American Journal of Animal and Veterinary Sciences 6 (3): 93-99, 2011
ISSN 1557-4555

Impact of Dietary Polydextrose on Clinical Signs of Canine Osteoarthritis

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Abstract: Problem statement: Osteoarthritis is an inflammatory joint disease associated with loss of cartilage matrix. There is suggestive evidence that the intake of polydextrose fiber has anti-inflammatory activity. It was reasoned that polydextrose may have a positive influence on canine osteoarthritis. **Approach:** A double-blind, placebo-controlled trial with privately owned dogs was carried out to assess the efficacy of STA-LITE® polydextrose in the treatment of osteoarthritis. With the use of a questionnaire, five clinical signs were evaluated by the owners. For a period of 8 weeks, the dogs received a complete dry food without or with 3% polydextrose. There were 16 control and 19 test dogs. **Results:** The baseline values of clinical scores for swelling of joints, stiffness and lameness indicated that the severity of osteoarthritis was much less in test dogs than in the controls. The initial scores for activity and pain were similar in two groups. Comparing the changes in clinical scores over time between control and test dogs would be biased by the difference in baseline severity of osteoarthritis. On strict terms, a maximum number of pairs of matched control and test dogs was formed for each clinical sign. It was found that all five clinical signs showed more group-mean improvement in the dogs fed the diet containing polydextrose than in those given the control diet. The difference between the pooled group-mean changes of the control and test dogs was statistically significant. As an overall index of the improvement of osteoarthritis, the sum of changes for the five clinical variables was calculated. Polydextrose was found to induce a marked improvement of osteoarthritis: The polydextrose-mediated increase in the osteoarthritis improvement index was 57%. **Conclusion:** Polydextrose can be considered safe and it is suggested that a dose of 3% in a dry food can be beneficial for dogs with osteoarthritis.

Key words: Dietary polydextrose, canine osteoarthritis, double-blind, placebo-controlled trial, joint disease, functional ingredient

INTRODUCTION

In dogs, osteoarthritis is a common joint disease with symptoms such as chronic pain, lameness and decreased mobility (Henrotin *et al*., 2005). Osteoarthritis is characterized by loss of cartilage matrix associated with a release of pro-inflammatory cytokines (Henrotin *et al*., 2005). It is not possible to cure osteoarthritis, implying that management aims at the relief of pain through reduction of inflammatory reactions and further breakdown of cartilage. Treatment generally consists of the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDS) to decrease inflammation and consequently pain. However, side effects such as vomiting and diarrhea may occur (Innes *et al*., 2003). As an alternative to NSAIDS, canine osteoarthritis may be managed by nutraceuticals that are administered as supplements or as ingredients of industrially produced dog foods. The efficacy of fish oil (Roush *et al*., 2010a), gelatin hydrolysate (Beynen *et al*., 2010) and beta-1,3/1,6-glucans (Beynen and Legerstee, 2010) has been demonstrated in double-blind, placebo-controlled dog trials. However, for optimum management of canine osteoarthritis, further research on potential functional ingredients remains necessary.

STA-LITE® polydextrose is a very pure fiber derived from dextrose. It is a well-tolerated soluble fiber with prebiotic properties, low glycemic response and low energy value (Auerbach *et al*., 2007; Flood *et al*., 2004; Knapp *et al*., 2008; Jie *et al*., 2000). STA-LITE® polydextrose is frequently used to increase the fiber content, provide texture, replace sugar and reduce calories in foods for human consumption (Cho, 2009). Research has shown that polydextrose may have specific biological effects, including anti-inflammatory activity. In rats fed a diet containing 2% of

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polydextrose, a significant increase in the concentration of IgA in the lumen of the caecum has been observed (Peuranen *et al*., 2004). In pigs fed a diet with 2% added polydextrose, the expression of cyclo-oxygenase-2 (COX-2) in the mucosa of the distal small intestine was found to be significantly decreased (Fava *et al*., 2007). In an experimental rat model of colitis, polydextrose had an anti-inflammatory effect that reduced myeloperoxidase activity, counteracted glutathione content and promoted reduction in lesions (Witaicenis *et al.*, 2010). The observed effects of polydextrose on IgA, myeloperoxidase, glutathione and COX-2 point at anti-inflammatory activity. Thus, it could be suggested that polydextrose may have a beneficial influence on canine osteoarthritis.

In the present study, the efficacy of a preparation of polydextrose in the treatment of canine osteoarthritis has been evaluated. In a double-blind, placebo-controlled trial, privately owned dogs were used and the clinical signs were evaluated by the owners. For a period of 8 weeks, the test dogs daily received a complete dry food without or with 3% polydextrose.

MATERIALS AND METHODS

Animals: Dogs with signs of osteoarthritis were recruited through breed associations. The (potential) participants were informed about the purpose and design of the trial and had to sign a statement on informed consent. Fifty three dogs were subjected to either the placebo or test group. Thirteen dogs did not finish the trial and the trial questionnaires for another five dogs were not complete so that the data for 35 dogs (16 dogs in the control group and 19 dogs in the test group) were available for analysis. Table 1 shows the characteristics of the dogs as based on the intake questionnaire completed by the owners. There was a wide variety of dog breeds; there were Labrador Retrievers (n = 4), Swiss white Shepherds (n = 4), St Bernard dogs (n = 3), Border Collies (n = 3), Shar Pei dogs (n = 3), Golden Retrievers (n = 2), Berner Mountain dogs (n = 2), Dutch Partridge dogs (n = 2), cross breeds (n = 4) and others (n = 8).

Table 1: General characteristics of the dogs

Characteristic	Placebo group (n = 16)	Polydextrose (n = 19)
Osteoarthritis diagnosed by veterinarian, yes/no	16/0	16/3
Mean age, years (range)	8.9 (5-13)	8.5 (1-12)
Mean body weight, kg (range)	36.8 (16-75)	31.1 (10-60)
Gender, female/male/castrated	3/3/10	4/8/7
Use of analgetics, yes/no	5/11	8/11
Use of supplements, yes /no	8/8	8/11

The analgetics used were as follows: Cortaphen forte (n = 4), Rimadyl (n = 3), Carprofen (n = 2) and others (n = 4). In 16 dogs various supplements were used. The owners were instructed to continue as usual with the administration of analgetic and/or supplement during the course of the trial. If no analgetic or supplement was used, this was maintained throughout the experiment.

Experimental design: Recruitment of the dogs, keeping contact with the dog owners, supplying of food, data collection and general coordination of the trial was done by LDJ and MS who were blinded to treatment modality. In the intake questionnaire, the owners indicated the severity of osteoarthritis as described below for the trial questionnaire. The eligible dogs were allocated to either the placebo or test group by DHJS, who kept the treatment code closed until statistical analysis of the data. The allocation was done so that the distribution of osteoarthritis severity would be similar for the control and test dogs.

All dogs were fed on the same complete dry food (Carocroc Chicken and Rice 23/12, Vobra Special Petfoods BV, Veghel, The Netherlands), which was supplied in 15-kg, blank packaging. The test food contained 3% of polydextrose (STA-LITE® polydextrose, Tate and Lyle, France). The polydextrose was added prior to extrusion to the ingredient mixture of the control food at the expense of the corn component. Testing with healthy dogs had indicated that an inclusion level of 3% polydextrose does not negatively affect feces consistency (Vasupen *et al*., 2011).

The foods were sent by courier to the dog owners. The trial lasted 10 weeks. The first week served as a baseline. During the second week the dogs were gradually transferred from their habitual diet to the food supplied. During the third week only the food supplied was fed, which was continued for another 8 weeks.

Trial questionnaire: The trial questionnaire was in the form of a booklet, which also provided instructions, including a completed example of a question in the format used. The severity of the signs of osteoarthritis was scored by the owners by marking with a cross a 10-cm, horizontal line. The line was without any unit, but functioned as a scale in combination with the description. The signs to be scored by owners were: activity (vitality), swelling of joint, stiffness, lameness, pain. Body condition was also scored. The signs were scored on day 0 (start) and weekly afterwards.

To aid in scoring the signs, the following descriptions were given. Activity (vitality). "How active and vital is your dog? Is your dog capable of playing? Does your dog reach the door earlier than you? Is your dog excited when you are taking her/him somewhere?" The scale ran from "Not active" (extreme left) to "Very active" (extreme right). Swelling of joint. "Does your dog have swelling on the site of osteoarthritis? Around the joint with diagnosed osteoarthritis, there may be swelling of either a tough or soft nature". The scale ran from "Marked swelling" (extreme left) to "No swelling" (extreme right). Stiffness. "How stiff is your dog? Does your dog easily get out of its basket in the morning or does it take time to get started when going for a walk?" The scale ran from "Very stiff" (extreme left) to "Smooth" (extreme right). Lameness. "Is your dog lame or does it not use one leg at all? Watch your dog carefully to ascertain whether or not there is a change of the degree of lameness during the trial". The scale ran from "Very lame" (extreme left) to "Not lame" (extreme right). Pain. "Does the osteoarthritis cause pain in your dog? Does your dog growl or scream when she/he gets up or makes a wrong movement. Does your dog indicate pain or does she/her try to bite you when touching certain joints". The scale ran from "Usually an expression of pain" (extreme left) to "Never an expression of pain" (extreme right). Body condition."What is the body condition of your dog? In an obese dog, the ribs are not visible and are covered by a layer of fat tissue. In addition, the belly is not slimmer than the chest and thus shows no waist. A dog with normal body condition has ribs that are just visible and shows a waist. A skinny dog has pronounced ribs". The scale ran from "Very skinny" (extreme left) to "Very fat" (extreme right).

Data analysis: The marked scales were transferred into values by using the distance, expressed in mm, of the crosses from the left side (= 0 mm). To calculate the baselines, the values for day 0 and week 1 were averaged per variable per dog. To calculate the final values, those for weeks 8, 9 and 10 were averaged. For each dog and each variable, the change over time was calculated. The data are presented without units. To identify treatment effects, the changes over time for the placebo and test group were subjected to the Student's t test with two-tailed $P<0.05$ as criterion of statistical significance.

The data were not only analysed for all animals in the control and test group, but also for the maximum number of matched control and test animals for each clinical sign. The baseline scores for the clinical signs of osteoarthritis were generally higher for the test animals, indicating less severity of osteoarthritis. This causes bias when comparing the changes over time within the two groups. The bias would be associated with the phenomenon of regression to the mean and that of baseline-dependent sensitivity to improvement. Animals with less severe signs of disease generally are less sensitive to treatment. To solve the problem of bias, for each clinical sign control and test animals were matched so that baseline values were similar. The matching was done by DHJS prior to data analysis and without consideration of the final values. The terms were that the two baseline values within a pair would not differ numerically by three and that for each clinical sign a maximum number of pairs had to be formed. Then again for each dog and each variable the change over time was calculated and subjected to statistical analysis as indicated above. In addition, the group-mean changes over time for the five clinical signs were added up to arrive at an overall index of improvement of osteoarthritis. The index was calculated for both the control and test dogs.

RESULTS

Table 1 shows that the general characteristics of the placebo and test group were similar. The intake values for the clinical signs of osteoarthritis (data not shown) changed erratically over time towards the beginning of the trial. As a result, the baseline values for the clinical signs of osteoarthritis were not comparable for the test and placebo group (Table 2). The test animals had higher scores for swelling of joint, stiffness and lameness. In particular, the difference between control and test animals was considerable for the severity of lameness. The control dogs had an average score of 49.9, whereas the score for the test animals was 72.1; this difference was highly statistically significant ($p = 0.005$). The higher score for swelling also reached statistical significance ($p = 0.036$). The scores for activity and pain were similar for the two groups.

Table 2 documents the data for the total groups of control and test dogs. When compared to the baseline values, the final values in the control dogs for all clinical signs, except for pain, showed a significant increase. In the dogs fed polydextrose, there only was a significant change in the signs of stiffness. When the changes over time of the two groups were compared, there were no statistically significant differences (Table 2). Apart from the pain variable, the group-mean increases were greater in the control animals.

Table 2: Group-mean baseline values and changes over time in the osteoarthritic signs (improvement is indicated by a + sign) for the total groups

	Placebo (n = 16)		Polydextrose (n = 19)		
Variable	Baseline	Change	Baseline	Change	P value for difference in change
Activity	50.8	+9.4	54.8	+4.6	0.287
Swelling	73.4	+ 4.2	83.2	+1.8	0.059
Stiffness	38.9	+12.3	49.2	+9.8	0.729
Lameness	49.9	+9.5	72.1	+3.7	0.446
Pain	74.3	+1.9	72.8	+3.1	0.664

Table 3: Group-mean baseline values and changes over time in the osteoarthritic signs (improvement is indicated by a + sign) for the matched groups

		Placebo		Polydextrose		
Variable	No. of pairs	Baseline	Change	Baseline	Change	P value for difference in change
Activity	9	51.7	+8.6	52.4	+13.3	0.475
Swelling	10	76.2	+3.0	76.9	+3.4	0.558
Stiffness	10	38.0	+14.0	38.1	+17.0	0.583
Lameness	8	60.9	+1.5	62.6	+6.3	0.332
Pain	12	73.5	+0.5	73.7	+3.3	0.252

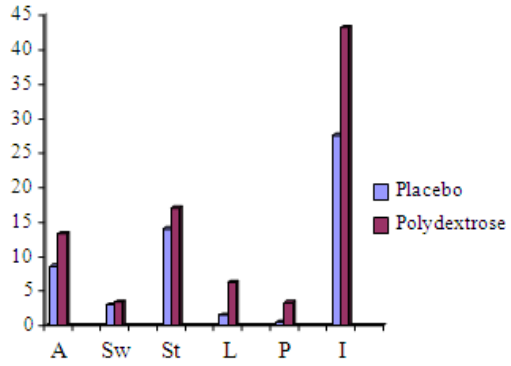

Fig. 1: Effect of polydextrose on clinical signs of osteoarthritis in matched control and test dogs. The bars represent the magnitude of improvement of clinical signs. The improvement was calculated as the difference between final and initial scores on a 0 (severe signs) to 100 (no signs) scale. A = activity; Sw = swelling of joints; St = stiffness; L = lameness; P = pain; I (index) = improvement of the five clinical signs combined. The group-mean changes were pooled for the five clinical signs and the difference between control and test dogs was found to be statistically significant (p = 0.018).

The data obtained after matching control and test animals are presented in Table 3. When the changes over time of the two groups were compared for each clinical sign, there were no statistically significant differences (Table 3). The group-mean increases for all five clinical signs were greater in the dogs fed the diet containing polydextrose (Table 3), which is illustrated by Fig. 1. The difference between the pooled group-mean changes for the control and test dogs was statistically significant (p = 0.018).

The changes over time for the five clinical signs were added up for each group to arrive at an overall index of improvement of osteoarthritis. The improvement index was 27.6 for the placebo group and 43.3 for the test group (Fig. 1). The extra improvement caused by the ingestion of polydextrose was 57%.

DISCUSSION

An evidence-based application of polydextrose in the treatment of canine osteoarthritis requires proven efficacy in double-blind, placebo-controlled clinical trials. After matching the control and test animals with regard to baseline scores for the clinical signs, the dogs fed the diet with polydextrose showed greater numerical improvement as to the scores of activity, swelling, stiffness, lameness and pain, but the differences between the control and test treatment did not reach statistical significance. The systematic, positive effects of polydextrose on osteoarthritic signs resulted in a clear improvement of the osteoarthritis index. Possibly, the lack of statistical significance of the polydextrose effects is caused by insufficient statistical power in combination with placebo effects rather than by an inefficacy of the supplement. The double-blind nature of the trial excluded any observer bias, but it is well-known that placebo effects occur in double-blind studies on canine osteoarthritis (Dobenecker *et al*., 2002; Gingerich and Strobel, 2003; Innes *et al*., 2003; Pollard *et al*., 2006). Likewise, in this study the clinical signs of the control animals were improved during the course of the study as observed by the owners.

This study does not provide absolute proof that polydextrose feeding has a beneficial effect on canine osteoarthritis. The baseline severity of osteoarthritis was less for the test animals than for the control dogs. It may be expected that the test animals were less

sensitive to improvement of the clinical signs so that an effect of polydextrose, if any, could not be demonstrated. Indeed, the data for the total groups show less improvement in the test animals than in the control dogs. In other words, the placebo effect may have been greater than the polydextrose effect. This is substantiated by analyzing the data after matching. For the control and test dogs matched with regard to baseline scores, the group-mean changes were greater in the polydextrose group than in the control group (Fig. 1). However, even after matching the polydextrose effects on the individual scores did not reach statistical significance. This may relate to insufficient statistical power because of the small sample size. When the group-mean changes were pooled for the five clinical signs, the difference between control and test dogs was found to be statistically significant. It should be noted that the posterior matching procedure may be criticized as it could have introduced allocation bias. Clearly, further clinical trials are required for definite proof that the feeding of polydextrose relieves canine osteoarthritis.

In addition to proven efficacy, the use of polydextrose in the treatment of canine osteoarthritis should have a scientific basis. It should be possible to explain in molecular terms how it inhibits inflammation and/or how it inhibits breakdown of the cartilage matrix. In vitro (Makivuokko *et al*., 2005) and in vivo research in pigs (Fava *et al*., 2007) has demonstrated that polydextrose reduces the expression of COX-2. This effect may lead to reduced production of prostaglandin E2 (PG-E2) which is responsible for the clinical signs like pain and swelling of joints. There appears to be similarity between polydextrose and fish oil. The intake of fish oil reduces the severity of canine osteoarthritis (Roush *et al*., 2010a; 2010b) and it inhibits both the activity of COX-2 and the breakdown of cartilage proteoglycans (Curtis *et al*., 2000). It is difficult to see that intake of polydextrose inhibits the degradation of cartilage. For rats fed polydextrose, an increase in the area of ileal mucosa with cells producing interleukin-1 (IL-1) has been reported (Peuranen *et al*., 2004). IL-1 stimulates the production of Matrix Metalloproteinase-3 (MMP-3) by chondrocytes (O'Connor and Fitzgerald, 1994) which is involved in the degradation of collagen molecules in the cartilage matrix.

In the control dogs, group-mean baseline and final scores for body condition were 46.7 and 47.1. During the course of the study, the group-mean scores of the test dogs increased from 51.4 to 64.7. Although the increase was not statistically significant ($p = 0.235$), it might point at some weight gain. In retrospect, it is unfortunate that the dogs in this study were not weighed. A general feeding schedule was supplied, but the amount of food provided was determined by the dog owners and thus was not controlled. It could be speculated that the relief of osteoarthritis as induced by polydextrose had improved wellbeing of the dogs and thereby stimulated appetite. Weight loss in obese dogs is associated with a decrease in the severity of canine osteoarthritis (Impellizeri *et al*., 2000; Mlacnik *et al*., 2006; Marshall *et al*., 2010). The test dogs were not obese as is indicated by the scores for body condition. Nevertheless, it is possible that the positive effect of polydextrose on osteoarthritis is somewhat underestimated because of the simultaneous tendency towards slight weight gain. It should be noted that the quantitative amount of weight gain of the test dogs, if any, is unknown and so is the relationship between weight gain, duration of overweight and the severity of osteoarthritis.

CONCLUSION

This study does not provide solid evidence that dietary polydextrose diminishes the clinical signs in dogs with osteoarthritis, but a beneficial effect of clinical relevance is acceptable. Polydextrose at a dietary inclusion level of 3% is safe in dogs (Burdock and Flamm, 1999). Polydextrose is heat stable and can be added to dog food prior to extrusion (Cho, 2009). This study indicates that a dose of 3% in a dry food would be beneficial for dogs with osteoarthritis.

ACKNOWLEDGEMENT

This study was funded by Tate and Lyle. The research and all publications arising out of or referable to it are considered proprietary data to which Tate & Lyle claims exclusive right of reference in accordance with Regulation (EC) no 1924/2006 of the European Parliament and of the Council on Nutrition and Health Claims Made on Foods.

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