ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

The use of Laser Technology and Aquacomplex Titanium Glycerol solvate in the Treatment of Chronic Osteomyelitis.

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ABSTRACT

Chronic osteomyelitis remains one of the most difficult problems of purulent surgery, which is associated, among other things, with a high incidence of up to 6% in the structure of the pathology of the musculoskeletal system and 6.8-12% in the structure of purulent-septic diseases, high risk of developing septic complications and relapses with disabilities reaching up to 55% of cases. The aim of the study was to improve the results of treatment of chronic osteomyelitis by using laser technologies and aqua-complex of titanium glycerol solvate. Experimental studies were performed in 5 groups on 175 white rats with chronic osteomyelitis: 2 control and 3 experimental ones. In the first control group were animals without treatment. In the 2nd control and all the experimental groups, the purulent focus was surgically sanitized. In the 1st experimental group, the sanitation of the bone cavity was supplemented by the application of low-intensity laser irradiation. In the 2nd experimental group, the aqua-complex titanium glycerol solvate was introduced into the bone cavity. In the third test group, treatment of the bone cavity with low-intensity laser radiation followed by the introduction of the aqua-complex titanium glycerol solvate into it. In the course of performing the work, we analyzed the following studies: clinical, hematological, microbiological and radiological. Modeling of chronic osteomyelitis according to the developed technique allowed to form a pathological process with fistulas and a purulent discharge by the 31st day, which was confirmed by the data of clinical, microbiological and radiological studies. The developed method of complex treatment of chronic osteomyelitis, based on combined application of laser technologies and aqua-complex of titanium glycerol solvate, helped to close the wound defect by 14 days; by the 28th day of the research we noticed a normalization of general condition, appetite and motor activity in the rats; on the 90th day of observation we noticed a normalization of the hip circumference of the injured limb, according to the free radical oxidation parameters, and biochemical data.
Keywords: titanium glycerosolvate aqua-complex, osteomyelitis.

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ISSN: 0975-8585

INTRODUCTION

Chronic osteomyelitis remains one of the most difficult problems of purulent surgery, which is associated, among other things, with a high incidence of up to 6% in the structure of the pathology of the musculoskeletal system and 6.8-12% in the structure of purulent-septic diseases, high risk of developing septic complications and relapses with disabilities reaching up to 55% of cases.

The aim of the study was to improve the results of treatment of chronic osteomyelitis by using laser technologies and aqua-complex of titanium glycerol solvate. Experimental studies were performed in 5 groups on 175 white rats with chronic osteomyelitis: 2 control and 3 experimental ones. In the first control group were animals without treatment. In the 2nd control and all the experimental groups, the purulent focus was surgically sanitized. In the 1st experimental group, the sanitation of the bone cavity was supplemented by the application of low-intensity laser irradiation.

In the 2nd experimental group, the aqua-complex titanium glycerol solvate was introduced into the bone cavity. In the third test group, treatment of the bone cavity with low-intensity laser radiation followed by the introduction of the aqua-complex titanium glycerol solvate into it. In the course of performing the work, we analyzed the following studies: clinical, hematological, microbiological and radiological.

Modeling of chronic osteomyelitis according to the developed technique allowed to form a pathological process with fistulas and a purulent discharge by the 31st day, which was confirmed by the data of clinical, microbiological and radiological studies.

The developed method of complex treatment of chronic osteomyelitis, based on combined application of laser technologies and aqua-complex of titanium glycerol solvate, helped to close the wound defect by 14 days; by the 28^{th} day of the research we noticed a normalization of general condition, appetite and motor activity in the rats; on the 90^{th} day of observation we noticed a normalization of the hip circumference of the injured limb, according to the free radical oxidation parameters, and biochemical data.

Chronic osteomyelitis remains one of the most difficult problems of purulent surgery, which is associated, among other things, with the characteristics of infectious foci, a high incidence of up to 6% in the structure of the pathology of the musculoskeletal system and 6.8-12% in the structure of purulent-septic diseases, septic complications and relapses. The use of new technologies in the complex treatment of chronic osteomyelitis cannot be recognized as sufficiently effective, which is also confirmed by the fact that about 70% of patients with chronic osteomyelitis lose their ability to work, and more than 55% become disabled [1, 3, 5-8, 10, 11].

Methods aimed at enhancing reparative osteogenesis, the research forosteoinductive and osteoconductive materials, local mechanical and physical effects show significant interest in improving methods of treating chronic osteomyelitis. Alsoan interesting method is the use of the properties of laser radiation, which possess anti-inflammatory, immunostimulating, reparative, bacteriostatic and bactericidal actions [1, 2, 4, 9, 10,11]

The aim of the study was to improve the results of treatment of chronic posttraumatic osteomyelitis by using an aqua-complex of titanium glycerol solvate and laser technologies.

Experimental studies were performed in 5 groups on 175 white rats with chronic osteomyelitis: 2 control and 3 experimental ones (Table 1). Each group included 35 animals.

Table 1: Characteristics of groups of animals

Group of animals	Number of animals	Nature of impact done to the animals
1st control	35	Without treatment
2nd control	35	Surgical sanitation of the wound (SSW)
1st experimental	35	SSW + Low-intensity laser irradiation (LILI)

2nd experimental	35	SSW + Aqua-complex of titanium glycerol solvate "Tizol" (Tizol)
3rdexperimental	35	SSW + Tizol + LILI

In the first control group the animals were without treatment.

In the 2nd control and experimental groups, the purulent focus was surgically sanitized.

In the 1st experimental group, bone grafting was supplemented by the application of low-intensity laser irradiation with a wavelength of 1062 nm and a radiation power of 3.5 W from a distance of 8-10 cm for 10 min.

In the 2nd experimental group, the aqua-complex of titanium glycerol solvate Tizol was injected into the bone cavity. With the help of an ophthalmic microsurgical membrane spatula, the aqua-complex of titanium glycerol solvate of 0.3 grams was added to the filling, and induced in the bone cavity (2 test group).

In the third test group, we treated the bone cavity with low-intensity laser radiation (wavelength-1062 nm, distance 8-10 cm, radiation power of 3.5 W, duration 10 min), followed by the introduction of the aqua-complex of titanium glycerol solvate "Tizol" (0 , 3 grams).

Modeling of chronic posttraumatic osteomyelitis was carried out in two stages: the first stage - the creation of the bone cavity and the modeling of aseptic inflammation in it (1-6 days); 2nd stage - modeling of chronic osteomyelitis (7-30 days).

In the first stage, under anesthesia ("Zolitil-100" in a dose of 8 μ / kg) under aseptic conditions on the shaved portion, a linear cut 1.5 cm of the skin, subcutaneous fat, fascia and muscle was introduced; the metaepiphyseal zone of the femur was exposed, where a cavity with a diameter of 3.5 mm was created using a manual micromotor device. The cavity was washed with physiological solution, dried by gauze. Further, the gauze was wetted with a 1% solution of ethoxiclerol and inserted into the cavity together with some bone fragments. With a silk thread of 1.0 diameter, a one total stitch was made on the skin.

At the second stage, on the 7th day after the operation, operative access to the resulting cavity was performed by excision of the postoperative scar and a blunt spreading of the soft tissues with the help of single-tooth hooks. A microbial culture of staphylococcus in a 2% agar solution was inserted into the perforation by Kassirsky's needle; this solution contained about 150-200 thousand microtubules of Staphilococcus aureus. It was injected by extruding the culture using amandren. The hole in the bone was sealed with erodont-cement, the wound was covered with penicillin powder and sutured tightly.

Experimental studies were carried out in strict accordance with the Convention for the Protection of Vertebrates used for experimental and other purposes (Strasbourg, France, 1986), Order of the Ministry of Health and Social Development of the Russian Federation of August 23, 2010 No. 708n "On the Approval of the Rules of Laboratory Practice", Order of the Ministry of Health of the USSR No. 755 of August 12, 1977 "On measures to further improve the forms of work using laboratory animals".

In the course of experimental studies, we assessed the following parameters: clinical (general condition of animals, local: severity of inflammatory signs, the nature of wound detachment), hematological (general blood test, determination of oxidative stress level), microbiological (qualitative and quantitative assessment of microbiological cultures), x-ray methods.

Statistical processing of the data was carried out using the StatSoftStatistica 6.1 Russian software package. Using the software we evaluated the following calculations: mean values, median and mode, error of mean, variance and standard deviation, confidence interval, quartiles and centile corridors. When the multimode character of the distribution was revealed, as well as from the asymmetry and excess data, the character of the distribution of the results of the study was determined using the graphical method-the construction of distribution histograms, and the methods of Kolmogorov-Smirnov and Lilliefors. The methods of parametric and nonparametric statistics (depending on the nature of the distribution) were used: one- and multivariate variance analysis, the Kruskal-Wallace H criterion; the criterion of Sheffe was used as a posteriori

criterion. As for criterial statistics, the upper 5% F-distribution region was used, as more stringent than the t-distribution, to ensure greater accuracy of estimates.

The results of objective research methods

Analysis of objective data on the 7th day, animals in all study groups revealed oppression of the general condition, decreased appetite, exhaustion, poor motor activity accompanied by lameness; withdrawal of the limb was observed during palpation in the projection of the bone cavity. In the 1 st control group, the circumference of the lower third of the thigh of the affected limb was 3.05 ± 0.14, in the 2nd control group, 3.02 ± 0.1, in the 1st test group - 2.98 ± 0.09 cm; in the 2nd experimental - 2.95 ± 0.1 cm, in the 3rd test group - 2.68 ± 0.08 cm (Table 2). In the control groups purulent fistulous passages were revealed. In the 1st and 2nd experimental groups, the diastasis of the edges of the wounds with poor serous-purulent discharge was determined. In the third test group, a serous-purulent discharge was observed.

Table 2: Dynamics of the circumference of the lower third of the thigh of the affected limb

Days	Control groups		Experimental groups		
	1st	2nd	1st	2nd	3rd
7th day	3,05±0,14	3,02±0,10	2,98±0,09	2,95±0,10	2,68±0,08**
14th day	3,02±0,10	3,00±0,09	2,75±0,10**	2,84±0,08	2,57±0,08**
28th day	2,99±0,10	2,84±0,09	2,65±0,09**	2,68±0,10**	2,42±0,08**
60th day	2,98±0,11	2,72±0,11**	2,43±0,08**	2,47±0, 08**	2,37±0,07**
90th day	2,92±0,13	2,54±0,12**	2,32±0,11**	2,39±0,08**	2,26±0,07**

** - the reliability of differences in comparison with the 1st control group, p <0.005

On the 14th day, the animals in the 1st and 2nd control groups of the study maintained very slow progression of the general condition; we noticed a decrease in appetite, a high level of exhaustion, poor motor activity accompanied by lameness and the formation of fistulas with hyperemia and a moderate amount of serous-purulent discharge.In the experimental groups, there was an improvement in general condition and appetite, motor activity, moderate brittleness of the animals' fur, complete closure of wound defects. In the 1st control group, the circumference of the lower third of the thigh of the affected limb was 3.02 ± 0.10 cm, in the 2nd control group - 3.00 ± 0.09 cm, in the 1st experimental group of animals - 2.75 ± 0, 10 cm, in the 2nd experimental -2.84 ± 0.08 cm, in the third experimental group - 2.57 ± 0.08 cm.

On the 28th day of the study, the animals of the 1st control group experienced depression of general state and appetite, exhaustion, fragility of the fur cover, weak motor activity, the presence of fistulous passages with the zone of hyperemia and a moderate amount of serous-purulent discharge. In the 2nd control group, the general condition of the animals corresponded to the norm, there was an appetite, but exhaustion was observed, weak motor activity was maintained. By 28 days of the study in the experimental groups there was a normalization of the general condition, appetite and motor activity, pathological fragility of the animals' fur was not detected. In the 1st control group, the circumference of the lower third of the femur of the affected limb was 2.99 ± 0.10 cm, in the 2nd control group - 2.84 ± 0.09 cm, in the 1st experimental group of animals - 2.65 ± 0 , 09 cm, in the 2 nd experimental - 2,68 ± 0,10 cm, in the 3rd experimental group - 2,42 ± 0,08 cm.

On the 60th and 90th day, objective research data of the animals of the 1st control group did not show any positive dynamics, fistulas with serous-purulent discharge were retained, severe edema (2.98 ± 0.11 and 3.00 ± 0.11, respectively). While palpating the animal, we refrained from palpating the injured limb. By the 60th day in the animals of the second control group, the diameter of the lower third of the thigh was 2.72 ± 0.11 cm, in the first experimental - 2.43 ± 0.08, in the 2nd experimental - 2.47 ± 0,08, in the third experimental - 2,37 ± 0,07 cm.

By 90 days the general condition of the animals of the 2nd control group was normalized, but the dullness of the covering of the fur. During the movement, the animals of the 2nd control and experimental groups completely used the injured limb, local signs of inflammation were absent. The circumference of the

hip of the injured limb on the 90th day in the animals of the 2nd control group was 2.54 ± 0.12 cm, the first experimental group - 2.32 ± 0.11, the 2nd experimental -2.39 ± 0.08, the third experimental - 2.26 ± 0.07 cm.

Thus, the most rapid relief of local and general manifestations of the clinical picture of chronic osteomyelitis was observed with the use of a complex treatment based on the combined use of surgical sanitation of a purulent focus, low-intensity laser irradiation and the aquacomplex of titanium glycerol solvate "Tizol" (3rd experimental group), which consisted in closure of the wound defect on the 14th day; normalization of the general condition, appetite and motor activity occurred on the 28th day, the investigation of the hip circumference of the injured limb to the 90th day of observation.

Indication of oxidative stress

The dynamics of oxidative stress processes were studied by analyzing free-radical processes in the body, which were assessed by the level of lipid peroxidation (malonic dialdehyde / MDA) and oxidative modification of proteins (the content of carbonyl groups in the reaction with 2,4-dinitrophenylhydrazine).

When analyzing lipid peroxidation on the 7th day, it was noted that in the 1st control group, the MDA level was 43.12 ± 4.17 nmol / L or more, which was almost 2 times higher than the value of this parameter in intact animals.The MDA value in the 2nd control group was 41.58 ± 2.9 nmol / L and indicated an increase in the intensification of lipid peroxidation processes. In the experimental groups, the process of lipid peroxidation proceeded less intensively than in the control groups.The MDA level was 34.02 ± 2.73 nmol / l in the 1st experimental group, 33.85 ± 2.35 nmol / l in the 2nd experimental group, 28.47 ± 3 in the third experimental t group, 05 nmol / l.

In the 1st and 2nd control groups, the level of DNPH was 80.97 ± 3.22 and 77.33 ± 2.23 nm / mg protein, respectively. In the experimental groups positive dynamics of OMB was revealed in comparison with the control groups. The level of DNPG in the 1st and 2nd experimental groups was 66.01 ± 3.14 and 64.05 ± 2.35 nm / mg protein, respectively. In the 3rdexperimental group, this indicator was 58.44 ± 3.28 nm / mg, which was significantly lower in comparison with the 1st and 2nd control groups.

By the 14th day of the study, the high levels of MDA, 40.54 ± 3.01 nmol / L and 39.81 ± 5.34 nmol / L, remained in the 1st and 2nd control groups, respectively, indicating a decrease in the regenerative processes of tissues in the focus of inflammation. When we used a complex of surgical and laser sanitation treatment of the pathological focus, we noticed a statistically significant decrease in the level of MDA (27.01 ± 2.93 nmol / L). In the group of laboratory animals, where the aqua-complex of titanium glycerol solvate was included in the treatment complex, a similar tendency as to the group with the use of laser sanitation was observed in relation to LPO - the MDA content was 26.02 ± 2.24 nmol / l. When the laser sanitation was combined with the titanium glycerol solvate and injected into the bone cavity, there was a statistically significant ($p < 0.05$) decrease in the MDA level in comparison with the 7th day (19.83 ± 1.56 nmol / l).

By the 28th day of the study in the 1st control group, high LPO activity persisted on the basis of the purulent-inflammatory process. The level of MDA in this group was 40.01 ± 3.26 nmol / l. In serum of laboratory animals of the 2nd control group, there were no statistically significant differences in the MDA content with respect to the 1st control group (37.27 ± 1.64 nmol / l). In the experimental groups, the LPO index decreased and approached the normal values, which confirmed the effectiveness of the treatment.

On the 28th day of the study, the OMB processes in the 1st control group had no significant differences compared to the 14th day, the DNPH level was 78.02 ± 2.15 nm / mg protein. In the 2nd control group there was a dynamics similar to the 1st control group. In this group, the level of DNPG was 65.11 ± 2.72 nm / mg protein. When assessing the level of carbonyl modification of proteins in experimental animals, we noted its increase in comparison with intact animals. However, it was significantly lower ($p < 0.05$) than in control animals and was 55.94 ± 2.72 nm / mg protein in the 1st experimental group, 53.58 ± 2.13 nm / mg protein in the second experimental group , in the 3rd test group - 50.24 ± 2.44 nm / mg protein.

By the 60th day of the study, the MDA level in the 1st control group was 39.28 ± 4.65 nmol / l, in the 2nd control group - 36.91 ± 3.12 nmol / l. In the 1st and 2nd experimental groups positive dynamics was observed in comparison with the 28th day. The level of MDA approached the index in intact animals and was

17.97 ± 1.54 nmol / l in the 1st experimental group; In the 2nd experimental group - 17.01 ± 0.92 nmol / l; In the 3rd experimental group - 14.86 ± 1.93 nmol / l, which practically corresponded to the level of the index in intact animals.

Free radical oxidation of lipids was accompanied by activation of the carbonyl modification of proteins. In the 1st control group, a high level of DNPH (77.07 ± 1.93 nm / mg protein) remained. In laboratory animals of the 2nd control group, the level of OMB decreased to a level of 59.61 ± 2.04 nm / mg. In the experimental groups, positive dynamics were noted. The level of DNPH in the 1st and 2nd experimental groups was 50.64 ± 2.18 and 50.07 ± 1.66 nm / mg, respectively. In the 3rd experimental group, this indicator approached the level of intact animals and was 48.59 ± 1.99 nm / mg protein.

By the 90th day of the study, the continuing high activity of LPO processes in the 1st control group was correspondent with the severity of the pathological process. The level of MDA in this group was 38.30 ± 4.20 nmol / l, which exceeded the same figure for intact animals by 165.97%.In the 2nd control group, the MDA content was positive and differed significantly from the 1st control group (35.30 ± 2.74 nmol / l). In the 1st and 2nd test groups, despite the pronounced positive dynamics, the MDA level remained above the normal values and amounted to 16.18 ± 0.82 and 15.98 ± 1.50 nmol / l. The analyzed index in the group of animals which received the complex treatment of the laser sanitation and "Tizol" was 14.40 ± 1.67 nmol / l.

In the whole course of this experimental period, high activity of OMB processes in laboratory animals of the 1st and 2nd control groups remained the same, the content of DNPG was 76.95 ± 1.73 and 56.99 ± 1.69 nm / mg, respectively. In the 1st and 2nd experimental groups, the level of DNPH decreased, similar to the level of MDA, but did not reach the values of intact animals. In the 3rd experimental group, the OMB process came into correspondence with the physiological norm and amounted to 46.26 ± 2.10 nm / mg.

Analysis of free radical processes in the body. Antioxidant defense of the organism.

In the course of the studies it was found that on the 7th day the level of SH-groups in the 1st control group was 107.45 ± 3.12 mg%, in the second control group - 112.74 ± 5.93 mg%. In the experimental groups, in response to the activation of LPO and OMB processes, we noted an adequate increase in the non-enzymatic link of the antioxidant defense system. In the first experimental group, the level of SH-groups was 117.11 ± 6.81 mg%. In the 2nd and 3rd experimental groups the level of SH-groups statistically significantly differed from the control groups and amounted to 118.51 ± 3.21 and 124.15 ± 2.53 mg%, respectively.

In the whole course of this experimental period, a statistically significant decrease in the level of the enzymatic link of the AOC was observed in the control groups. The content of SOD in the 1st control group was 0.40 ± 0.03 units, in the 2nd control group - 0.50 ± 0.07 units; In the 1st experimental group was 1.52 ± 0.04 units, in the 2nd experimental group - 1.60 ± 0.03 conv. units; In the 3rd experimental group - 1.96 ± 0.02 conventional units.

By the 14th day of the study in the control groups there was a decrease in the content of SH-groups based on the background of high activity of free-radical processes. The content of SH groups was 107.82 ± 6.13 mg% in the 1st experimental group, 109.22 ± 3.76 mg% in the 2nd experimental group, and 115.29 ± 5.71% in the third experimental group Mg%.

In the control groups on the 14th day of the study there was a significant inactivation of SOD. The SOD level in the 1st control group was 0.35 ± 0.03 units, in the 2nd control group - 0.43 ± 0.04 units.

On the 28th day of the study, the content of SH-groups was 68.25 ± 4.62 mg% in the 1st control group, and 70.09 ± 4.50 mg% in the 2nd control group. In the experimental groups there was a decrease in the level of SH-groups. However, this indicator was significantly higher than in the control groups. There was a correlation between the decrease in the level of SRO and the index of the non-enzymatic link of the AOS. In the first experimental group, the level of SH-groups was 73.97 ± 5.14 mg%, in the second experimental group - 74.60 ± 7.26 mg%, in the third experimental group - 78.59 ± 11.24 Mg%.

By the 28th day, the activity of the SOD enzyme in the control groups decreased similarly to the SH groups. In the experimental groups, the level of SOD based on a decrease in the activity of LPO and OMB was

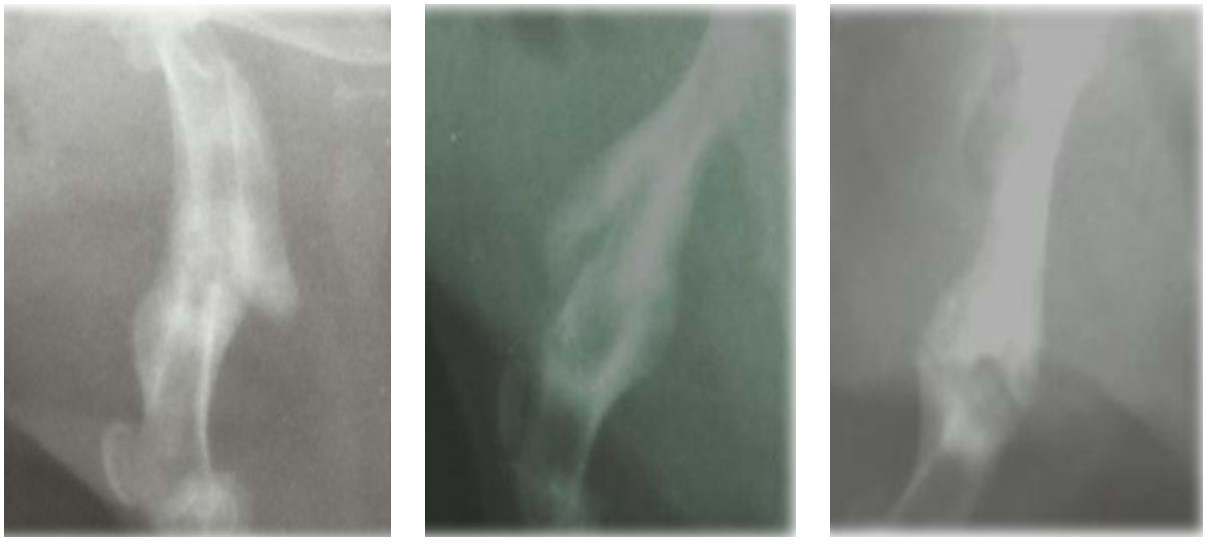
significantly higher in comparison with the control groups (p <0.05). Adequate functioning of the AOS prevented the formation of oxidative stress.

At the 60th, as well as on the 90th day in the control groups, oxidative stress was maintained, reducing the reserve capacity of AOS and aggravating endogenous intoxication. In the experimental groups, the processes of the system of free radical oxidation and antioxidant protection were balanced, this was based on the therapy induced on them. The most pronounced positive dynamics was noted in the group where the combined usage of laser sanitation and aqua-complex titanium glycerol solvatewas induced; the values of the indices did not exceed the level found in intact animals.

Thus, in the modeling of chronic osteomyelitis, the development of pathological activity of free radical oxidation processes was studied, on the basis of the low activity of the antioxidant defense system. The obtained data testify to the advisability of injecting, low-intensity laser irradiation and aqua-complex of titanium glycerol solvate in the complex of treatment of chronic osteomyelitis, which is confirmed by the revealed normalizing effect on the parameters of free radical oxidation, which contributes to stabilization of metabolic processes and a more favorable course of inflammation.

Results of X-ray methods of investigation

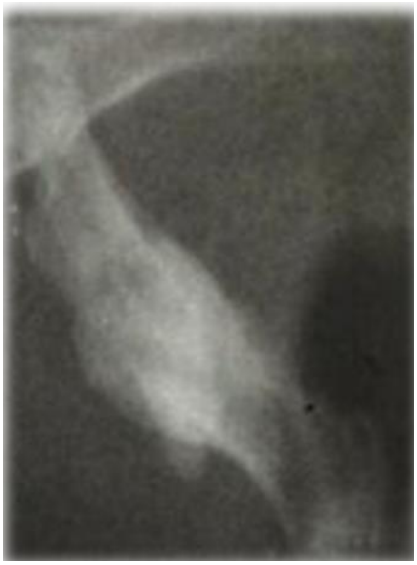
According to the X-ray study, we assessed the shape and size of bone cavities, bone sequesters, the degree of their demarcation, the state of the remaining bone sections, the degree of development of the bone sequestral cavity, the effectiveness of the removal of the bone sequesters, the rejection of the remaining unsuccessfully removed bone sequesters and the formation of new ones. In the 1st control group on the 14th and 28th day we were able to diagnose the osteomyelitis of the femur according to the following parameters: sequesters, with uneven edges, surrounded by a sequestral bone cavity with thick, dense walls. In the 2nd control group, a long lamellar sequestrum was noted; it was located centrally in the medullary cavity and surrounded by thick, dense walls consisting of an old cortical layer and a newly formed bone merged with it (Fig. 1).In all control groups, fistulas were observed in the middle third of the femur along the anterolateral surface. In the 1st and 2nd experimental groups, on the 14th and 28th day, we observed the sclerosis zones and bone thickening several cavities with lamellar sequesters inside on X-rays.



A *B* *C*

Pic.1. X-ray of the rat femur, the 28th day

A) 1st controlgroup; Б) 2nd control group; B) 1st experimental group



Pic.2. X-ray of the rat femur, 1st experimental group, 60th day

Pic. 3. X-rayfemur of the rat, 3rd test group, 90th day

In the late periods of the study, on the 60th and 90th days the foci of bone tissue destruction were less noted; they were located in the thickness of the cortical layer and in the spongy substance of the metaphysis (Figure 2). They were multiple, small, irregularly rounded or elongated, with fuzzy contours. The fussy contours of the bones with each other created a picture of spotted enlightenment. The bones became transparent. The cortical layer appeared to be unevenly thinned. In the 2nd experimental group there was a noticeable decrease in the foci of destruction and a combination of osteosclerosis foci with osteoporosis foci. In some cavities, small sequestrations were visible. The bone structure of the metaphysis was not clearly seen. In the 2nd experimental group, the signs of regeneration in the form of regenerative shadows located along the edges of the bone defect were more visibly noticed (in comparison with the 1st experimental group) (Figure 3). In the 1st and 2nd experimental groups there was a fusion of the outer cortical plate with the rest of the metaphysisinto a single whole one. There were no differentiations to the cortex and bone marrow space. The area of the created defect was not traced. In the X-ray study, the animals of the 3rd test group retained periosteal thickening of the bone.

When the growth plate was destroyed, the metaphysis and epiphysis were partially or completely connected. The diaphyseal part in chronic osteomyelitis is thickened, sclerosed, its structure is not uniform, the medullary canal is narrowed or absent altogether. On the 90th day, the femoral bones of laboratory animals of the 3rd experimental group had a clear pattern and well-defined boundaries of the cortical layer. The bone defect was completely filled with homogeneous shadows of the newly formed bone tissue. Fistulas and bone sequesters were not observed.

CONCLUSION

Modeling of chronic osteomyelitis according to the developed method allowed to form chronic osteomyelitis with fistulas with purulent discharge by the 31st day, which was confirmed by clinical, bacteriological, and x-ray studies. The developed method of complex treatment of chronic osteomyelitis, based on combined application of laser technologies and aqua-complex of titanium glycerol solvate promotes the closure of the wound defect by 14^{th} day; normalization of the general condition, appetite and motor activity by the 28^{th} day of the study; normalization of the hip circumference of the injured limb, and normalization of free radical oxidation, biochemical data to the 90^{th} day of observation.

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