

SILVER-MODIFIED MONTMORILLONITE IN THE TREATMENT OF PATIENTS WITH AN INFECTED WOUND

Research article

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Abstract

Infection of the skin and soft tissues occupies one of the dominant places among surgical pathology. It is known that about 40% of the total number of patients in surgical hospitals suffer from purulent diseases of the skin and soft tissues. According to statistics, from 500 to 700 thousand people annually in the Russian Federation receive treatment for purulent-inflammatory processes of the skin and soft tissues. The aim of the study was to evaluate the effectiveness of the use of silver-modified montmorillonite in the treatment of skin and soft tissue infections.

Material and Methods. In accordance with the tasks assigned, the following groups of patients were identified: The main group (60 people) used the original silver-modified montmorillonite (Ag-MMT) for local treatment of patients. The control group (52 people) used a silver-containing ATRAUMAN AG dressing for local wound treatment.

Results. In the main group, the complex application of the proposed method of treatment using Ag-MMT made it possible to achieve a pronounced effect in cleansing (4.9 ± 1.1 days) and epithelization (12.2 ± 1.8 days) of the wound compared with the control group (6.2 ± 0.9 , 13.8 ± 1.1 days, respectively, $p < 0.05$). Against the background of treatment, positive dynamics of morphological changes in wounds were revealed in patients of both groups, characterized by a sequential change of cytogram types from necrotic (type I) and degenerative-inflammatory (type II) to inflammatory-regenerative (type IV) in the control group and regenerative (type V) in the main group. The regenerative type of cytograms (type V) was not achieved by the 14th day in the control group, whereas in the main group this type of cytograms was determined by 11.2 ± 1.8 days ($p < 0.05$).

Conclusions. Studies have shown the clinical effectiveness of the use of silver-modified montmorillonite in the local treatment of purulent wounds. This effect is probably due to a combination of two factors: the absorption property of MMT and the antimicrobial action of silver.

Keywords: silver-modified montmorillonite, skin and soft tissue infection, contamination, degenerative-inflammatory.

МОДИФИЦИРОВАННЫЙ СЕРЕБРОМ МОНТМОРИЛЛОНИТ В ЛЕЧЕНИИ ПАЦИЕНТОВ С ИНФИЦИРОВАННЫМИ РАНАМИ

Научная статья

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Аннотация

Проблема лечения инфекции кожи и мягких тканей занимает одно из доминирующих мест среди хирургической патологии. Известно, что около 40% от общего числа пациентов хирургических стационаров страдают гнойными заболеваниями кожи и мягких тканей. По статистике, ежегодно в Российской Федерации от 500 до 700 тысяч человек получают лечение от гнойно-воспалительных процессов кожи и мягких тканей. Целью исследования была оценка эффективности применения модифицированного серебром монтмориллонита при лечении инфекций кожи и мягких тканей.

Материал и методы. В соответствии с поставленными задачами были выделены следующие группы пациентов: Основная группа (60 человек), в которой применялся оригинальный модифицированный серебром монтмориллонит

(Ag-ММТ) для местного лечения пациентов. В контрольной группе (52 человека) для местной обработки ран применяли повязку АТРАУМАН АГ, содержащую серебро.

Результаты. В основной группе комплексное применение предложенного способа лечения с использованием Ag-ММТ позволило добиться выраженного эффекта в очищении ($4,9 \pm 1,1$ дня) и эпителизации ($12,2 \pm 1,8$ дня) раны по сравнению с контрольной группой ($6,2 \pm 0,9$, $13,8 \pm 1,1$ дней соответственно, $p < 0,05$). На фоне лечения у пациентов обеих групп выявлена положительная динамика морфологических изменений в ранах, характеризующаяся последовательной сменой типов цитогрaмм с некротических (тип I) и дегенеративно-воспалительных (тип II) на воспалительно-регенеративные (тип IV) в контрольной группе и регенеративные (тип V) в основной группе. Регенеративный тип цитогрaмм (тип V) не был достигнут к 14-му дню в контрольной группе, тогда как в основной группе этот тип цитогрaмм был определен к $11,2 \pm 1,8$ суткам ($p < 0,05$).

Выводы. Исследования показали клиническую эффективность применения модифицированного серебром монтмориллонита при местном лечении гнойных ран. Этот эффект, вероятно, обусловлен сочетанием двух факторов: абсорбирующими свойствами ММТ и антимикробным действием серебра.

Ключевые слова: монтмориллонит модифицированный серебром, инфекции кожи и мягких тканей, обсемененность, дегенеративно-воспалительный процесс.

Introduction

Currently, wound surgical infection is one of the main problems with which patients seek medical help [1], [3], [12], [23]. The relevance of this problem is also confirmed by the fact that 14.0-16.0% of all nosocomial infections are postoperative wound infections. The vast majority of gram-negative microorganisms, including *Pseudomonas aeruginosa*, as well as *Staphylococcus aureus*, according to the results of studies in general surgical hospitals, demonstrate resistance to drugs such as Rivanol, Furacilin, Chloramine and Decamethoxin [2], [4], [13], [19]. At the same time, multicenter studies show that the frequency of wound suppuration after surgical interventions can reach 17.0- 27.0% [5], [6], [7], [20]. Slightly more than 75.0% of hospital rooms are "contaminated" with methicillin-resistant strains of *Staphylococcus aureus* [8], [11], [14], [24], 98.0% of chronic wounds are seeded with aerobic organisms [12], [16], [18], [19]. Local treatment of infected wounds includes the use of bioactive dressings, the action of which is mostly strictly directed and carried out in one or another phase of the wound process. On the other hand, since ancient times, silver preparations have been used for the treatment of wound infections, which has a persistent antiseptic effect [13], [15], [22], [25]. Along with the fact that there is more and more data in the literature on the growth of the number of bacteria resistant to modern drugs, the identification of microorganisms resistant to silver preparations is single and scattered [4], [17], [24], [26]. The wounded coatings existing on the market today with immobilized various forms of silver do not provide a stable and sufficient duration of antimicrobial action. At the same time, the results of studies on the high antibacterial activity of nanoscale silver particles began to appear in the literature [9], [19], [21], [23]. Thus, the study of the clinical efficacy of modern materials, including those with the inclusion of silver nanoparticles, in the treatment of skin and soft tissue infection, is an urgent and timely study.

Material and methods

In 2020-2021, 112 patients with infectious soft tissue lesions were treated at the surgical infection's clinic of the Belgorod Regional Clinical Hospital of St. Joasaph. Primary processes were registered in 20 (17.86%), secondary processes – in 92 (82.14%) patients. Of these, 60 are men (53.57%), 52 are women (46.43%).

Upon admission to the department, bacterial agents were found in the wounds of all patients, while the number of colony-forming units ranged from 105 to 109 CFU/ml. In 27.6% of cases, associated wound infection with nosocomial polyresistant strains of bacteria was diagnosed.

The following microorganisms were isolated from the wounds: *Staphylococcus aureus* – 23.8%; *Escherichia coli* – 19.23%; *Klebsiella pneumoniae* – 17.31%; *Pseudomonas aeruginosa* – 13.46%; *Enterococcus faecalis* – 9.62%; *Staphylococcus epidermidis* – 5.77%; *Acinetobacter baumannii* – 3.85%; *Corynebacterium striatum* – 3.85%; *Staphylococcus haemolyticus* – 3.85%.

In accordance with the tasks set, the following groups of patients were identified:

- The main group (60 people) for the local treatment of patients used the original montmorillonite modified with silver (Ag-ММТ), obtained at Belgorod State University in laboratory conditions by treating the substance montmorillonite with a solution of silver nitrate (patent No. 2522935. Russian Federation).

- Control group – (52 people) for the local treatment of wounds, a silver-plated АТРАУМАН АГ dressing containing silver dressing with antibacterial properties made of polyamide mesh coated with elemental silver was used.

Thus, according to the mechanism of action and composition, these funds are similar and are in states similar in form, which gave us the right to compare their effectiveness with each other.

The distribution of patients in the main and control groups by age and nosological forms is presented in *Table 1*.

Table 1 - Distribution of patients by age and nosological forms of diseases

Age, years	Group of patients										Total
	Main					Control					
	Primary infections of the skin and soft tissues		Secondary infections of the skin and soft tissues			Primary infections of the skin and soft tissues		Secondary infections of the skin and soft tissues			
	Necrotic celluli	Necrotic fasciit	Infect ed trophi	Diabetic foot	Infecti on of the	Necrotic celluli	Necrotic fasciit	Infect ed trophi	Diabetic foot	Infecti on of the	

	te		is		c ulcers, Bedsores		syndr ome		surgic al interv ention area		te		is		c ulcers, Bedsores		syndr ome		surgic al interv ention area									
	a b c.	%	a b c.	%	a b c.	%	a b c.	%	a b c.	%	a b c.	%	a b c.	%	a b c.	%	a b c.	%	a b c.	%	a b c.	%						
1 8 - 4 4	-		-		1	0.89	-		9	8.04	-		-		2	1.79	4	3.57	1	0	8.93	2	2.6	2	3.21			
4 5 - 5 9	3	2.68	-		1	0.89	-		7	6.25	1	0.89	1	0.89	2	1.79	2	1.79	5	4.46	2	2	1	9.64				
6 0 - 7 4	5	4.46	1	0.89	3	2.68	1	0.89	9	8.04	2	1.79	1	0.89	2	1.79	1	0.89	7	6.25	3	5	3	1.25				
7 5 - 9 0	1	0.89	1	0.89	1	0.89	1	0.89	6	5.36	2	1.79	1	0.89	4	3.57	1	0.89	7	6.25	2	5	2	2.32				
9 0 +	-		-		1	0.89	-		1	0.89	-		1	0.89	-		-		1	0.89	4	3.57	3	5.7				
T o t a l	9	8.04	2	1.79	7	6.25	4	3.57	3	3.92	4	3.57	4	3.57	1	3	1	2.5	8	7.14	2	3	2	0.53	1	1	0	0

The treatment was performed in an open way "under a bandage". The protocol of local treatment in all patients was the same. In the main group, after treating the wound surface with saline solution, a silver-modified montmorillonite was applied with a sterile spatula. After that, the wound was closed with a sterile transparent self-fixing film (*Figure 1*), (patent № 2775878. Russian Federation), in the control group it was closed with an ATRAUMAN AG bandage.



Figure 1 - Infected chest wall wound after treatment with modified silver monmorillonite

In 33% of patients in the main group (20 patients) and 26.92% of patients in the control group (14 patients), with abundant wound separations, VAC therapy was used at the time of admission – treatment of purulent wounds with negative pressure, which is created using a closed system consisting of a vacuum source and a vacuum attached to it located in the wound-assisted dressing (Vivano. Hartmann. Germany) (*Figure 2*).



Figure 2 - Treatment of an infected foot wound with VAC therapy

Note: Vivano. Hartmann. Germany

Bandages were performed daily for the first 5 days, and then every other day. The average duration of treatment, as a rule, did not exceed three weeks. All patients underwent daily visual examination of wounds with photo documentation, the following were analyzed: the severity of edema, the amount of wound discharge, hyperemia, granulation, epithelization [3], [7], [20], [24]. The area and depth of wounds were assessed using the mobile application +WoundDesk (Figure 3).

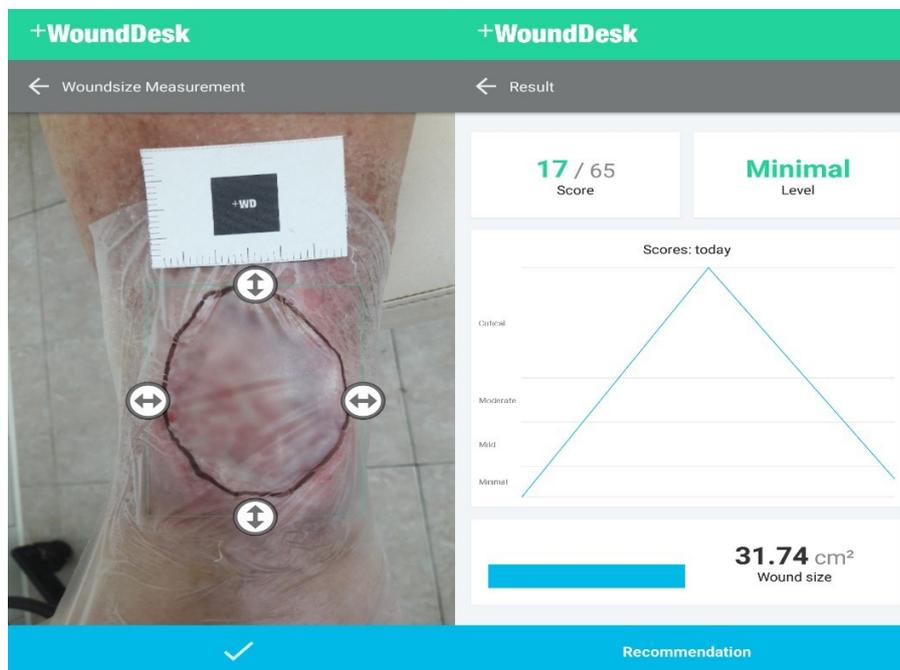


Figure 3 - Determination of the area of the infected ulcer of the lower leg using the mobile app +WoundDesk

Thermometry of the paravular zone, as well as symmetrical intact areas, was carried out using a standard electronic thermometer. The temperature index of blood circulation (TIC) was also calculated, which is the ratio of the difference in the temperature of the skin of the study area and the ambient air to the difference in the temperature in the armpit and the temperature of the skin of the study area (norm < 3).

Isolation of strains of microorganisms was carried out by standard methods using an automatic bacteriological analyzer VITEK2 (BioMerieux). The sensitivity of microorganisms to antibacterial drugs and the silver form of montmorillonite was determined by the diffusion method. The reading of growth inhibition zones was carried out automatically using the Adagio antibioticogram analyzer. During bacteriological studies, the quantitative composition of the microflora was also determined.

All patients underwent cytological examination of scrapings from the surface of wounds, upon admission, after 7 and 14 days of treatment. The scraping was taken by carefully scraping the surface with a spatula or scalpel. The following types of cytograms were distinguished according to Kamaev M.F.: necrotic, degenerative-inflammatory, inflammatory, inflammatory-regenerative and regenerative.

The work was carried out under the supervision and with the approval of the local ethics committee of the Belgorod Regional Clinical hospital Prelate Ioasaf, Belgorod, Russia (Protocol of February 25, 2020, No. 1); he is the winner of the "YMNİK" program of the Foundation for the Promotion of Innovations in the direction of "Medicine and Health-Saving Technology" in 2021.

Initially, we performed a visual assessment of wounds upon admission to the hospital (initial examination in the dressing room) on the 7th and 14th days of the treatment. The results of the visual assessment of the wounds at the specified study dates are presented in *Table 2*.

Table 2 - Visual assessment of wounds at all study periods in all 112 patients observed (100%)

Signs		Upon admission				7th day				14th day			
		Main		Control		Main		Control		Main		Control	
		aбс.	%	aбс.	%	aбс.	%	aбс.	%	aбс.	%	aбс.	%
Swelling of the paravascular area	expressed	10	16.66	10	19.23	3	5	7 *	13.46*	0	0	3 *	5.77*
	moderate	22	36.66	16	30.77	13	21.67	11	21.15	1	1.67	7 *	13.46*
	pasty	23	38.33	20	38.46	13	21.67	16 *	32.69*	5	8.33	14 *	26.92*
	no	5	8.33	6	11.54	31	51.67	18 *	34.62*	54	90	28 *	53.85*
Separated from the wound	significant amount	28	46.67	26	50	9	15	20	38.46	2	3.33	6 *	11.54*
	moderate	14	23.33	14	26.92	5	8.33	12 *	23.08*	2	3.33	10 *	19.23*
	minor	13	21.67	7	13.46	20	33.33	6 *	11.54*	9	15	14 *	26.92*
	no	5	8.33	5	9.62	26	43.33	14 *	26.92*	47	78.33	22 *	42.31*
Hyperemia of tissues	expressed	26	43.33	23	44.23	8	13.33	17 *	32.69*	0	0	6 *	11.54*
	moderate	28	46.67	22	42.31	12	20	18 *	34.62*	1	1.67	8 *	15.38*
	minor	4	6.67	5	9.62	13	21.67	10	19.23	8	13.33	16 *	30.77*
	no	2	3.33	2	3.85	27	45	7 *	13.46*	51	85	22 *	42.31*
Granulation	coarse-grained (the whole wound)	0	0	0	0	9	15	2 *	3.85*	46	76.67	28 *	53.85*
	fine-grained (single)	2	3.33	2	3.85	51	85	40 *	76.92*	14	23.33	16	30.77*
	absent	58	96.67	50	96.15	0	0	10 *	19.23*	0	0	8 *	15.38*

Marginal epithelization	pronounced distinct border of the epithelium	0	0	0	0	22	36.67	8 *	15.38*	48	80	19 *	36.54*
	not expressed	4	6.67	4	7.69	24	40	16 *	30.7*	11	18.33	24 *	46.15*
	absent	56	93.33	48	92.31	14	23.33	28 *	53.8*	1	1.67	9 *	17.31*
Wound area, cm ²		62.46 ± 1.2		64.21 ± 1.4		47.14 ± 1.5		58.23 ± 1.9*		16.30 ± 1.9		38.56 ± 1.7*	
Blood Circulation Temperature Index(TIC)		5.21 ± 1.2		5.94 ± 1.1		3.30 ± 0.4		4.30 ± 0.5*		2.20 ± 0.3		3.3 ± 0.3*	

Note: * – the difference is statistically significant, $p < 0.05$

Upon admission, all patients (both groups) had typical signs for all infected wounds: tissue edema, wound discharge (purulent, purulent-necrotic, etc.), hyperemia of the paravular region (Table 2). There were no significant differences in the frequency of certain signs and their severity in the studied groups.

On the 7th day of the treatment, we noted significant differences in the frequency and nature of such signs as:

- tissue edema (48.3% in the main group, 65.38% in the control group ($p < 0.05$));
- the number of patients with wound discharge (56.6% in the main group, 73.07% in the control group);
- hyperemia of the paravular region (55% in the main group, 86% in the control group).

Granulations were recorded in all patients of the main group, whereas in the control group granulations appeared in 80.7% of cases (10 patients had no granulation).

Also on the 7th day, we documented the appearance of distinct signs of marginal epithelialization of wounds in 76.6% in the main group and 46.1% in the control group. The area of wounds significantly decreased from (62.46 ± 1.2 cm²) to 47.14 ± 1.5 cm². in the main group, and in the control group, these indications were 64.21 ± 1.4 cm² and 58.23 ± 1.9 cm² ($p < 0.05$), respectively.

On the 14th day of the treatment, further improvement in the characteristics of these signs was recorded in the main group, which was characterized by the absence of tissue edema in 90% of patients, wound discharge in 78.3%, hyperemia of the paravular region in 85% of patients. Pronounced granulation occurred in 100% of patients, epithelialization was detected in 98.3% of patients. The area of the wound decreased by more than 3.8 times in relation to the initial indicators ($p < 0.05$).

In the control group, similar changes were diagnosed aimed at cleansing and closing wounds, but they were less pronounced, which was characterized by the preservation of tissue edema in 46.1%, wound discharge and tissue hyperemia in 37.6%, granulation was absent in 15.38%, epithelialization in 17.31%. The area of the wound was reduced by less than 2 times from the initial figures ($p < 0.05$).

When analyzing changes in the temperature index of blood circulation, we found a significant decrease of 2.3 times ($p < 0.05$) by the 14th day of treatment in the main group. In the control group, there was also a decrease in this index to 1.8 times ($p < 0.05$) from the baseline, these changes were also less pronounced than in the main group (2.2 ± 0.3 in the main and 3.3 ± 0.3 in the control, respectively, $p < 0.05$).

The analysis of the cytograms of the compared groups against the background of the treatment revealed a significant difference in the composition of cells and types of cytograms compared with the initial data at all study periods (Table 3).

Table 3 - Cytological studies of the dynamics of the reparative process of the wounds

Indicators	Upon admission		7th day		14th day	
	Main	Control	Main	Control	Main	Control
Number of white blood cells	66.7 ± 3.2	70.1 ± 2.8	38.6 ± 2.8	52.3 ± 2.2*	1.2 ± 0.05	16.8 ± 2.6*
Proportion of destroyed leukocytes,	70.2 ± 2.8	72 ± 3.2	58.2 ± 2.8	60.2 ± 2.1	0	56.2 ± 4.6*

%						
Cells, %						
neutrophils	80.6 ± 3.2	78.9 ± 3.2	58.5 ± 2.8	76.2 ± 1.8*	2.1 ± 0.08	16.3 ± 2.8
eosinophils	0.99 ± 0.05	0.88 ± 0.07	0.86 ± 0.07	0.9 ± 0.07	0.86 ± 0.06	0.67 ± 0.1
lymphocytes	2.2 ± 0.6	2.1 ± 0.7	5.6 ± 0.7	2.21 ± 0.8*	16.3 ± 2.1	4.1 ± 1.0*
polyblasts	7.2 ± 0.3	8.6 ± 1.1	13.6 ± 1.8	10.2 ± 0.9*	16 ± 1.6	11.2 ± 1.2*
macrophages	1.2 ± 0.08	1.3 ± 1.0	8.1 ± 0.72	3.9 ± 0.8*	14.2 ± 2.2	6.6 ± 1.6*
fibroblasts	0.6 ± 0.08	0.8 ± 0.05	2.46 ± 0.17	1.2 ± 0.2*	4.6 ± 1.8	2.2 ± 0.6*
multicore cells	0.03 ± 0.01	0.038 ± 0.01	0.05 ± 0.01	0.04 ± 0.01	0.06 ± 0.01	0.07*0.02
epithelium	0	0	units	0	cell groups	cell groups

Note: * – the difference is statistically significant, $p < 0.05$

When there were no significant differences in the cytograms of the compared groups. Changes characteristic of type I cytograms (necrotic type) were noted in all preparations: the visual fields are represented by destroyed neutrophils, a single number of microphages with no esterase activity, erythrocytes, microorganisms, as well as tissue detritus (Figure 4).

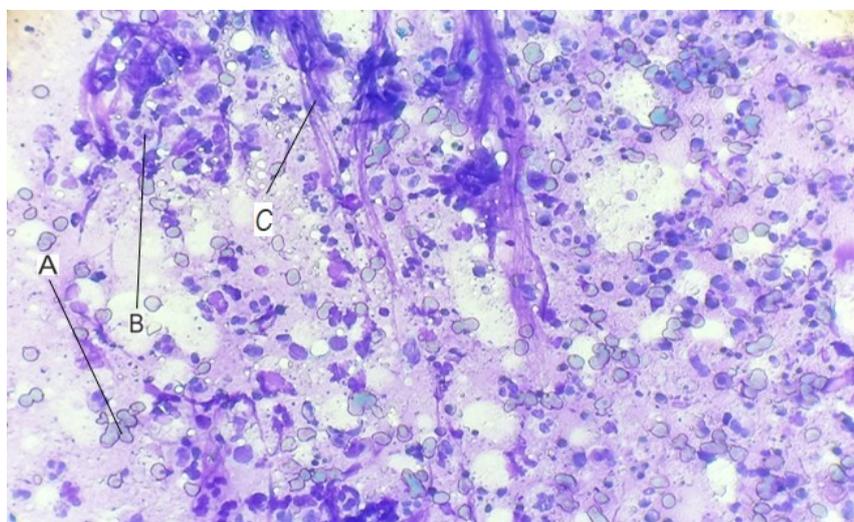


Figure 4 - Upon admission

Note: a – erythrocytes; b – neutrophils; c – fibrin

On the 7th day, against the background of ongoing treatment, cytogram analysis revealed a significant decrease in cellular detritus and elements of wound exudate. Clusters of neutrophils in a degenerative state with bright purple nuclei and pale pink cytoplasm are determined, the number of unchanged neutrophils is minimal (single). The macrophage reaction is pronounced – multiple macrophage cells with signs of high esterase activity are detected. This pattern is characteristic of type II cytograms (degenerative-inflammatory). In the control group, all fields of vision are occupied by cellular and tissue detritus, exudate, and a large number of microorganisms. Neutrophilic leukocytes with signs of degeneration and destruction, the minimum number of macrophages with moderate esterase activity are determined. The described changes are characteristic of type I cytograms (necrotic) (Figure 5).

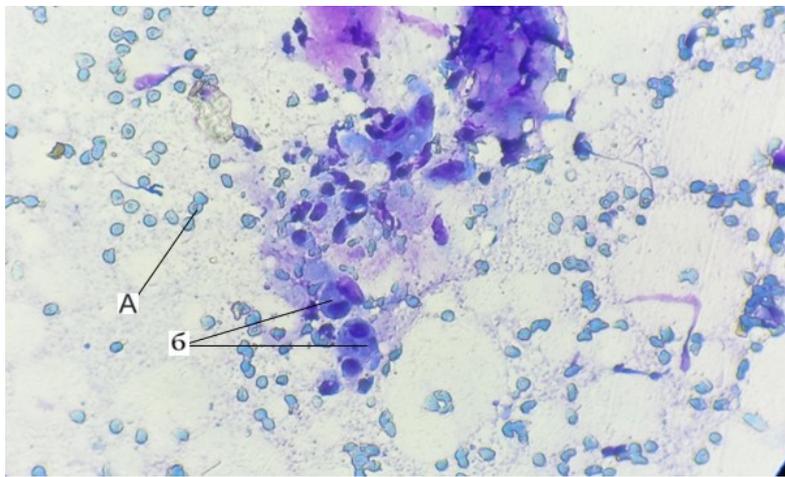


Figure 5 - On 7th day

Note: a – erythrocytes; b – macrophages

On the 14th day in the main group there was a change in the type of cytograms from type II (degenerative-inflammatory) to type IV (inflammatory-regenerative) and type V (regenerative), by this time neutrophilic leukocytes with signs of degeneration were practically undecided. There was a significant increase in the number of cellular elements of granulation tissue, epithelial cells, fibrillar structures, fibroblastic cells, macrophages and polyblasts. Microflora was not determined. In the control group, changes characteristic of inflammatory (type III) and inflammatory-regenerative (type IV) cytograms were revealed. Groups of destroyed and degeneratively altered neutrophils, a large number of macrophage cells in a state of active phagocytosis, polyblasts, lymphocytes, a minimum number of fibroblasts, a small number of microorganisms were determined (Figure 6).

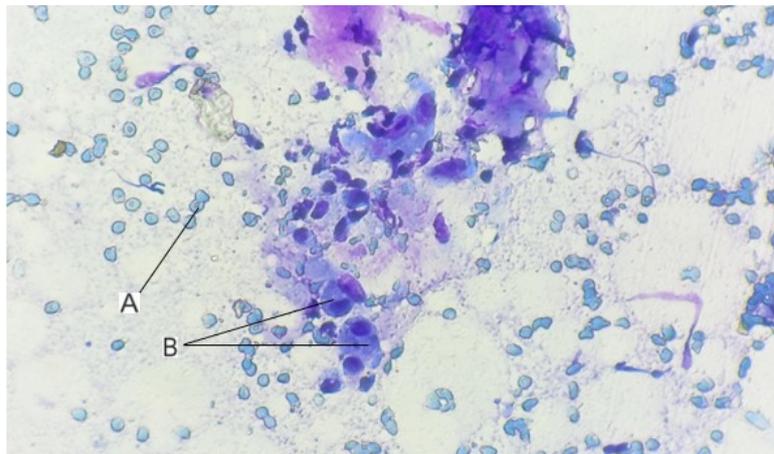


Figure 6 - On 14th day

Note: a – erythrocytes; b – macrophages

Discussion

In the main group, the complex application of the proposed method of treatment using Ag-MMT made it possible to achieve a pronounced effect in cleansing (4.9 ± 1.1 days) and epithelization (12.2 ± 1.8 days) of the wound compared with the control group (6.2 ± 0.9 , 13.8 ± 1.1 days, respectively, $p < 0.05$). Against the background of treatment, positive dynamics of morphological changes in wounds were revealed in patients of both groups, characterized by a sequential change from cytograms of types I and II (necrotic, degenerative-inflammatory) to type IV in the control and type V in the main groups (inflammatory-regenerative and regenerative, respectively). The regenerative type of cytograms (type V) was not achieved by the 14th day in the control group, whereas in the main group this type of cytograms was determined by 11.2 ± 1.8 days ($p < 0.05$).

Conclusion

Thus, studies have shown the clinical effectiveness of the use of silver-modified montmorillonite in the local treatment of purulent wounds. This effect is probably due to a combination of two factors: the absorption properties of MMT and the antimicrobial action of silver.

Конфликт интересов

Не указан.

Рецензия

Все статьи проходят рецензирование. Но рецензент или автор статьи предпочли не публиковать рецензию к этой статье в открытом доступе. Рецензия может быть предоставлена компетентным органам по запросу.

Conflict of Interest

None declared.

Review

All articles are peer-reviewed. But the reviewer or the author of the article chose not to publish a review of this article in the public domain. The review can be provided to the competent authorities upon request.

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