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Changes in the Number of White Blood Cells and Non-Specific Markers of Inflammation in the Body of Rabbits in Experimental Osteoarthritis of the Knee Joint

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Abstract. Osteoarthritis is the most common joint disease in animals, which is not always treatable. Both in veterinary and in human medicine, laboratory research methods are used to effectively diagnose this pathology. The purpose of this study was to establish the dynamics of markers of the acute phase of inflammation in the blood using experimental modelling of knee osteoarthritis in rabbits. Artificial reproduction of the pathological process in the knee joints of animals was performed by intra-articular administration of Yellow peel 2*5 ml. The BC-2800Vet automatic haematology analyser (China) was used to calculate the number of white blood cells and their subpopulations in the blood. The content of C-reactive protein in blood serum was found using enzyme-linked immunosorbent assay. The rate of erythrocyte sedimentation in the blood was investigated according to the Panchenkov method. Thus, on Day 7, a sharp increase in the number of white blood cells (2.7 times) and their subpopulations was noted in sick rabbits, which indicates an active inflammatory process of a systemic nature. On Day 14, their number in the blood of sick animals was characterized by a tendency to decrease, but it had not yet reached the values of the control group. On Days 21 and 28, all the indicators under study tended to decrease in sick animals. Specifically, the number of white blood cells and their subpopulations acquired reference values. The content of C-reactive protein significantly increased by 40.8 times in sick animals on Day 7 of the study and decreased by 1.7 times on Day 14 compared to its values at the previous stage. At the same time, on Day 28, this indicator increased by 19.3 times compared to the indicators of the control group of animals. The rate of erythrocyte sedimentation in the blood of sick rabbits significantly increased by 2.3 times compared to the control group. On Day 21, this indicator in the blood of sick rabbits decreased by 1.4 times compared to its values on Day 14 of the experiment. On the other hand, on Day 28, its value increased by 1.7 times compared to the control (4.3 mm/h). The results obtained will contribute to further targeted laboratory diagnostics of knee osteoarthritis in animals, which will ensure the proper effectiveness of therapeutic and preventive measures and improve their overall health

Keywords: laboratory diagnostics, leukogram, C-reactive protein, erythrocyte sedimentation rate

Introduction

Osteoarthritis is a dystrophic joint lesion that develops due to degeneration of the articular cartilage. Therewith, the inflammatory process occurs with damage not only to the cartilage, but also to all components of the joint.

This disease is a substantial problem in veterinary practice and the most common joint pathology in animals. The incidence rate is 2.5-20% in young animals and 35-55% in geriatric animals (according to statistics from the veterinary clinic "Dunai", Kyiv).

New effective methods and means of treatment that give rapid results and substantially reduce the risk of side effects are being actively developed [1-3]. Intra-articular administration of autologous enriched plasma is performed, stem cells, joint replacement, or arthroplasty are

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used. Therewith, the economic efficiency of using these methods is important.

In rabbits and other domestic animals, osteoarthritis is described by certain changes in morphological and biochemical parameters of the blood. These biomarkers can be used both in preclinical and clinical studies. The main purpose of such studies is to establish the diagnosis, figure out the stage of the disease and monitor its course, confirm the pharmacological mechanism of action, demonstrate the biological mechanism of action and predict the clinical outcome of the disease [4-6].

It is believed that most animals with osteoarthritis do not have specific changes in the results of blood and urine tests, except for cases of synovitis with significant effusion of synovial fluid into the articular capsule. Therewith, hypergammaglobulinemia is registered in the blood of sick animals, which provokes a substantial increase in the rate of erythrocyte sedimentation, leukocytosis develops with changes in the leukogram and an increase in the level of acute phase indicators – C-reactive protein, fibrinogen, etc. [4; 6; 7].

C-reactive protein is one of the most common test indicators used in clinical laboratory practice to assess, diagnose, and predict inflammation. However, its role in physiological processes is not yet fully understood. This protein is the most sensitive indicator of tissue damage due to inflammation, necrosis, and trauma. It is the very first of the acute phase proteins actively produced by hepatocytes under pathogenic factors. Its content is mainly regulated by circulating interleukin-6. C-reactive protein belongs to the family of pentraxins, shows a 1000-fold or greater increase in concentration during the development of pathological processes in tissues [7; 8].

The half-life of C-reactive protein from the blood is about 19 hours and stays stable regardless of the animal's health status. Its high sensitivity and ease of analysis have made it an ideal marker of inflammation. It was discovered in 1930 by William Tillett [8] and Thomas Francis [8] of Rockefeller University. The researchers reported that the third serological fraction, or "fraction C," isolated from patients infected with pneumococci, differed from the capsule polysaccharide and nucleoprotein fractions that were detected by a specific antibody response. Oswald Avery and McLean McCarthy [8], who postulated the "transformation principle" and the concept that genes are made up of DNA, also described that the levels of C-reactive protein as an "acute phase protein" were elevated in the serum of patients with inflammatory processes. Volanakis and Kaplan [8] later identified specific ligands capable of binding to C-reactive protein. It was found that this protein performs the function of conjugating pathogens and inducing their destruction by the complement system. It has also been investigated as a screening marker of inflammation, disease activity, and as a diagnostic supplement. The exact role of C-reactive protein as an acute phase protein requires further evaluation. Such information focuses on its diagnostic significance in various diseases, as well as on established and contradictory evidence for its physiological role [7; 8].

The half-life of serum C-reactive protein in both clinically healthy rabbits and animals treated with inflammatory stimuli is 4-6 hours [7; 8]. The content of C-reactive protein in the blood serum of rabbits during an experimental study of the pathological process immediately increases, and its peak level is noted on the 3rd day after inoculation. Thus, it is believed that serum C-reactive protein is an informative marker of inflammatory processes existing in the animal body [7; 8].

The purpose of this study lies in the investigation of changes in the number of white blood cells and their subpopulations, the content of C-reactive protein and the rate of erythrocyte sedimentation in the blood of rabbits in experimental osteoarthritis of the knee joint.

Literature Review

Osteoarthritis is a degenerative-dystrophic joint disease that occurs due to the gradual physical destruction of articular cartilage [9].

Osteoarthritis is also known as the most common type of degenerative joint disease (DJD) and develops more often with age. Changes in osteoarthritis usually occur slowly over many years, although there are exceptions. Inflammation and joint damage cause bone changes, destruction of tendons and ligaments, and destruction of cartilage, leading to pain, swelling, and deformity of the joint [9; 10].

Dogs of different breeds are prone to developing osteoarthritis due to poor breeding. Dog breeds such as Labrador, springer spaniel, German shepherd, golden retriever, Rottweiler, and Bernese Mountain Dog are more susceptible to this joint pathology [2; 3; 9].

Any dog can develop osteoarthritis, especially with age [6-8]. However, there are some factors that can lead to its development in animals of large breeds (German shepherd, Labrador, golden retriever). These include obesity, age, especially middle-aged and older dogs; long-term exposure to stress factors during sports activities (flyball, diving); injuries such as fractures or torn ligaments; hip or elbow dysplasia; infections affecting the joints (Lyme disease); unbalanced diet and genetics [8; 9].

Osteoarthritis is also a severe problem in horses, which can develop regardless of their breed and age. On the territory of Ukraine, there are certain problems with the diagnosis of this disease in horses at an early stage because not all veterinary clinics can conduct such in-depth examinations of animals.

Unfortunately, osteoarthritis is a rapidly progressive disease, and there are no effective medications. Stabilization of the patient's condition is focused on relieving pain, reducing the inflammatory process, improving the quality of life, and slowing down the development of the disease. Treatment of osteoarthritis is usually multimodal, i.e., diverse treatment methods are used simultaneously to achieve the best result [9; 11; 12].

To improve joint function, reduce inflammation, and slow the progression of damage, dietary supplements are prescribed to animals [11; 12]. Glucosamine and chondroitin are two common ingredients in joint supplements used in both dog and human treatments. These supplements reduce inflammation, promote healing, and increase water retention in the cartilage, which provides better cushioning for the joint. Green-lipped mussel (GLM) is another proven dietary supplement ingredient for treating joint pathology in both animals and humans, which contains beneficial nutrients such as omega-3 fatty acids, glycosaminoglycans, and antioxidants. It is a powerful anti-inflammatory agent that reduces pain and preserves joint function. Supplements are

often used is animal diet during the progression of osteoarthritis because they are safe for long-term use [12].

Therefore, the use of dietary supplements in animals and the control of pain sensitivity by introducing nonsteroidal anti-inflammatory drugs are the basis for the treatment of osteoarthritis. The most common medications for pain relief in the more severe form of osteoarthritis are nonsteroidal anti-inflammatory drugs, which can both reduce pain and the progression of inflammation in the joints. However, these preparations have significant side effects with prolonged use, especially in patients with poor liver or kidney function. That is why it is necessary to consider the risks and benefits of treating animals with nonsteroidal anti-inflammatory drugs for osteoarthritis. Therewith, regular morphological and biochemical blood tests should be performed [10; 11; 13].

Notably, keeping an optimal body weight of animals and an active lifestyle affects the activity of the joints. In overweight animals with osteoarthritis, an increase in pain is observed, and the processes of cartilage destruction are accelerated [10; 11].

Timely and effective laboratory diagnosis of this pathology in animals is relevant precisely because standard treatment protocols for osteoarthritis of animals do not give positive results, and even lead to complications from the digestive system, liver, and kidneys.

Materials and Methods

The study was conducted in the scientific laboratory of the I.O. Povazhenko Department of Surgery and Pathophysiology of the Faculty of Veterinary Medicine of the National University of Life and Environmental Sciences of Ukraine during 2021-2022.

The study material was 24 clinically healthy male rabbits with a body weight of 2.5 to 2.8 kg. They were divided into two groups: control and experimental with 12 animals each. Animals of the control group were intra-articularly injected with isotonic (0.9%) NaCl solution in a dose of 0.7 ml. Experimental development of osteoarthritis was modelled in the animals of the experimental group by intra-articular administration of a 4% solution of retinol acetate and kojic acid (Yellow Peel preparation, Medicare, Germany) in a dose of 0.7 ml. Intra-articular injections were performed using a 23 G needle (0.6*32 mm) at intervals of 7 days, twice.

During the simulation of experimental osteoarthritis, a clinical examination of animals was performed, as well as a study of the number of white blood cells and their subpopulations in the blood, the content of C-reactive protein and the rate of erythrocyte sedimentation.

Blood for these studies was taken from animals of the control and experimental groups on Days 7, 14, 21, and 28 after modelling experimental osteoarthritis of the knee joint.

Experiments using laboratory animals were conducted in compliance with the requirements of the "General ethical principles for conducting experiments on animals", approved by the National Congress on Bioethics (09/20/2004, Kyiv, Ukraine) [14] and the provisions of the "European Convention for the protection of vertebrates used for experimental and other scientific purposes" (Strasbourg, 1986) [15], the Law of Ukraine "On the Protection of Animals from Ill-treatment" [16; 17].

The groups of values of indicators in dynamics were compared according to the Student's parametric criterion with the determination of the arithmetic mean (M) and its error (m). Differences between the two indicators of the compared samples at $P < 0.05$, $P < 0.01$, and $P < 0.001$ were considered statistically significant [18].

Changes in the number of white blood cells and their subpopulations in the blood were evaluated using BC-2800VET automatic haematology analyser (Mindray Building, Keji 12th Road South, High-tech Industrial Park, Nanshan, Shenzhen 518057, P. R. China) [19], within three hours after sampling.

The content of C-reactive protein was examined in the blood serum of rabbits using the Vcheck kit (manufactured by Bionote, Korea). The Vcheck kit is based on a fluorescent enzyme-linked immunosorbent assay for quantitative measurement of C-reactive protein concentrations. The concentration of this protein was found using a BIONOTE Vcheck analyser (manufacturer Bionote, Korea) based on the calibration curve data [20].

The rate of erythrocyte sedimentation in the blood was investigated according to the Panchenkov method [21]. According to this method, an anticoagulant was used – a 3.8% solution of sodium citrate. A chemical solution was added to a test tube containing capillary blood and placed vertically for 60 minutes. Therewith, red blood cells settled to the bottom of the test tube. The time it takes for them to settle is considered the rate of erythrocyte sedimentation.

The list of 20 criteria corresponding to the diagnosis of rheumatoid arthritis classified by the American Rheumatism Association includes an indicator of increased erythrocyte sedimentation rate. Most rheumatologists believe that an important diagnostic criterion is a thorough examination, which should confirm inflammation of the synovial membrane of the joint (synovitis). However, the erythrocyte sedimentation rate is a useful indicator in case of a doubtful diagnosis [10; 11; 22].

Results and Discussion

In case of joint diseases, it is important in diagnosis not only to take an anamnesis and a clinical examination, but also laboratory tests – counting the number of leukocytes, changes in the leukogram, the level of the erythrocyte sedimentation rate and the content of C-reactive protein in the blood serum. The research results are consistent with the results of a study by other authors [11; 23; 24].

It was found that on Day 7 of the experiment, changes in the number of white blood cells and their subpopulations in the blood of rabbits of the experimental group were noted (Table 1).

Table 1. The number of leukocytes and their subpopulations in the blood of rabbits on Day 7 of the experiment with experimental osteoarthritis (M ± m, n = 12)

Indicator	Control group	Experimental Group	Reference values
White blood cells (g/l)	5.4 ± 0.1	14.6 ± 0.2***	5-13
Neutrophils (%)	48.2 ± 0.9	52.5 ± 0.6***	34-70

Table 1, Continued

Indicator	Control group	Experimental Group	Reference values
Eosinophils (%)	0.9 ± 0.2	8.8 ± 0.5***	0-2
Basophils (%)	0.0 ± 0.0	0.3 ± 0.2*	0-0.8
Lymphocytes (%)	50.2 ± 1.1	23.2 ± 1.1***	43-80
Monocytes (%)	0.8 ± 0.3	15.2 ± 0.5***	0-4

Note: *P < 0.05; ***P < 0.001 compared to the control group of rabbits.

Based on the results of the study given in Table 1, it follows that on Day 7 of the experiment, a significant 2.7-fold (p < 0.001) increase in the number of white blood cells in the blood of sick rabbits (experimental group) is observed compared to the animals of the control group. This indicates an acute inflammatory process in the body of rabbits of the experimental group. The number of neutrophils, eosinophils, basophils, and monocytes in their blood was also significantly higher, 1.1 times (P < 0.001), 9.7 times (P < 0.001), 33% (P < 0.05), and 19 times (P < 0.001), respectively, compared to the control animals. At the same time, the number of lymphocytes in the blood of sick rabbits was significantly less by 2.2 times (P < 0.001) compared to the control. These changes indicate an inflammatory process caused in response to preparation administration and activation of nonspecific immunity in experimental osteoarthritis in animals of the experimental group. In rabbits of the control group, these indicators corresponded to the limits of reference values.

Consequently, experimental osteoarthritis causes a general inflammatory process in the body of animals of the experimental group, which is also consistent with experimental data of S. Chandrashekara [7].

The results of the study of the number of leukocytes and their subpopulations in the blood of rabbits on Day 14 of the experiment with experimental osteoarthritis are presented in Table 2.

Table 2. The number of white blood cells and their subpopulations in the blood of rabbits with experimental osteoarthritis on Day 14 of the experiment (M ± M, n = 12)

Indicator	Control group	Experimental Group	Reference values
White blood cells (g/l)	6.0 ± 0.1	14.2 ± 0.2***	5-13
Neutrophils (%)	47.6 ± 1.0	49.8 ± 0.6	34-70
Eosinophils (%)	0.8 ± 0.2	2.5 ± 0.2***	0-2
Basophils (%)	0.0 ± 0.0	0.6 ± 0.2**	0-0.84
Lymphocytes (%)	50.9 ± 1.2	42.1 ± 1.5***	43-80
Monocytes (%)	0.7 ± 0.2	7.1 ± 0.3***	0-4

Note: **P < 0.01; ***P < 0.001 compared to the control group of rabbits

Table 2 suggests that on Day 14 of the experiment, the number of white blood cells in the blood of rabbits of the experimental group significantly increased by 2.4 times (P < 0.001) compared to the control group of animals. Therewith, the number of eosinophils, basophils, and monocytes significantly increased, respectively, by 3.1 times (P < 0.001), by 60% (P < 0.01) and by 10.1 times (P < 0.001) compared to the control group. However, the number of lymphocytes in the blood of rabbits of the experimental group significantly decreased by 1.2 times (P < 0.001). There was no statistically significant difference between the neutrophil count in the experimental and control groups of animals.

Such changes in white blood cells in the blood of rabbits of the experimental group indicate the activation of specific factors of the immune system on Day 14 of the experiment (in the study, this is a response to the introduction of the preparation, but its concentration decreases).

As data in Table 2 suggests, in the control group of animals, the indicators of the number of white blood cells and their populations in the blood correspond to the limits of reference values, which is consistent with the research results of E. Oohashi *et al.* [8]. The research results on the number of white blood cells and their subpopulations in the blood of rabbits on Day 21 of the experiment with experimental osteoarthritis are presented in Table 3.

Table 3. The number of white blood cells and their subpopulations in the blood of rabbits with experimental osteoarthritis on Day 21 of the experiment (M ± M, n = 12)

Indicator	Control group	Experimental Group	Reference values
White blood cells (g/l)	5.4 ± 0.1	12.6 ± 0.2***	5-13
Neutrophils (%)	43.3 ± 1.1	48.1 ± 0.9	34-70
Eosinophils (%)	0.5 ± 0.2	2.4 ± 0.3***	0-2
Basophils (%)	0.0 ± 0.0	1.5 ± 0.2***	0-0.8
Lymphocytes (%)	51.9 ± 1.0	45.9 ± 0.9***	43-80
Monocytes (%)	0.4 ± 0.2	1.5 ± 0.2***	0-4

Note: ***P < 0.001 compared to the control group of rabbits

According to the results presented in Table 3, on Day 21 of the study, the number of white blood cells in the blood of sick rabbits was significantly higher by 2.3 times (P < 0.001), eosinophils – by 4.8 times (P < 0.001), basophils – by 1.5% (P < 0.001), monocytes – by 3.8 times (P < 0.001) compared to the control. At the same time, the number of lymphocytes significantly decreased by 1.1 times (P < 0.001). The number of neutrophils tended to increase in the blood of rabbits of the experimental group by 1.1 times. Changes in the number of leukocytes and their subpopulations in the blood of sick rabbits indicate an inflammatory process caused by a foreign agent (in the conducted study, this is a response to the administration of the preparation at a reduced concentration).

In the blood of the control group of animals, indicators (Table 3) correspond to the limits of reference values, which indicates the absence of an inflammatory process in the animal body.

The results of the study of the number of white blood cells and their subpopulations in the blood of rabbits on Day 28 of the experiment with experimental osteoarthritis are presented in Table 4.

Table 4. The number of white blood cells and their subpopulations in the blood of rabbits with experimental osteoarthritis on Day 28 of the experiment (M ± M, n = 12)

Indicator	Control group	Experimental Group	Reference values
White blood cells, (g/l)	5.3 ± 0.1	10.8 ± 0.1***	5-13
Neutrophils (%)	42.9 ± 0.9	46.5 ± 0.9**	34-70
Eosinophils (%)	0.5 ± 0.2	1.3 ± 0.2*	0-2
Basophils (%)	0.0 ± 0.0	0.7 ± 0.2***	0-0.8
Lymphocytes (%)	56.2 ± 0.9	49.3 ± 0.9***	43-80
Monocytes (%)	0.4 ± 0.2	2.4 ± 0.3***	0-4

Note: *P < 0.05; ***P < 0.001 compared to the control group of rabbits

As data from the Table 4 suggests, on Day 28 of the experiment, the number of white blood cells in the blood of rabbits of the experimental group significantly increased by 2.0 times (P < 0.001), neutrophils – by 1.1 times (P < 0.01), eosinophils – by 2.6 times (P < 0.05), basophils – by 0.7% (P < 0.001) and monocytes – by 6.0 times (P < 0.001) compared to animals of the control group. At the same time, the number of lymphocytes in the blood of rabbits in the experimental group significantly decreased by 11 times (P < 0.001) compared to the control group. These changes indicate an inflammatory process in the animal body, but the more time passes from the date of the last injection of the irritant, the less pronounced this inflammatory process becomes. In the blood of rabbits of the control group, the indicators corresponded to the limits of reference values.

It is known from the literature that C-reactive protein is a sensitive marker and is used to monitor inflammatory processes [2]. In animals of the experimental group for osteoarthritis, the content of C-reactive protein depended on the stage of development of experimental osteoarthritis. As Figure 1 shows, the content of C-reactive protein in the blood serum of animals of the experimental and control groups differed significantly, which corresponds to the research results of A. Hillström [2].

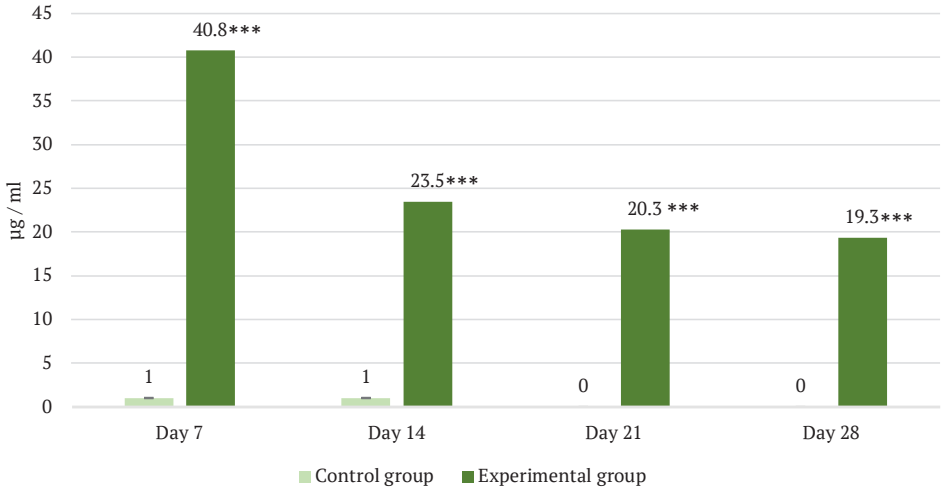

Figure 1. Evaluation of the level of C-reactive protein in the blood serum of rabbits of the control and experimental groups

Thus, on Day 7 of the study, the content of C-reactive protein in the blood serum of control rabbits was within the control values. In the blood serum of rabbits of the experimental group, the content of C-reactive protein significantly increased by 40.8 times ($P < 0.001$) compared to the control group (1 μg/ml), which indicates an acute inflammatory process in the animal body with experimental osteoarthritis.

On Day 14 of the study, the content of C-reactive protein in the blood serum of rabbits in the experimental group increased by 23.5 times ($P < 0.001$) compared to animals in the control group, where its concentration stayed unchanged and on average corresponded to the value of 1 μg/ml. Therewith, the content of this protein decreased by 1.7 times compared to that on Day 7 of the study. At the same time, in the control group of rabbits, the content of C-reactive protein in the blood serum was within the control values. This points to a decrease in the concentration of an irritating substance in the animal body, which was used to simulate experimental osteoarthritis.

On Day 21 of the study, the C-reactive protein content in the blood serum of rabbits in the control group corresponded to the range of reference values. In rabbits of the experimental group, the indicator of this protein content significantly increased by 20.3 times ($P < 0.001$) compared to animals of the control group, where it was 0 μg/ml. Notably, the concentration of this protein in the blood of rabbits of the experimental group was 1.2 times lower ($P < 0.001$) compared to the indicator on Day 14, as well as 2.0 times relative to Day 7.

On Day 28 of the experiment, the content of C-reactive protein in the blood serum of rabbits in the control group corresponded to the limits of reference values. In the blood serum of animals of the experimental group, this indicator increased by 19.2 times ($P < 0.001$) compared to the control (0 μg/ml). The content of C-reactive protein in the blood serum of rabbits of the experimental group decreased by 1.1 times compared to its value on Day 21 of the study. This indicates the course of an acute inflammatory process.

Thus, the study of the content of C-reactive protein in the blood serum of animals can be used for rapid diagnosis of inflammatory diseases of the joints. The presence of this inflammation marker in the blood serum of rabbits of the experimental group indicates that after modelling the inflammatory process in the knee joint during the first week of the study, an acute inflammatory process occurred as a reaction to an irritating substance. In the period up to the fourth week of research, the content of this protein decreased, but compared to its values in the control, it stayed elevated. The results of these studies are consistent with the data of other authors [2].

Therewith, a study was conducted to find the rate of erythrocyte sedimentation in the blood of rabbits with experimental osteoarthritis (Fig. 2). Thus, on Day 7 of the experiment, in the blood of animals of the experimental group, the value of this indicator increased by 2.3 times ($P < 0.001$) compared to that in animals of the control group (4.8 mm/h).

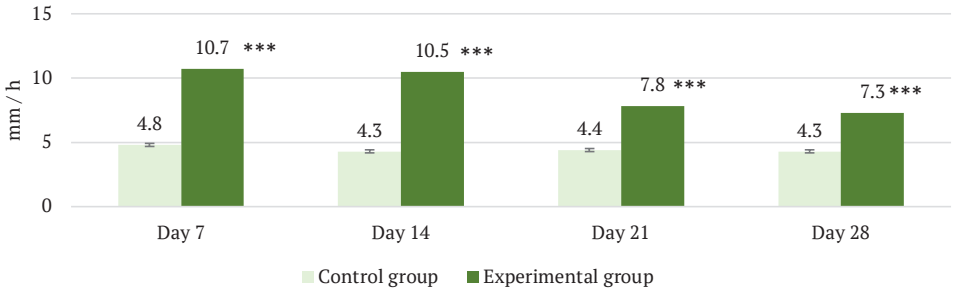

Figure 2. Changes in the rate of erythrocyte sedimentation in the blood of experimental rabbits

It is known from the literature sources that an increase in the rate of erythrocyte sedimentation indicates an inflammatory process in the animal body [21; 25; 26]. The mechanism of this phenomenon is explained by a decrease in the electrical charge of blood cells due to the adsorption of acute phase inflammatory proteins on their surface.

On Day 14 of the study, a 2.4-fold increase in the erythrocyte sedimentation rate ($P < 0.001$) was observed in the blood of animals of the experimental group compared to the control (4.3 mm/h). On Day 21 of the experiment, a 1.4-fold decrease in the value of this indicator was noted in the blood of these rabbits compared to the previous period. However, the rate of erythrocyte sedimentation in the blood of rabbits of the experimental group increased by 1.8 times ($P < 0.001$) compared to animals of the control group (4.4 mm/h).

On Day 28 of the study, a decrease in the rate of erythrocyte sedimentation in the blood of rabbits was noted compared to that on Day 21 of the study. Therewith, this indicator in the blood of rabbits of the experimental group increased by 1.7 times ($P < 0.001$) compared to animals of the control group (4.3 mm/h).

Thus, an increase in the rate of erythrocyte sedimentation in the blood of animals of the experimental group is connected with the fact that modelling experimental osteoarthritis in rabbits provokes not only a local, but also a systemic inflammatory process. The results of these studies are consistent with the data of other authors [21; 24].

Therefore, leukocytosis, an increase in the level of C-reactive protein, and an increase in the rate of erythrocyte sedimentation in the blood of rabbits with experimental osteoarthritis are a significant sign of the presence of an inflammatory process in the body, which is consistent with the results of the study by Legrand *et al.* [4].

Conclusions

It was found that in the blood of rabbits with artificial modelling of osteoarthritis of the knee joint, the development of leukocytosis is observed, which is especially pronounced on Days 7 and 14 of the experiment. An increase in the

number of leukocytes in the blood of sick animals indicates not only a local inflammatory process in this joint, but also a generalized nature of the pathology, to which the body's immune system reacts.

A significant increase in the number of neutrophilic granulocytes in the blood of sick animals during the experiment also indicates an inflammatory process in the body. The number of eosinophils in the blood of these rabbits increases by Day 7 and decreases by Day 28, which indicates a direct dependence of the synthesis of immune system cells in such animals in response to the irritating effect of intra-articular administration of retinol acetate and kojic acid. The increase in the number of basophils during the experiment is obviously caused by the active proliferation and differentiation of haematopoietic stem cells in the bone marrow of animals. The decrease in the number of lymphocytes in the peripheral blood of sick rabbits is probably explained by the accumulation of lymphocyte clones in the peripheral organs of the immune system (lymph nodes, spleen) to activate the synthesis of immunoglobulins and cytokines, which ensure the cooperation of cellular-humoral links of immunity in experimental osteoarthritis in the knee joint. Therewith, monocytosis is associated with the reaction of immune system cells to a local inflammatory process in the animal body.

The content of C-reactive protein in the blood serum of rabbits with experimental osteoarthritis of the knee joint increases by 40.8 times on Day 7 of the experiment and decreases on Days 14, 21, and 28.

In experimental osteoarthritis of the knee joint, the blood of rabbits shows an increased rate of erythrocyte sedimentation, which is also one of the markers of the inflammatory process in their body.

Further research in this area may accelerate the early diagnosis of osteoarthritis of the knee joint, which will improve the effectiveness of treatment in the preliminary stages of the development of the pathological process. This will also contribute to further quality control of therapy to improve the clinical condition of animals and timely prevent further joint destruction.

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Зміни кількості лейкоцитів і неспецифічних маркерів запалення в організмі кролів за експериментального остеоартрозу колінного суглобу

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Анотація. Остеоартроз є найпоширенішим захворюванням суглобів у тварин, яке не завжди піддається лікуванню. Як у ветеринарії, так і в медицині для ефективної діагностики цієї патології використовують лабораторні методи дослідження. Метою роботи було визначення динаміки маркерів гострої фази запалення в крові за експериментального моделювання остеоартрозу колінного суглоба в кролів. Штучне відтворення патологічного процесу в колінних суглобах тварин здійснювали шляхом внутрішньосуглобового введення препарату Yellow peel 2*5 ml. Для підрахунку кількості лейкоцитів та їх субпопуляцій в крові використовували автоматичний гематологічний аналізатор BC-2800Vet. Уміст С-реактивного білка у сироватці крові визначали за допомогою імуноферментного аналізу. Швидкість осідання еритроцитів у крові досліджували за методом Панченкова. Так, на 7 добу в хворих кролів відмічали різке підвищення кількості лейкоцитів (у 2,7 раза) та їх субпопуляцій, що вказує на активний запальний процес системного характеру. На 14 добу їх кількість в крові хворих тварин характеризувалася тенденцією до зменшення, проте вона ще не досягала значень показників контрольної групи. На 21 і 28 добу всі досліджувані показники в хворих тварин мали тенденцію до зменшення. Зокрема, кількість лейкоцитів та їх субпопуляцій набувала референтних значень. Уміст С-реактивного білка вірогідно підвищувався в 40,8 раза у хворих тварин на 7 добу дослідження та зменшувався в 1,7 раза на 14 добу порівняно з його значеннями на попередньому етапі. Водночас на 28 добу цей показник зростав у 19,3 раза порівняно з показниками контрольної групи тварин. Швидкість осідання еритроцитів у крові хворих кролів вірогідно зростала в 2,3 раза порівняно з контрольною групою. На 21 добу цей показник у крові хворих кролів знижувався в 1,4 раза порівняно з його значеннями на 14 добу експерименту. Натомість, на 28 добу спостереження його величина зростала в 1,7 раза порівняно з контролем (4,3 мм/год). Отримані результати сприятимуть надалі проведенню прицільної лабораторної діагностики остеоартрозу колінного суглобу в тварин, що забезпечить належну ефективність лікувально-профілактичних заходів та покращення загального стану їхнього здоров'я

Ключові слова: лабораторна діагностика, лейкограма, С-реактивний білок, швидкість осідання еритроцитів