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SHORT-TERM CHANGES IN LIPID PROFILE FOLLOWING EXPERIMENTAL OSTEOARTHRITIS IN DOGS

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Summary

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Changes in plasma lipid profile of dogs following experimental knee osteoarthritis (OA) were evaluated to determine the possible cardiovascular risk associated with OA in dogs. Ten dogs (mean weight 12.4 ± 1.8 kg) were used. Experimental OA was induced in the right knee, using the groove model and confirmed by radiography. Gait was assessed subjectively and respective gait scores (GAS) were assigned. Blood was obtained for determination of total plasma cholesterol (TC), triglycerides (TRIG), high density lipoproteins (HDL) and low density lipoproteins (LDL) fortnightly for twelve weeks. Radiographic scores (RAS), GAS, TC, TRIG, HDL and LDL were compared by means of ANOVA. Correlation between parameters was evaluated using Pearson's correlation test. A P value less than 0.05 was considered significant. The blood TC of the dogs progressively decreased from week 4 to week 12 of OA. The TRIG however, decreased progressively from the baseline values up to the second week and thereafter, there were no significant differences up to week 12. The LDL decreased progressively from the baseline value until the 10th week, while the HDL decreased progressively from baseline up to week 2 of experimental knee OA, and thereafter increased until the 10th week. It was therefore concluded that there were no significant changes in the lipid profile of dogs following experimental OA. However, these changes might be related to the duration of observation period.

Key words: cholesterol, dog, lipoproteins, osteoarthritis, triglycerides

INTRODUCTION

The developmental orthopaedic diseases and associated osteoarthritis (OA) are the most common articular diseases in dogs. They account for about 70 percent of hospital visits for articular disease and related problems (Richardson & Toll, 1997). Incidence of canine OA is increased by trauma, obesity, aging and genetic abnormalities. Fifty percent of OA cases are observed in dogs aged between 8–13 years. OA have been reported in several joints including elbow, shoulder, hip and knee (Mele, 2007) and is more prevalent in male dogs than in females (Duval *et al.*, 1999).

Vascular diseases and cardiovascular risk factors are high amongst people with OA (Plumb & Aspden, 2004). Emerging evidence suggests that these conditions may share similar risk factors (Conaghan *et al.*, 2005). Hypercholesterolaemia and hypertriglyceridaemia, the risk factors for cardiovascular disease, have been related to risk of OA and its progression in

epidemiologic studies (Findlay, 2007). It has been reported that humans with OA had altered lipid profiles characterised by increased concentration of total cholesterol (Borman *et al.*, 1999). It was recently demonstrated that serum cholesterol and triglyceride levels were associated with incidence of bone marrow lesions in humans (Davies-Tuck *et al.*, 2009).

However, till now there is little information on the relationship between OA and lipid alterations in dogs. This study aimed to evaluate the changes in lipid profiles of dogs following experimental OA and its relationship with the progression of disease.

MATERIALS AND METHODS

Ten adult local dogs of both sexes with mean weight of 12.4±1.8 kg and age ranging from 1–3 years were used. They were adjudged to be free of any musculoskeletal disease based on the visual assessment of gait and radiographic evaluation of the joints. The dogs were housed individually in concrete-floored kennels and were fed once daily cooked rice supplemented with sufficient amount of fish and palm oil, and water *ad libitum*. Ethical approval for this study was obtained from the Research Ethics Committee, College of Veterinary Medicine, Federal University of Agriculture, Abeokuta, Ogun State.

Dogs were premedicated with intramuscular injections of 0.04 mg/kg atropine (Amopin®, Yanzhou Pharmaceuticals, China) and 1 mg/kg xylazine (XYL-M2®, V.M.D, Germany). Fifteen minutes later, anaesthesia was induced with intravenous injection of 0.5 mg/kg diazepam (Calmpose® Ranbaxy, India) and 15 mg/kg ketamine (Ketamin hydrochloride USP®, Rotex Medica, Germany). Following induction of anaesthesia, the right knee was prepared aseptically. Thereafter, a 5 cm para-patellar incision was made. Bleeding was controlled and soft tissue damage was kept to the minimum. Cartilages of the lateral and medial femoral condyles were then grooved using an intramedullary pin held to a T-chuck. The grooves were about 0.5 mm in depth and were made with the joint in utmost flexion. Grooves were made on the weight bearing parts of the femoral condyles without damaging the subchondral bone. Following cartilage grooving, the joint was rinsed with saline and the joint capsule was closed with chromic catgut size 1 (Sterile Absorbable Suture USP®, Ogotex, China) using simple continuous suture pattern. The subcutis was closed with a subcorticular suture pattern using chromic catgut size 1, while the skin was closed with nylon sutures size 0 (Sterile Non-absorbable Suture USP®, Ogotex, China) using horizontal mattress suture pattern.

The dogs were allowed to recover for two weeks. During this period, the dogs were treated with penicillin/streptomycin (PenStrep®, Kepro, Holland) and pain was controlled using a combination of dipyrone and sodium salicylate (Febralgina®, Agrovet, Peru) administered for three days after the arthrotomy. In addition, the operated joint was loaded for 30 min daily, by fixing the contralateral leg to the trunk. This was done three times a week for two weeks.

The dogs were assessed radiographically, two weeks after arthrotomy of the right knee until confirmation of OA (week 0) and then fortnightly for twelve weeks. Scores were assigned to the observable radiographic changes by a surgeon using criteria shown in Table 1. Similarly, the gaits of the dog were assessed subjectively every two weeks starting from the time OA

Table 1. Radiographical assessment of dogs with experimentally induced osteoarthritis (OA) (maximum score = 12 points)

Score	Criteria
No OA (0)	Presence of osteophytes
Mild OA (1)	Joint space narrowing
Moderate OA (2)	Subchondral bone sclerosis
Severe OA (3)	Mineralisation of joint soft tissue

Table 2. Gait assessment evaluation for dogs with experimentally induced osteoarthritis (maximum score 32 points)

Locomotion	Score
Walking	Excellent (4) Good (3) Fair (2) Poor (1)
Trotting	
Pacing	
Jumping	
Descending stairs	
Lying down	
Getting up	
Difficulty moving after major activity	

was radiographically confirmed (week 0) up to the 12th week, using a modification of criteria established by Millis (Millis *et al.*, 2006) (Table 2).

Five mL of blood wereobtained from the cephalic vein before knee arthrotomy, the day after knee arthrotomy, immediately after radiographic confirmation of OA (week 0) and thereafter fortnightly up to the 12th week for the determination of total cholesterol (TC), triglycerides (TRIG), high density lipoproteins (HDL) and low density lipoproteins (LDL). The biochemical parameters were determined using Randox Laboratory kit reagents as described by Jeusette *et al.* (2005).

Data were expressed as mean ± standard deviation. Gait assessment scores (GAS) and radiographic scores (RAS) were compared at six and twelve weeks using Wilcoxon sign rank test, while time-related differences in TC, TRIG, HDL and LDL were compared with ANOVA. Correlation between parameters was evaluated using Pearson's correlation test. at a level of significance less than 0.05.

RESULTS

The total plasma cholesterol (TC) of the dogs ranged between 2.8±0.6 mmol/L and 4.1±0.5 mmol/l. The TC concentrations increased significantly ($P<0.05$) vs the baseline value after arthrotomy and then returned back to this value by week 2 of OA. Thereafter, the TC of the dogs progressively decreased from week 4 to week 12 of OA (Table 3). The TRIG of the dogs ranged between 1.0±0.4 mmol/L and 1.5±0.3 mmol/L. The TRIG however, decreased progressively from the baseline values up to week 12 of OA except at weeks 0, 4 and 10 of OA. There was no significant difference in the TRIG up to week 12 of OA. The LDL of the dogs ranged between 0.4±0.2 mmol/L and 1.1± 0.2 mmol/L. The LDL decreased progressively from the baseline value up to ten weeks of OA (Table 3). The HDL of the dogs ranged between 2.3±0.6 mmol/L and 3.1±0.7 mmol/L. The HDL decreased gradually from baseline up to week 2 and thereafter increased up to week 10 of OA (Table 3). In general, there was no significant difference in blood HDL of dogs within the 12-week duration of OA.

Both TC and TRIG were negatively correlated to RAS following experimental OA in the dogs. Similarly, both TC and TRIG were negatively correlated to the GAS following experimental OA in the dogs (Table 4).

Table 3. Short-term changes in blood lipid parameters (TC: total cholesterol; TRIG: triglycerides; LDL: low density lipoprotein; HDL: high density lipoprotein), gait assessment score (GAS) and radiographic score (RAS) following experimental knee osteoarthritis in dogs

Time intervals	TC (mmol/L)	TRIG (mmol/L)	LPL (mmol/L)	HDL (mmol/L)	GAS	RAS
Before arthrotomy	2.8 ± 0.6	1.5 ± 0.3	1.1 ± 0.3	2.1 ± 0.7	ND	0
1 day after arthrotomy	4.1 ± 0.5**	1.2 ± 0.2	0.7 ± 0.3	2.6 ± 0.3	ND	0
Week 0*	4.0 ± 0.7**	1.4 ± 0.2	0.6 ±0.4	2.6 ± 0.5	17.0 ± 5.5	1.2 ± 0.5
Week 2	2.8 ± 0.8	1.3 ± 0.1	0.8 ± 0.4	2.3 ± 0.6	18.4 ± 6.4	1.6 ± 0.5
Week 4	4.1 ± 0.5**	1.4 ± 0.4	0.6 ± 0.2	3.1 ± 0.6	21.1 ± 2.8	2.8 ± 0.5
Week 6	3.8 ± 0.5	1.1 ± 0.2	0.7 ± 0.2	2.9 ± 0.8	17.4 ± 6.1	3.2 ± 0.8
Week 8	3.3 ± 0.9	1.0 ± 0.4	0.7 ± 0.2	2.4 ± 0.6	16.4 ± 7.2	3.0 ± 0.8
Week 10	3.0 ± 0.5	1.5 ± 0.2	0.5 ± 0.2	3.1 ± 0.7	16.4 ± 7.2	2.8 ± 0.5
Week 12	3.2 ± 1.1	1.1 ±0.3	1.1 ± 0.2	2.4 ± 0.5	17.0 ± 6.6	2.8 ± 0.8

* After radiographic confirmation of OA; ND – not determined; ** $P<0.05$.

Table 4. Pearson's correlation coefficients of blood lipid parameters, gait assessment score (GAS) and radiographic score (RAS) following experimental osteoarthritis in dogs. In brackets, the levels of significance are presented

Parameters	TC	TRIG	LDL	HDL	GAS	RAS
TC		–0.185 (0.691)	0.491 (0.263)	0.601 (0.153)	0.328 (0.473)	0.458 (0.302)
TRIG	–0.185 (0.691)		–0.445 (0.317)	0.739 (0.058)	0.071 (0.850)	–0.125 (0.789)
LDL	0.491 (0.263)	–0.445 (0.317)		–0.510 (0.243)	0.027 (0.954)	0.271 (0.556)
HDL	0.601 (0.153)	0.739 (0.058)	–0.510 (0.243)		0.318 (0.487)	0.286 (0.533)
GAS	0.328 (0.473)	0.071 (0.850)	0.027 (0.954)	0.318 (0.487)		0.153 (0.496)
RAS	–0.458 (0.302)	–0.125 (0.789)	0.271 (0.556)	0.286 (0.533)	0.153 (0.496)	

TC: total cholesterol; TRIG: triglycerides; LDL: low density lipoprotein; HDL: high density lipoprotein.

DISCUSSION

The results of this study showed that there were no significant short-term changes in the blood lipid profiles of the dogs following experimental OA in dogs, neither was there a positive association between changes in lipid profiles and the progression of OA as earlier reported in humans (Borman *et al.*, 1999). However, this finding may be due to the short duration of the study which may have not

allowed for sufficient time to produce significant alterations in the biochemical profiles of dogs.

Changes in the lipoprotein fractions of blood during inflammatory and non-inflammatory arthropathies have been reported to be related to the degree of inflammation in the course of the disease (Davies-Tuck *et al.*, 2009). Results of experimental studies indicated that in the course of inflammation, the liver preferentially utilises amino acids for the production of inflammatory mediators rather than for manufacturing of enzymes important in lipid metabolism, with the resultant reduction in the production of lipoproteins (Borman *et al.*, 1999). Since the inflammatory component of OA is minimal, it is thus expected that the changes in the lipid profiles during OA will be less compared with those of rheumatoid arthritis. This might explain the absence of significant changes in the lipid profile of the dogs during the twelve weeks monitoring of OA in the dogs.

In humans with rheumatoid arthritis, altered lipoprotein patterns were reportedly characterised by low levels of serum TC, LDL, VLDL and TRIG, while in OA patients, altered levels of lipids were characterised by increased concentration of TC (Hurt-Camejo *et al.*, 2001; Dessein *et al.*, 2002). Dogs with hip OA were also shown to have increased serum lipid levels with evidence of hypofibrinolysis and increased platelets aggregation (Ghosh & Cheras, 2001). This has been associated with decreased physical activity of the patient. The results of this study did not reflect any significant change in the lipid profiles of the dog except for the interval between weeks 2 and 4 of OA when both TC and TRIG increased significantly and between weeks 10 and 12 when LDL was significantly higher. The exact reason for the decline in the plasma levels of the measured lipid parameters by week 2 of OA is not known but is thought to be due to increased turnover of lipids for energy production or an increased degradation through lipid peroxidation or a combination of both (Damyanovich *et al.*, 1999). The major limitation to this study was the short duration of the monitoring period which may not have provided sufficient time for the expected changes to occur. In an experimental model of osteoarthritis, this limitation is because of welfare concerns.

One of the aims of this study was to assess if there was any association between the severity of OA as quantified by gait assessment and radiological scores of the knee and the lipid profile of the dogs. Previous studies in both humans (Borman *et al.*, 1999; Ghosh & Cheras, 2001; Davies-Tuck *et al.*, 2009) and animals (Alam *et al.*, 2006) failed to establish associations between serum cholesterol levels and the severity of OA. In this study both TC and TRIG were negatively correlated with the gait assessment and radiographic scores, further confirming earlier reports of no association between the progression of OA and the lipid profile changes.

In conclusion, findings of this study failed to confirm a significant increase in the serum levels of TC and TRIG as earlier reported for knee OA in humans and hip OA in dogs but instead there were insignificant reductions in the serum concentration of the lipids as OA progressed. Owing to the limitation of the study stated and the dearth of data regarding the lipid changes following OA in dogs, it is therefore suggested that further long-term studies on dogs with natural OA should be carried out to assess if changes in the lipid profile of dogs can be used as a predictor for the progression of OA in dogs.

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