Regular Article

Effect of an Oral Joint Supplement When Compared to Carprofen in the Management of Hip Osteoarthritis in Working Dogs

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The goal of this study was to evaluate the effectiveness of an oral joint supplement in working dogs with hip osteoarthritis compared with a positive control group (CG). Fifteen animals were divided in treatment group (TG, $n = 10$) and CG ($n = 5$). To TG a commercially available joint supplement, containing glucosamine HCl, chondroitin sulphate, and hyaluronic acid was given for 40 days and a 70-day course of a placebo, to be administered as if it was carprofen. The CG received carprofen for 70 days, and a placebo to be administered as the joint supplement. Response to treatment, measured by the canine brief pain inventory (CBPI) and the Hudson visual analog scale, was evaluated before treatment (T0), after 15 days (T1) and 1 (T2), 2 (T3), 3 (T4), 4 (T5), and 5 (T6) months. With CBPI, no differences were found in pain interference score and pain severity score between TG and CG throughout or when comparing results within groups. Individual results were considered successful in a maximal of three dogs of the TG by T3 (30%) and 1 in CG (25%). With Hudson visual analog scale, improvements where registered with individual results, for 40%-50% of the animals in TG and 60%-80% of cases in CG. The oral joint supplement and carprofen produced some improvements in individual scores but where unable to do so when overall results were considered. Each of these options may not be able, by itself, to fully address the demands of a working dog with joint disease and related pain.

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Introduction

Osteoarthritis in dogs is a slowly progressive, degenerative, and active disease, affecting up to 20% of all dogs over 1 year of age.[1] It can impose severe changes over articular cartilage, with loss of matrix, a reduction in the rate of synthesis and imbalance between proteolytic enzymes, their inhibitors and proinflammatory cytokines, that eventually lead to complete cartilage surface loss.[2-4] It is the most commonly diagnosed arthropathy in animals and is due to a variety of factores, like laxity or malalignment of joints, trauma, excessive work, and genetic factors. Diagnosis is based on history and sign, such as pain and stiffness, and radiographic examination of affected joints, commonly featuring periosteal proliferation, deformity of subchondral bone, and narrowing of joint spaces.[5-7]

The most common treatment for the management of osteoarthritis related pain and symptoms, consist of nonsteroidal anti-inflammatory drugs (NSAIDs), given per os. The risk of side-effects associated with long-term courses of NSAIDs, has led to an have increased interest in disease modifying agents such as nutraceuticals, even though there is some evidence to support the long-term use of NSAIDs for an increased clinical effect.[8] Nutraceuticals have also been proposed to reduce clinical signs, while preventing the degenerative process evolution, although there are limited numbers of rigorous randomized controlled trials available.[4,5,9-12]

Glucosamine is considered a "chondroprotective" agent, since it modulates the metabolic activity of chondrocytes, having a disease-modifying effect. In vitro, it has shown to have the ability of reducing matrix molecule degradation and enhancing synthesis.[6,13] Chondroitin is the major glycosaminoglycan found in the cartilage of moving joint surfaces while hyaloronic acid is one of the major molecular components of joint fluid.[1] The previous two (Glu/CS) act as the substrate for the production of aggrecans and inhibit IL-1 induced COX-2 and PGE_2 synthesis.[2] The use of

multicomponent formulations seem to be a trend, with the idea that several components will act in multiple targets, with a combined optimal effect.[14]

The canine brief pain inventory (CBPI) was developed as a questionnaire destined to the owner, for the assessment of their perception of the effect of chronic pain in their own dog and validated as a health-assessment questionnaire.[15] It has been used to detect improvements in the treatment of osteoarthritis in dogs receiving NSAIDs and autologous platelet therapy.[16,17]

The Hudson visual analog scale (HVAS) has been found to be repeatable and valid in the assessment of mild-to-moderate lameness in dogs. This questionnaire was elaborated having as a criterion-reference standard force plate analysis.[18] Both these assessment tools have been used before with good correlation with hip osteoaoarthritis related chronic pain in dogs.[11]

The objective of this study was to evaluate the effectiveness of a commercial available joint supplement in working dogs, its effect in reducing pain and compare its results with a positive group. To our knowledge, the effect joint supplements and even carprofen in working dogs has not been accessed before. We hypothesize that joint supplements can reduce individual pain scores in police working dogs with hip osteoarthritis for a period longer than that of administration of the supplement.

Materials and Methods

The study's protocol was approved by the Ethical Review Group of the Association of Veterinary Anaesthetists (No. 2017-002) and complies with the NIH guidelines for Humane Care and Use of Animals. Animals were signaled from the population of police working dogs of the Guarda Nacional Republicana (Portuguese Gendarmerie), based on history, trainer complaints, physical and radiographic examination consistent with degenerative joint

disease of the hip joint. Other illnesses were ruled out through physical examination, complete blood count, serum chemistry profile, and urinalyses. Animals that presented complaints compatible with osteoarthritis in any other joint were submitted to radiographic examination and, if it was verified, animals were excluded. Animals included in the study were not under any other treatment, making a washout period unnecessary.

Fifteen animals comprised the sample for this study. Ten animals were randomly assigned to the treatment group and provided with a commercially available joint supplement (Cosequin HA, Bioiberica), containing a combination of glucosamine HCl (purity > 99%) 400 mg, chondroitin sulphate (purity 100%) 300 mg, and hyaluronic acid 15 mg. The supplement was administered according to the manufacturer's indication, at a dose adjusted to the animal's weight for 40 days. They also received a 70-day course of a placebo, administered according the manufacturer's indications for carprofen. Both carprofen and the placebo were packed in a similar fashion.

Five animals were randomly assigned to a positive CG that received carprofen (Rimadyl, Zoetis) for 70 days at a loading dose of 2 mg/kg (4.4 mg/lb) body weight twice daily for 7 days followed by a once daily maintenance dose of 2 mg/kg (4.4 mg/lb). As osteoarthritis is a painful condition, a positive control was elected instead of a placebo.[19] Carprofen was chosen because it is a commonly prescribed NSAID for postoperative pain and osteoarthritis related pain and inflammation.[14] From day 0, they were also be started on a placebo with the same physical appearance of the joint supplement and followed the treatment protocol for the treatment group (TG). The manufacturer of the chosen joint supplements indicates that it has an effect that lasts for 3 months with a 40 day course of treatment. To compare both treatments, a long period of carprofen administration is required.

The animals were rested for 3 days and resume normal activity over a period of 5 days.[19] All animals were examined by the assisting veterinarian after the 3 days of rest and accompanied by the same veterinarian on the first 5 days of reintroduction of normal activity, point at which the animal were allowed to resume normal activity. Response to treatment, as measured by the CBPI and the HVAS (completed by the trainers, who were blinded to the dog's assigned group and questionnaires were completed without possible confounding comments by the veterinarian), were evaluated before treatment (T0), after 15 days (T1) and 1 (T2), 2 (T3), 3 (T4), 4 (T5), 5 (T6), and 6 (T7) months after starting the treatment. Additional evaluations were to be performed as necessary, if the animal exhibited a decrease in performance, showed any sign of pain during exercise or manipulation, a change in appetite, vomit or diarrhea or a decrease in the results of the CBPI or HVAS was observed, leading to a return to the initial values. By days 30 and 70, blood and urine complete blood count, serum chemistry profile, and urinalyses were repeated.

Normality of results was accessed with a Shapiro-Wilk test and results of both group by instant were compared using a Mann-Whitney test. When comparing each instant with T0 within each group, a paired samples t-test was used. All results were analyzed with IBM SPSS Statistics Version 20 and a significance level of $P < .05$ was set.

Results

Of the animals enrolled in the study, one of the dogs in the CG was excluded after T4 due to a degradation of its condition, having started other treatments.

When comparing CBPI results of both groups, no differences were found in pain interference score (PIS) and pain severity score (PSS) between TG and CG throughout the study. Even when
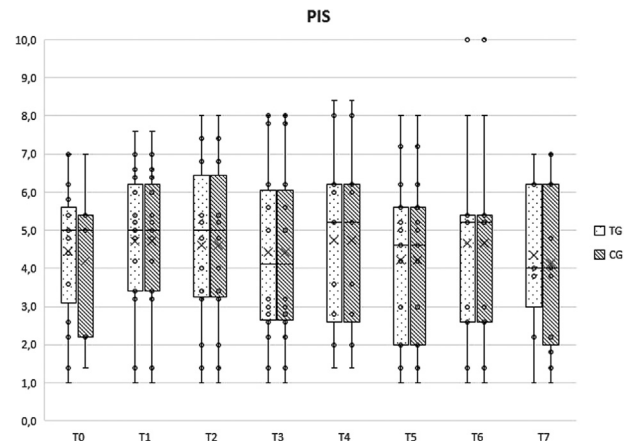

Fig. 1. Overall pain interference scores (PIS) scores by instant for treatment (TG) and control (CG) groups. Box plots represent median, 25th and 75th percentiles, and whiskers represent 10th and 90th percentiles.

comparing results from each instant with T0 within each group, no significant differences were observed. Overall score evolution for PIS and PSS can be observed in Figs 1 and 2, respectively.

Individual treatment success, as measured by the CBPI, has been defined as a reduction of ≥1 in PSS and ≥2 in PIS.[20] Treatment was successful in reducing PIS in 1 animal of the TG at T1 (10%) and 2 at T2 (20%). A reduction bellow 2 was registered in 3 other animals at T3-T5. This remained true until T6, and by T7 the treatment was considered successful only in 1 case. In the CG, treatment was not considered a success in any of the animals of the group.

When considering PSS, treatment was successful in one animal of the TG at T1 (10%), 2 at T2 (20%), and 3 at T3 (30%). From T4-T6, in only 2 cases (20%) was the treatment registered as successful, and this value was reduced to 1 at T7. A reduction bellow 1 point was registered on other animal at T4. In the CG, treatment was only classified as a success by this definition in one animal, and the results maintained up to T7. In 3 other, a reduction bellow 1 was also observed.

Trainers were also asked to classify the animals' overall quality of live in a qualitative scale, that comprised 5 levels, bad, reasonable, good, very good and excellent. In the TG, 40% of animals was classified as having a reasonable quality of live at T0 60% as good. This distribution of classifications changed at T1, with 50% of animals classified as having a good quality of live and 50% as reasonable, and these results remained until to T3. From T4 on 60% of animals were classified as having a reasonable quality of
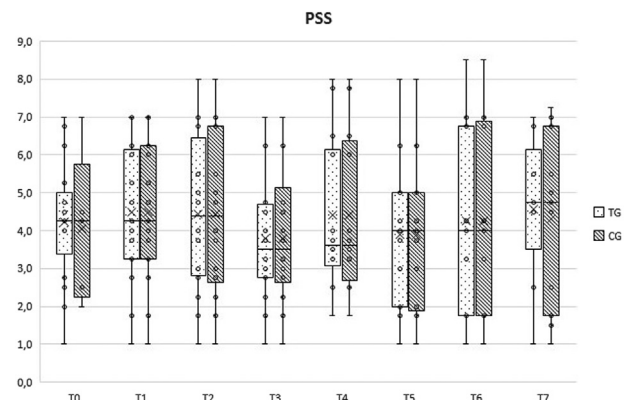

Fig. 2. Overall pain severity scores (PSS) scores by instant for treatment (TG) and control (CG) groups. Box plots represent median, 25th and 75th percentiles, and whiskers represent 10th and 90th percentiles.