

NOLTREX IN THE TREATMENT OF CANINE OSTEOARTHRITIS

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Summary

There are presented data on the use of the substitute synovial fluid Noltrex to 18 dogs of different breeds and ages in two veterinary clinics in Moscow and Kurgan in 2015 – 2016. An assessment of its clinical efficacy for dogs with primary and secondary osteoarthritis of various geneses of shoulder, elbow, hip and knee joints was carried out.

Key words: synovial fluid, osteoarthritis, dog, endoprosthetics.

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INTRODUCTION

Osteoarthritis is a joint disease with predominance of degenerative and dystrophic changes in the cartilage and then in the surrounding bone tissue. It is the most common pathology of locomotor system in mature dogs of larger breeds and dogs of breeds which are genetically prone to osteodystrophy at any age. Primary osteoarthritis appears as a natural biological aging process, but the secondary osteoarthritis is the consequence of congenital abnormalities of the joint, trauma, infectious or endocrine disease, obesity, long periods of joint overloads and etc. Osteoarthritis in the generalized form can affect several joints at once, which leads to a conjoint lameness or complete refusal of the animal to move.

Age related cartilage tissue degeneration becomes a cause of low joint mobility and increases the risk of development of this pathology [9]. Additionally, such condition is characterized in an animal by discomfort, the decrease of motor activity and pain. More than 75% of cases are resulted in lameness [6]. Pain syndrome as the main osteoarthritis symptom [10] leads to the muscular mass decrease in the affected limb and requires various NSAIDs, that cause complications such as erosive gastritis, intestinal hemorrhages, etc.

There are usually three osteoarthritis grades identified depending on the joint damage severity (Fig 1).

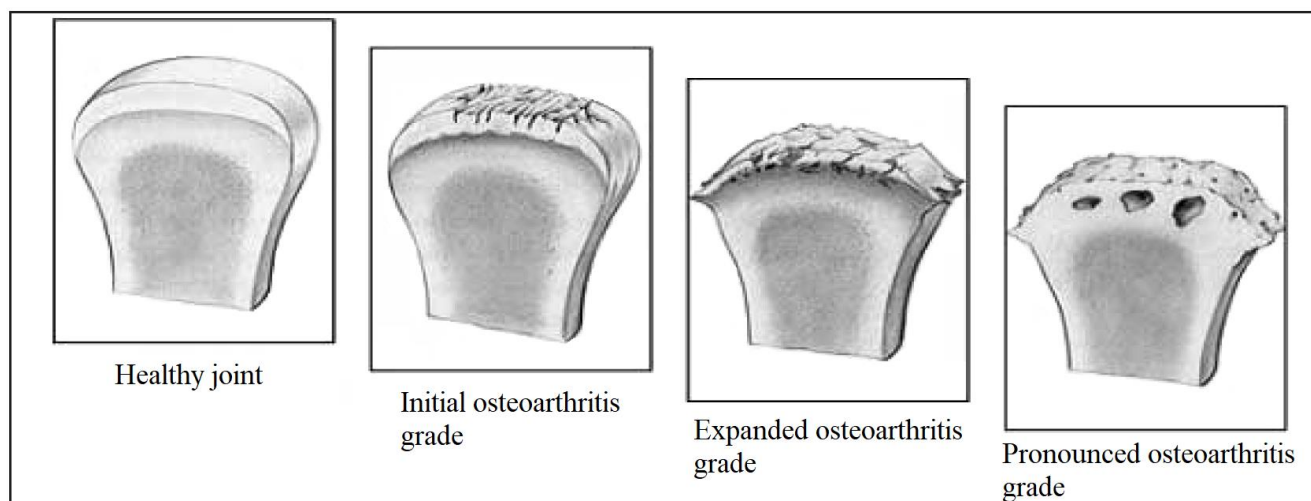


Fig.1. Joint changes during osteoarthritis.

Despite the widespread development of methods of surgical treatment of affected joints, in many cases this is not possible due to the risk of using anesthesia in elderly patients. Should also take into account that endoscopic operations and total arthroplasty of joints require complex equipment of the veterinary clinic.

In osteoarthritis, the secondary reactive synovitis develops against the background of a decrease in the concentration and average molecular weight of hyaluronic acid in the synovial fluid. This fact served as the basis for injecting hyaluronic acid into the joints of dogs. Almost all veterinarians, specialized in surgery and orthopedics of small domestic animals, at inflammatory processes in the joints of animals use Lidase, Hyastat®, Ostenil®, Fermathron® and other products containing hyaluronic acid or its derivatives. The duration of their action depends on the molecular weight. The most effective are hyaluronic acids with an average molecular weight of about 2000 kDa. Often at the site of their injection there is pain and an acute inflammatory reaction occur. Exogenous hyaluronic acids are removed from the joint in three phases (half-life of 2 hours; 1.5 days and 4 weeks). Therefore, in order to achieve a long-term therapeutic effect, it is necessary to inoculate them at least 5 times [5].

Injecting the synthetic synovial fluid substitute into the affected joint helps to reduce the friction of the articular surfaces, hyperpression and mediated pain syndrome. In many cases, the therapeutic effect is short-lived.

In 2004 Research Center Bioform LLC registered a new endoprosthesis of synovial fluid Noltrex. By composition it is a high-viscosity biopolymer, a mixture of 3D polyacrylamide ($4.0 \pm 1.5\%$), purified water ($96 \pm 1.5\%$) and silver ions ($0.0001 - 0.0025\%$). **Noltrex molecular weight is over 10 million Dalton!** The product is a high-density gel. It compensates the lack of synovial fluid in the joints affected by osteoarthritis of any stage. The manufacturer claims that the layer of hydrogel creates cushioning effect, which dampens

mechanical stress on the joint, and that in turn preserves the cartilage integrity and prevents its further destruction. At the same time, the articular cavity expands as the synovial fluid viscosity is restored to normal (so the contacting surfaces in the joint are physically moved away from each other) and the mechanical protection of the articular cartilages is ensured. By neutralizing the pain syndrome this synovial fluid prosthesis increases the affected joint mobility for a long period due to slow biodestruction of the polymer. In medical practice Noltrex injections allow doctors to delay or avoid surgical prosthetic reconstruction of the joint [1].

The product is supplied ready for use in the plastic syringe with Luer-Lock™ fitting. The consumer package includes sterile injection needles 18Gx½” and 21Gx½”. The volume of gel contained per syringe and the shelf-life (24 month) are indicated on the package. Noltrex is stored at temperature from 1 to 30 °C. It is not recommended to expose to the direct sunlight or freeze. Before injection it is recommended to evacuate any free joint fluid or inflammatory exudate (if any). Since this product does not contain any antimicrobial components, it is not used as the main remedy for infectious arthritis.

Noltrex is a low-contrast object, at ultrasound examination it is barely seen inside the joint.

In 2012 the product was assessed in regards to its use for the induced arthritis treatment in laboratory animals at the Federal State Budgetary Educational Institution of Higher Professional Education Skryabin Moscow State Academy of Veterinary Medicine and Biotechnology (FGBOU VPO n.a. Skryabin KI MSAVMB). The viscoprosthesis optimized chondro- and osteogenesis in the damaged knee joint, with the formation of integral articular tissue covering [8].

The purpose of this work is to evaluate the effectiveness of Noltrex in osteoarthritis (OA) in dogs.

MATERIALS AND METHODS

The work was conducted in veterinary clinics “Vetmir” (Moscow) and “Endovet” (Kurgan) on 14 and 4 dogs respectively of different breeds (German Shepherd, Great Dane of Bordeaux, African Boerboel, Labrador, Cane Corso, Bedlington Terrier, Dachshund, Chihuahua, Yorkshire Terrier, mestizo dogs) at age of 1-12 years. Owners addressed the lameness, decreased motor activity and the pain go syndrome in their pets. Their clinical examination revealed moderate swelling, crepitation and pain at joint flexion, and partial atrophy of the flexor muscles of the extremities.

On X-rays of various joints affected by osteoarthritis, a narrowing of the joint space was

usually observed, subchondral osteosclerosis, osteophytosis (Fig. 2-6).

In the Moscow clinic, as a result, the animals with osteoarthritis caused by hip dysplasia, habitual dislocation of the patella, rupture of the anterior cruciate ligament, and dysplasia of the cubitus joint were selected, as well as dogs with complications after operations on the knee joint. This pathology was determined based on the results of X-ray and ultrasound examinations. In the clinic in Kurgan the dogs with osteoarthritis of the shoulder and elbow joints (the diagnosis was made taking into account the data of X-ray and arthroscopic studies) were

selected. The animals had a history of joint dysplasia and delaminating osteochondritis.

Prior Noltrex injection all the animals were subjected to the treatment with medications including NSAID injections without significant

clinical improvement. Two of the dogs, according to their medical history, had previously undergone surgery to repair a torn anterior cruciate ligament of the knee joint and remove the menisci, and the other two had arthroscopic operations.



Fig.2. Great Dane of Bordeaux.

Hip joint with OA caused by dysplasia and chronic subluxation. There are additional bone tissue layers on the femoral neck, pathological changes in the femoral head and acetabulum.



Fig.3. African Boerboel.

The knee joint with OA, accompanied by osteophytes on the articular surfaces of the femur and tibia, as well as on the patella.



Fig.4. Great Dane of Bordeaux.

Shoulder joint with OA, caused by cartilage usuration and degenerative changes in the subchondral space of the shoulder howling bone.

After diagnosis, the animals were fixed in a lateral position, the injection site was antiseptically prepared with iodine-free antiseptics, and a synovial fluid substitute was injected into the affected joints. Then, a slight flexion, extension, adduction, abduction, and rotation of the treated joint was performed, and they were placed on an even surface for assessing gait and the pain severity (Fig. 7).

The animals were observed regularly for 6 to 12 months, assessing the change in the musculoskeletal function of the affected extremities. The speed and duration of the clinical effect of the synovial fluid substitute were also taken into account. The locomotor function of the affected extremity was compared before and after its inoculation, the signs of muscle atrophy and contractures, the intensity of pain and crepitation in the joint area, as well as

negative side effects. The degree of pain and the functional state of the affected joints were determined immediately after the injection of the

product, the next day, 2 weeks later and a few months later.



Fig.5. German Shepherd dog.
Elbow joint with OA, accompanied by narrowing of the articular space and osteophytosis of the joint capsule.



Fig.6. Bedlington Terrier.
Wrist joint of a with OA, caused by the syndrome of weakness of the wrists at a young age.

When using Noltrex, no other treatment methods were used. In the vast majority of cases, it was administered as single injection into 1 or 2 affected joints of the same name. In several animals, the product was injected twice with the 2-week interval.

This procedure was performed without sedation, with the exception of 1 animal. In 2 cases, inhalation anesthesia was required, since one dog underwent arthroscopy, and the other (Chihuahua) required anesthesia for any type of manipulation.

Large breed dogs with generalized osteoarthritis Noltrex was simultaneously injected into 3 and 4 joints. So, in a 12-year-old German Shepherd, the synovial fluid substitute was injected into both elbow joints and into one knee joint; the African Boerbol was injected into both elbow and both knee joints. For small-breed dogs the preparation was used at a dose of 1 ml/joint, for large-breed animals - 2.5 and 5 ml/joint.

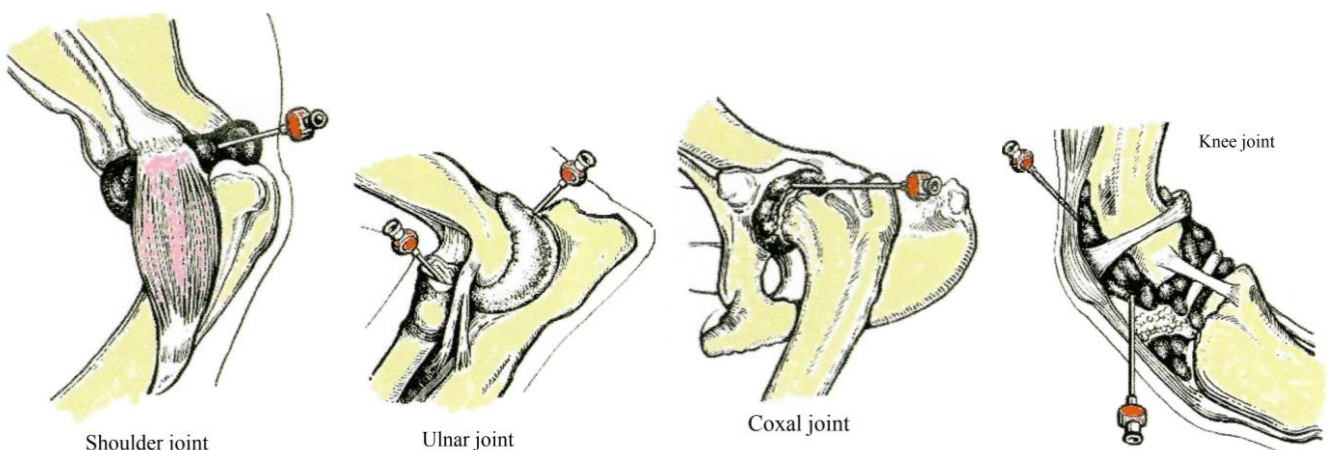


Fig.7. Injection of Noltrex into several joints.

RESULTS

At intra-articular administration of Noltrex, 2 dogs of small breeds showed a pain reaction, 4 individuals experienced discomfort directly in the process of conducting the procedure, but after walking this effect disappeared within 15-20 minutes.

Starting from the next day after the administration of the product, the pain syndrome in the animals decreased or completely stopped. In 6 cases, the therapeutic effect became more pronounced after repeat injections carried out at intervals of 2 weeks.

In one dog after injection of Noltrex in 3 joints, clinical and functional effects could not be achieved in one of the elbow joints. The pain syndrome and partial lameness in this patient remained, but the

dynamic capabilities of the limbs were improved through the reduction of loads on the joints and muscles. In 17 (94 %) animals the lameness significantly decreased or completely disappeared. Also, over time the pain syndrome disappeared. Improvement of the motor function of the joints was manifested in 1 dog for 6 months, and in all others - 12 months (see the table). Among 4 animals, joint crepitation was still registered after 6 months of observation, but the locomotor function of limbs was preserved. One animal (German Shepherd) after Noltrex injection was still limping and had pain syndrome, but it should be mentioned that this particular dog had insufficient exercise and was overweight.

Table. Noltrex effectiveness for osteoarthritis treatment in dogs (number of animals/ %), comparison.

| Assessment criterion/time | Before the product injection | After the injection | 2 weeks after | 6 months after | 12 months after |
|---------------------------|------------------------------|---------------------|---------------|----------------|-----------------|
| Lameness | 18 / 100% | 2 / 11% | 3 / 17% | 1 / 6% | 1 / 6% |
| Pain syndrome | 17 / 94% | 6 / 33% | 3 / 17% | 1 / 6% | 1 / 6% |
| Crepitation | 17 / 94% | 4 / 22% | 5 / 28% | 4 / 22% | 4 / 22% |
| Muscle atrophy | 18 / 100% | - | 4 / 22% | 3 / 17% | 2 / 11% |
| Contracture | 8 / 44% | 8 / 44% | 2 / 11% | 1 / 6% | 1 / 6% |

CONCLUSION

Noltrex allows for the correction of the synovial fluid viscosity lost as a result of the disease, helps to reduce further degeneration of articular cartilage. With its help it is possible to suppress the pain syndrome and restore the motor function of the joints, which significantly improves the quality of life of dogs at any osteoarthritis stage. The method of application of product is not complicated, but

because of its significantly high density, it is administered for 15 to 20 seconds per dose, which in some cases requires sedation of animals. It can be periodically administered to dogs with chronic osteoarthritis (1- 2 times in 6-12 months). The widespread use of Noltrex in veterinary practice is also justified from an economic point of view against the background of expensive surgical intervention.

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