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Methods for modeling osteoarthrosis of large joints

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Abstract. The methods of modeling osteoarthritis of large joints in the experiment are described. Based on the literature data, the technological methods of modeling osteoarthritis in laboratory animals were analyzed and summarized. It is shown that the existing experimental models are not universal and, as a rule, reflect one of the links of etiopathogenesis. Practical recommendations are given on the choice of technological methods depending on the research objectives.

Keywords: osteoarthritis, experimental models, large joints.

The great interest in experimental models of osteoarthritis is explained by the widespread prevalence and high social significance of this pathology. Among all joint diseases, osteoarthritis is the main nasology, its frequency in the population can be compared with that in colds and viral diseases [1-3]. The economic damage from this disease amounts to millions of dollars, for example, in the United States, the cost per patient suffering from osteoarthritis in 2004 amounted to 5700 dollars. [4]. Modeling osteoarthritis in laboratory animals when studying the effectiveness of certain methods of treatment is a common practice. Since mechanical stress is essential in the

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pathogenesis of degenerative-dystrophic and inflammatory processes in cartilaginous tissue [5–7], the most clinically significant is the modeling of osteoarthritis of large joints, in particular of the knee [8,9]. Currently, a significant number of such models have been proposed, each of them has its own characteristics. First of all, this concerns the methods of formation, timing, severity and dynamics of the development of pathological processes in the joint. Various types of laboratory animals are used. The variety of the described experimental models of osteoarthritis dictates the need to structure and generalize the available information.

The purpose of the review is to analyze the technological methods of modeling osteoarthritis in animals.

The analysis of sources of scientific libraries, medical databases of the Internet (PubMed, ScienceDirect), patents.

In the modern scientific literature, osteoarthritis is considered as a heterogeneous group of diseases of various etiologies with similar biological, morphological and clinical manifestations [10–12].

Often, osteoarthritis is modeled by injecting agents into the joint that have a significant damaging effect on the elements of the joint. For example, work [13] describes a method for modeling osteoarthritis by two intra-articular administration of 1 unit to mice. collagenase VII (from Clostridium histolyticum) 2 days apart; possible introduction into the knee joint of sodium salt of monoiodoacetic acid [14], dexamethasone [15]. The known method consists in the introduction of vitamin A into the joint of laboratory rats once a day, at the rate of 13.5-13.9 mg per 1 kg of body weight, for 2 days, which disrupts the processes of synthesis / resorption of joint tissues and leads to pronounced inflammatory and destructive changes in the joint and paraarticular tissues [16].

A large number of surgical methods for modeling osteoarthritis have been proposed. One of the most radical can be considered the method of forming experimental arthritis of the knee joint by removing the lateral femoral condyle in

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rabbits [17]. A more gentle method is the application of defects of varying severity to the articular surface and damage to the ligamentous apparatus. For example, there is a known method for modeling post-traumatic arthrosis of the hip joint in rats by applying a standard defect in the form of a round hole 2 mm in diameter, penetrating through the articular cartilage into the subchondrial bone [18]. In [19], to simulate osteoarthritis in dogs, a defect in the form of a groove was applied in the loaded area of the femoral condyle without damaging the subchondral bone. Inflammatory and degenerative-dystrophic changes by damage to the ligamentous apparatus, as a rule, are caused in the knee joint. The anterior cruciate ligament is often transected - this technique is used in dogs [20], rabbits [21–23], and rats [24]. In addition to the anterior cruciate ligament, other elements of the joint can also be damaged. So, in [25], the removal of the medial meniscus was added to the intersection of the indicated ligament, the article [26] describes the modeling of osteoarthritis by transection of the medial collateral ligament and complete (full thickness) dissection of the meniscus; in the study [27], the intersection of the medial collateral and both cruciate ligaments with resection of the medal meniscus of the knee joint.

In addition to causing mechanical trauma, when modeling osteoarthritis, the effect of low temperatures can be used, as reported in [28, 29]. There is a known method for modeling a destructive-dystrophic process in the joint, which consists in a direct effect on the articular cartilage with a stream of para-liquid nitrogen under a pressure of 0.2–0.6 atm for 4–8 s [30].

It should be noted that osteoarthritis can be caused without directly affecting the joint. In this regard, of interest is the message [31], which proposes a method for the formation of osteoarthritis in guinea pigs, the essence of which is bilateral oophorectomy. Signs of the disease, according to electron microscopy, appear as early as 6 weeks, after 12 weeks severe degenerative damage to the cartilage is noted.

A special place is occupied by models of spontaneous osteoarthritis, developed for various animals: guinea pigs [32], dogs [33], Syrian hamsters [34], mice [35].

Today they are quite popular in experimental studies, especially when it comes to the use of genetically modified transgenic mice, in which premature cartilage degeneration occurs [36].

A certain influence on the dynamics of the course of osteoarthritis can be exerted by regulating the load on the affected joint. For example, in a study [5] on a model of spontaneous osteoarthritis, it was demonstrated that in guinea pigs on a restricted diet, osteoarthritis developed less frequently and was less severe. In the article [36], it is proposed to regulate the severity of the pathological changes that arise after the intersection of the anterior cruciate ligament and removal of the medial meniscus, varying the amount and duration of physical activity on the damaged joint.

When planning experimental work, the researcher is faced with the need for a critical analysis of the advantages and disadvantages of experimental models of osteoarthritis in relation to specific conditions, which, due to their sufficiently large number and variety, presents certain difficulties.

For convenience of consideration, all experimental models of osteoarthritis on the basis of their common features can be conditionally divided into groups (table). First of all, non-surgical and surgical methods of modeling can be distinguished.

The non-surgical group of experimental models favorably differs in "non-invasiveness", but it also has a significant drawback - it takes a long time for the development of serious pathological changes in the cartilage tissue. In addition, in these cases, the contralateral joint cannot be used as a control joint.

Surgical models of osteoarthritis are the most numerous and used most often. As a rule, a direct effect is exerted on the joint: the introduction of chemicals, the use of physical factors, the application of mechanical trauma. The disadvantages of these models include their rather high trauma, a certain labor intensity, the risk of infection of the joint.

Thus, all existing experimental models reflect the polyetiology of osteoarthritis associated with the pathogenetic mechanisms of the process,

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in which an imbalance between catabolic and anabolic processes leads to the degradation of cartilage tissue. Changes in the mechanical properties of cartilage are observed, which depend on the correct ratio of collagen, proteoglycans and water in the tissue; as a result, its shock-absorbing and mechanical properties decrease. This condition can be caused in different ways, the main thing is that the influence of the pathogenetic factor is sufficient in strength and duration. With the progression of osteoarthritis, the cartilage softens, loosens, cracks appear in it, extending to the bone. Bony articular surfaces, deprived of shock absorption due to the destruction of cartilaginous tissue, experience increased and uneven mechanical stress. Zones of dynamic overload appear in the subchondral bone, causing disturbances in microcirculation. This situation contributes to the occurrence of microfractures, subchondral osteosclerosis, cystic restructuring, changes in the curvature of the articular surfaces, which in turn can lead to the formation of bone and cartilaginous growths - osteophytes.

When modeling osteoarthritis, such risk factors as age, gender, as well as mechanical and hormonal factors must be taken into account [17]. The more risk factors are taken into account in the development of a particular experimental model, the easier it is to form characteristic changes in the cartilage tissue and other elements of the joint. It should not be forgotten that none of the experimental models in animals can reproduce a pathological process identical to that in human osteoarthritis [27].

Consequently, the existing experimental models of osteoarthritis are not universal and, as a rule, reflect one of the links in etiopathogenesis. When choosing technological methods for modeling osteoarthritis of large joints, it is necessary to focus on the tasks of the study: studying one or another link of pathogenesis or determining the effectiveness of therapeutic measures. The choice of this or that model depends on the goal set by the experimenter. If it is necessary to obtain a pronounced destructive process in the shortest possible time, then preference should

be given to methods involving the destruction of the articular surface with damage to the subchondral bone plate. To study the repair processes of only cartilaginous tissue, the defect must be localized within the cartilage. In the case when it is necessary to assess the effect of any therapeutic agent on all elements of the joint washed by the synovial fluid, with minimal trauma of the procedure, models with the use of intra-articular injections can be recommended. For the development of methods for the correction of pathological processes developing in violation of the biomechanics of joints in athletes, it is most expedient to dissect the ligaments and / or menisci. In a situation where it is important not to exert a direct effect on the joint, you can resort to bilateral ovarian removal in guinea pigs or choose models of spontaneous osteoarthritis.

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