and around the wound, and it occupied a smaller area. The underlying layers, represented by fibrous connective tissue, consisted of uneven, dense fibrous tissue forming hyalized foci. Among them, small hair cylinders and thick-walled vessels were determined. Epithelialization of the wound surface due to hyperplasia of the squamous epithelium was detected along the edges of the wound. At the same time, on the 7th day, the activity of proliferation of structural elements was noted in the form of proliferation of young connective cells and hyperplasia of the integumentary epithelium. Outgrowths of different sizes and shapes were formed, on the surface of which hyperkeratosis was detected.

At later stages of observation, it was noted that the wound was surrounded on all sides by predominantly fibrous scar tissue. However, by the 9th day, this scar tissue was inferior and was characterized by the presence of foci of pathological hyperplastic changes in the form of persistence of inflammatory infiltrates, hyalized foci, and pathological regeneration of skin appendages. At the bottom and around the wound, an increase in regenerative processes was noted, where the foci of inflammation decreased in size and activity, while layers of fibrous connective tissue remained only around the vessels, the number of vessels decreased, and their walls normalized in the form of fibrosis.

Cytological indices on the third day corresponded to those in animals of group I. However, by the 5th-7th day, the picture was characterized by the content of neutrophils of average preservation, constituting 90%, the rest of the cells were represented by lymphocytes, monocytes, macrophages and polyblasts. It should be noted that on the third day, the species composition of the microflora in most animals was represented by a microbial association. In dynamics, by the 5th-7th day, the average geometric concentration of microbes in the wound was $10^{5\text{-}7}$ mt/g. On the 9th-10th day, a decrease in the number of neutrophils by up to 60%, an increase in the number of young connective tissue cells and a decrease in the amount of microflora were observed; the average geometric concentration of microbes in the wound was $10^{4\text{-}5}$ mt/g of tissue.

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All this indicated the beneficial effect of 10% Povidone-iodine solution, which promoted the cleansing of necrotic tissue. At the same time, the area of inflammatory granulation tissue remains extensive, and inflammatory hyalized foci remain within its thickness. In the dermis and epidermis, dysregenerative changes occur in the form of hyperplasia of the hair follicles and papillomatous proliferation of the epidermis. Cytological studies confirmed the transition of the wound process to the second phase only by the 7th-9th day of treatment.

As noted above, animals of the third group underwent local sanitation of the wound surface with a two-component ointment Sulfargin, which contains silver ions Ag+ and sulfadiazine (Sulfanilamide). The studies revealed that the morphological picture on the third day of treatment was practically identical to that of animals of groups I and II. On the 4th-5th day it was similar to the morphological picture observed in animals of group II on the 5th-7th day. However, during subsequent observation periods, although no purulent-necrotic deposits were detected at the bottom of the wound and the surface of the surrounding areas, there was sufficient inflammatory granulation tissue at the bottom and around the wound, and they occupied a large area. The inflammatory-proliferative infiltrate spread to all layers of the wound and was represented by leukocyte infiltration. The underlying layers, like the overlying ones, were loose and edematous. Myxomatosis and fibrinoid swelling were determined in places. Among them, well-developed full-blooded thick-walled vessels were determined. At the edges of the wound, slight epithelialization of the wound surface was determined due to hyperplasia of the squamous epithelium with pronounced dysregenerative changes.

The results of the cytological examination on the third day were the same as in the previous groups. The picture typical for group II on the 5th-7th day could be observed in group III already on the 3rd-4th day. At the same time, there was no microbial association during these periods, and their average geometric concentration in the wound was 10^{3-4} mt/g of tissue. All this indicated a regression of the inflammatory process and its transition to the second phase. Its further use in the second phase of the wound process activated the processes of reparation and regeneration.

Thus, the results of the experimental study of animals of group III allowed us to conclude that the use of the two-component ointment Sulfargin, which contains silver ions Ag+ and sulfadiazine (with an antibiotic of the sulfanilamide group), can, in a short time, reduce the microbial colonization of the wound below the critical level and promote the early transition of inflammation to the second phase of its course and activate the processes of reparation and regeneration. The results of morphological studies indicated the disappearance of purulent-necrotic, dysregenerative and hyperplastic changes in the wound area. Acceleration of scarring and epithelialization of the wound surface was noted. In the early stages after using the ointment based on silver ions, less pronounced circulatory and inflammatory changes in the edges of the wound were observed. Only a small layer of necrotic detritus was detected. Inflammatory infiltration involved shallow layers of surrounding tissue and was represented by an infiltrate of hematohistiogenic cells.

In experimental animals of group IV, local treatment differed depending on the phase of the wound healing process and was carried out by combined use of Povidone-iodine solution and Sulfargin in the first phase of inflammation, in the second phase of the wound healing process only Sulfargin ointment was used once a day.

The studies revealed that the morphological picture on the third day of treatment was similar to the morphological picture observed in animals of group III on the 5th-7th day. The results of morphological studies indicated the disappearance of purulent-necrotic, disregenerative and

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hyperplastic changes in the wound area already at early stages from the start of treatment. Acceleration of scarring and epithelialization of the wound surface was noted. At the same time, less pronounced discirculatory and inflammatory changes in the wound edges were observed.

The results of the cytological examination on the third 3rd day showed that no microbial association was observed during this period, while the average geometric concentration of microbes in the wound was 10^{3-4} mt/g tissue, that is, it was below the critical level. All this indicated a regression of the inflammatory process and its transition to the second phase. On the 5th day of treatment, a negative bacteriological result was noted. At the same time, further treatment of the wound process continued with the use of Sulfargin ointment as a monotherapy without a combination of 10% Povidone-iodine solution, which contributed to the activation of repair and regeneration processes. It can be stated that already on the 4-5th day of treatment, an inflammatory-regenerative type of cytogram was detected in animals of group IV. This picture is typical of an uncomplicated inflammatory process. The number of neutrophils decreased to 60%, and 30% of the cells were represented by lymphocytes, fibroblasts and macrophages. The content of the latter reached 7%, which is an objective criterion for wound cleansing from purulent-necrotic tissues.

Thus, summarizing the results of experimental studies, it can be noted that a differentiated approach to the local use of 10% Povidone-iodine solution in combination with a two-component ointment Sulfargin containing silver ions Ag+ and sulfanilamide, taking into account the phase of the wound process in the treatment of purulent wounds, in contrast to conventional treatment methods, has a number of positive aspects.

In particular, the wound is cleared of infection 2.0-2.5 days faster, the transition of the wound process from phase I to phase II is accelerated 2.5-3.0 days, the number of purulent-necrotic, dysregenerative complications in the wound is significantly reduced, which contributes to rapid scarring and epithelialization of its surface.

Conclusions:

1. The results of experimental studies on animals using a 10% Povidone-iodine solution as a local treatment for wound infection indicate a significant decrease in the purulent-necrotic process over time.
2. Experimental studies have led to the conclusion that the use of a two-component ointment Sulfargin in the treatment of wound infection, which contains silver ions Ag+ and sulfadiazine, can, in a short time, reduce the microbial colonization of the wound below the critical level and promote the early transition of inflammation to the second phase of its course and activate the processes of reparation and regeneration.
3. A differentiated approach to the treatment of wound infection using locally 10% Povidone-iodine solution in combination with a two-component ointment Sulfargin containing silver ions Ag+ and sulfanilamide, taking into account the phase of the wound process, unlike conventional treatment methods, accelerates the cleansing of the wound from infection by 2.0-2.5 days faster, the transition of the wound process from phase I to phase II is accelerated by 2.5-3.0 days, the number of purulent-necrotic, dysregenerative complications in the wound is significantly reduced.

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