Original Article

Comparison of the Efficacy of Firocoxib and Carprofen in Clinical Use for Canine Coxofemoral Osteoarthritis

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Abstract

Firocoxib and carprofen, non-steroidal anti-inflammatory drugs (NSAIDs), are used in the treatment of canine osteoarthritis. This study evaluated the efficacy and provided information of these NSAIDs in clinical practice. Sixteen healthy dogs of large breeds over 5 years old without systemic diseases and pregnancy that had coxofemoral osteoarthritis were divided into 2 groups, firocoxib group (n=9) and carprofen group (n=7). The study was conducted for 16 weeks. Firocoxib (5mg/kg body weight) or carprofen (4.4mg/kg body weight) was administered to all dogs once daily for 2 weeks, on alternate days for 6 weeks and every 2 days for 8 weeks. Of all samples, serum OA biomarkers (hyaluronan (HA) and chondroitin sulfate epitope WF6), hematological profiles together with physical, orthopedic and radiographic examination, passive range of motion measurement, pain and lameness scoring, urinalysis, fecal examination and owner preference scoring were assessed. Evaluations of the study took place at weeks 0, 2, 4, 8, 12 and 16. Although the serum WF6 levels of the firocoxib group were gradually increased until week 12 and decreased at week 16 and those of the carprofen group were decreased at week 2 and then gradually increased until week 16, the levels of WF6 revealed that the chondroprotective effect of firocoxib and carprofen was still indistinct. Passive range of motion (ROM) measurement revealed evidences of increased hip flexion of the firocoxib group at weeks 2, 4 and 16 (p<0.05) and increased hip extension of the carprofen group at weeks 2, 8 and 12 (p<0.05). These improved ranges of motion indicated that both NSAIDs ameliorated the clinical signs.

Keywords: canine osteoarthritis, carprofen, firocoxib, non-steroidal anti-inflammatory drugs

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Introduction

Osteoarthritis (OA) is non-infectious degeneration of articular structures that occurs in movable or weight-bearing joints. As a result of unstable joints, some structures such as osteophyte are formed to stabilize the osteoarthritic joints and may cause pain and inflammation (Allan, 2007; Thompson, 2007; Bennett, 2010). OA are divided into primary and secondary OA. Primary OA with obscure etiology is usually found in old dogs. Secondary OA is found in dogs with diseases or abnormalities of joints such as congenital anomalies, trauma and joint laxity. These factors conduce to degeneration of affected joints and periarticular structures (Todhunter and Johnston, 2002; Taylor, 2003; Allan, 2007; Edge-Hughes, 2007; Thompson, 2007; Bennett, 2010).

Cartilage matrix turnover in normal articular cartilage reveals the balance of catabolism and anabolism that are controlled by enzymes such as matrix metalloproteinases (MMPs) and the inhibitors of matrix metalloproteinases (TIMPs) (Bennett, 2010). In OA joints, some inflammatory cytokines such as interleukin (IL)-1, tumor necrosis factor (TNF)-α and interleukin (IL)-6 induce the abnormalities of proteoglycan synthesis and structures. Moreover, these cytokines induce synthesis and release of degradation enzymes, leading to promotion of catabolism predominated over anabolism (MacPhail, 2000; Uesaka et al., 2001; Henrotin et al., 2005; Thompson, 2007; Nganvongpanit et al., 2008; Bennett, 2010; Fox, 2010).

Nowadays, the late stage of OA is diagnosed by physical, orthopedic and radiographic examinations (Nganvongpanit and Ong-Chai, 2004a; Nganvongpanit and Ong-Chai, 2004b; Pothacharoen et al., 2006). Some studies used analysis of the levels of OA biomarkers to detect the early stage. These OA biomarkers such as hyaluronan (HA) and chondroitin sulfate epitope WF6 are the components of articular cartilage; therefore, the change in levels of these biomarkers may represent the destruction of articular cartilage (Arican et al., 1994; Hardingham, 1995; Nganvongpanit and Ong-Chai, 2004a; Pothacharoen et al., 2006; Nganvongpanit et al., 2008; Trakulsantirat et al., 2010).

Aims of treatment of canine osteoarthritis are to relief pain, reduce inflammation, prevent increased degeneration and improve the use of affected joints (MacPhail, 2000; Todhunter and Johnston, 2002; Trakulsantirat et al., 2010). Selective non-steroidal anti-inflammatory drugs (NSAIDs) such as firocoxib and carprofen are used to relief pain and inflammation from osteoarthritis because their selective cyclooxygenase (COX) -2 (inducible form) inhibition property leads to reduction in the inflammatory-mediated prostaglandin synthesis and spares COX-1 (constitutive form), which is necessary for protective prostaglandin synthesis. Therefore, selective COX-2 NSAIDs reduce the commonly adverse effects of NSAIDs such as gastrointestinal irritation and ulceration, hepatic toxicity and coagulation disorders (Mathews, 2002; Lascelles et al., 2005; Luna et al., 2007; Scott, 2007; Papitch, 2008; Bennett, 2010).

Firocoxib is a selective cyclooxygenase (COX) -2 inhibitor that inhibits COX-2 350-430 times greater than COX-1 in canine whole blood (McCann et al., 2004; Hazewinkel et al., 2008). Recommended dosage is 5 mg/kg body weight (Hanson et al., 2006; Papich, 2008). Overdose or concurrent use with other NSAIDs or corticosteroid could induce gastrointestinal ulcer (Steagall et al., 2007).

Carprofen is a preferential COX-2 inhibitor that inhibits COX-2 6.5-16.8 times greater than COX-1 in canine whole blood (Streppa et al., 2002; Hanson et al., 2006). Recommended dosages are 2.2 mg/kg body weight twice a day or 4.4 mg per 1 kg of body weight once a day (Plumb, 2005; Papich, 2008). Long-term use of carprofen did not increase the incidence of gastrointestinal adverse effect compared with short-term use (Autefage and Gosselin, 2007).

Although the study of Pollmeier et al. (2006) revealed that osteoarthritic dogs treated with firocoxib showed greater improvement of clinical sign than those treated with carprofen, the authors questioned whether firocoxib had more efficacy than carprofen in decreasing articular cartilage degradation, pain, inflammation and progression of osteoarthritis. The objectives of this research were to study the efficacy of firocoxib compared with carprofen in the treatment of canine osteoarthritis by evaluation of serum OA biomarker (hyaluronan and WF6) levels and clinical assessments including physical, orthopedic and radiographic examinations, passive range of motion measurement, pain and lameness scoring and owner assessment and preference.

Materials and Methods

Sixteen over five-year-old dogs of large breeds with signs of coxofemoral osteoarthritis including altered gait, joint pain, palpable crepitus, limitation of joint movement and decreased passive range of motion (ROM) (Todhunter and Joneston, 2002) were included in the study. All samples in this study were without pregnancy, systemic and infectious diseases. In addition, all dogs had never been treated with NSAIDs or had appropriate withdrawal period as shown in Table 1. The dogs were divided into firocoxib group (n=9) and carprofen group (n=7) by randomization. This study was approved by the Ethic Committee of Faculty of Veterinary Science, Chulalongkorn University.

Both groups were treated with firocoxib or carprofen for 16 weeks once daily for 2 weeks, on alternate days at weeks 3-8 and every 2 days at weeks 9-16. Recommended dosage of firocoxib was 5 mg/kg body weight once a day (Hanson et al., 2006; Papich, 2008) and carprofen was 4.4 mg/kg body weight once a day (Plumb, 2005; Papich, 2008).

Both groups were assessed by gait observation, temperature measurement, mucous membrane and capillary refill time observation, heart and lung sound auscultation and joint palpation. All samples were assessed by the same veterinarian with double-blind procedure.

To analyze all blood profiles, 5 milliliters of blood was collected and divided into 4 ml for serum OA biomarker (HA and WF6) analysis and 1 ml for

hematology (Fig. 1). The blood samples for analysis of serum OA biomarkers were organized in 7,000 rounds/second-centrifuge for 10-15 min to separate serum and blood cells, then the serum was collected at -20°c and transferred for analysis at Thailand Excellence Center for Tissue Engineering, Department of Biochemistry, Faculty of Medicine, Chiang Mai University. The remaining 1-millitter blood samples were analyzed for hematological profiles including complete blood count and blood chemistry (serum glutamic-pyruvic transaminase (SGPT), alkaline phosphatase (ALP), blood urea nitrogen (BUN), creatinine and total protein) by Small Animal Hospital, Faculty of Veterinary Science, Chulalongkorn University.

Table 1 Withdrawal period of other anti-inflammatory drugs and nutraceuticals

Drugs	Withdrawal period (weeks)
Oral non-steroidal anti-inflammatory drugs	2
Oral corticosteroid	3
Injectable non-steroidal anti-inflammatory drugs	12
Oral nutraceuticals	4
Injectable nutraceuticals	24

(Modified from Moreau et al., 2003)

Table 2 Pain and lameness score

Criteria	Score
1. Lameness on standing	
No lameness	0
Decreased weight bearing but paws touch the ground completely	1
Decreased weight bearing and paws touch the ground partially	2
No weight bearing	3
2. Lameness on walking	
No lameness and normal weight bearing	0
Mild lameness and decreased weight bearing	1
Moderate lameness and decreased weight bearing	2
Severe lameness and no weight bearing	3
3. Lameness on running	
No lameness and normal weight bearing	0
Mild lameness and decreased weight bearing	1
Moderate lameness and decreased weight bearing	2
Severe lameness and no weight bearing	3
4. Pain on palpation	
No pain expression	0
Mild pain, e.g. turning the head to look at the affected joint	1
Moderate pain, e.g. pulling the affected limb back	2
Severe pain, e.g. crying, refusing to let anyone touch the affected limbs, aggression	3
5. Radiographic change	
No radiographic lesion	0
Mild remodeling of acetabulum and femoral neck, Morgan line, mild sclerosis of femoral head	1
Remodeling and osteophyte formation of acetabulum, remodeling of femoral neck, sclerosis of femoral head, enthesiophytosis	2
Severe remodeling and osteophyte formation of acetabulum and femoral neck and severe sclerosis of femoral head	3

(Modified from Moreau et al., 2003 and Reymond et al., 2012)

In each visit, passive ROM as coxofemoral joint flexion and extension of all dogs were evaluated twice and mean of the angles was calculated by the same veterinarian with double-blind procedure. The flexion and extension angles were measured by creating a line between the tuber sacrale and ischiadicum and connecting it with a line formed between the greater trochanter and lateral femoral epicondyle (Jaegger et al., 2002; Millis et al., 2004).

Lameness of all dogs was evaluated while they were standing, walking and running. Joint pain was appraised by palpation. Pain and lameness scoring was assessed by the same veterinarian with double-blind procedure following the criteria in Table 2.

Coxofemoral joint radiography of ventrodorsal and lateral views of all samples were evaluated and lesions were scored (following the criteria in Table 2) by the same veterinary radiologist of Small Animal Hospital, Faculty of Veterinary Science, Chulalongkorn University with double-blind procedure.

Urinalysis and fecal examination were evaluated to monitor adverse effects from urinary and gastrointestinal tracts. Urine was collected by natural voiding before the examinations occurred and divided into 2 parts. The first part was observed for physical properties (such as color, transparency and specific gravity measurement) and tested for chemical properties by chemical dipstick (Combur[10] Test, Roche Diagnostics GmbH, Mannheim, Germany) for pH, leukocyte, nitrite, protein, glucose, urobilinogen, bilirubin, erythrocyte and hemoglobin in urine. The other part of urine was organized in 1,000-1,500 rounds/second-centrifuge for 3-5 min to separate the

sediment for Sternheimer-Malbin staining and microscopic examination (Buranakarl et al., 2001). Fecal examination took place by fecal collection, fresh smear and microscopic examination. The urinalysis and fecal examination were assessed at weeks 2, 4, 8, 12 and 16 after treatment.

All owners were taught to evaluate their dogs' symptoms together with observing adverse effects such as vomiting, diarrhea, etc. They also signed informed consent forms before enrolling in the study. Additionally, they were informed about the types of NSAIDs used to treat their dogs. The owner assessment and preference scoring followed the criteria in Table 3.

Table 3 Owner assessment and preference score

Criteria	Score
1. Standing up and lying down	
No pain	0
Occasionally difficult to stand up and lie down especially after long-term rest	1
Sometimes difficult to stand up and lie down	2
Always difficult to stand up and lie down	3
Refuse to stand up and lie down	4
2. Walking	
Normal gait	0
Decreased hip flexion then returns to normal gait after short walking	1
Decreased hip flexion or mild lameness	2
Moderate lameness	3
Severe lameness	4
3. Running	
Normal running	0
Mild lameness after rest then normal running	1
Lameness after long running or doing exercise	2
Lameness while running	3
Refuse to run	4
4. Jumping up and down	
Normal jumping	0
Occasionally have mild difficulty jumping	1
Always have mild difficulty jumping	2
Always have severe difficulty jumping	3
Refuse to jump	4
5. Going up or down the stairs	
Normal going up or down the stairs	0
Occasionally have mild difficulty going up or down the stairs	1
Always have mild difficulty going up or down the stairs	2
Always have severe difficulty going up or down the stairs	3
Refuse to jump	4
6. Playing or doing exercise	
Long-time playing or doing exercise without excess tiredness	0
Occasionally excess pain or tiredness after long-time playing or doing exercise	1
Ignore playing after short-time exercise	2
Sudden pain or tiredness after starting playing or doing exercise	3
Refuse to play or do exercise	4
7. Improvement	
No pain or lameness	0
Greatly decreased pain or lameness	1
Moderately decreased pain or lameness	2
Mildly decreased pain or lameness	3
No improvement	4

(Modified from Autefage and Gosselin, 2007 and Pollmeier et al., 2006)

All examinations except urinalysis and fecal examination took place at weeks 0, 2, 4, 8, 12 and 16 after treatment. The data of OA biomarkers and passive ROM were analyzed by repeated measures ANOVA and T-test (SPSS version 19). Pain and lameness score, radiographic score and owner assessment and preference were analyzed by Wilcoxon signed rank test and descriptive statistics.

Results

The signalment of samples in this study is shown in Table 4. There was no statistically significant difference in the age and weight between the firocoxib and carprofen groups.

The physical examination of all dogs revealed no clinical abnormality except hindlimb lameness and pain on extension of coxofemoral joints.

Comparison of the serum HA levels within and between the firocoxib and carprofen groups revealed no statistically significant difference ($p>0.05$). The mean of serum HA levels is shown in Figure 2. In the firocoxib group, the mean of serum chondroitin sulfate epitope WF6 levels at week 4 was greater than at pre-treatment (week 0), but the levels at week 16 were less than at weeks 8 and 12 ($p<0.05$). In the carprofen group, the mean of serum WF6 levels at week 12 was greater than at weeks 2, 4 and 8 and the levels at week 16 were greater than at week 2 ($p<0.05$)

(Fig 3). Comparison of the levels of serum WF6 between both groups revealed statistically significant difference at weeks 2 and 4 (Fig 4).

The passive ROM of coxofemoral joints of the firocoxib group was improved on flexion at weeks 2, 4 and 16 after treatment (p<0.05). The improvement in passive ROM in the carprofen group was found on extension at weeks 2, 8 and 12 after treatment (p<0.05) (Fig 5). There was no statistically significant difference in the passive ROM between the firocoxib and carprofen groups.

Table 4 Signalment of dogs

Group	Number	Age (year±SD)	Gender (number(%))		Weight (kg±SD)	Breed (number (%))*
			male	female		
Firocoxib	9	6.67±2.35	8(88.89)	1(11.11)	35.75±5.74	LR 1 (11.11) GR 4 (44.44) Rott 3 (33.33) Mixed 1 (11.11)
Carprofen	7	5.86±1.78	4(57.14)	3(42.86)	36.44±6.14	LR 2 (28.57) GR 1 (14.29) Rott 2 (28.57) GS 1 (14.29) Mixed 1 (14.29)

*Breeds: LR=Labrador retriever, GR=Golden retriever, Rott=Rottweiler and GS=German shepherd

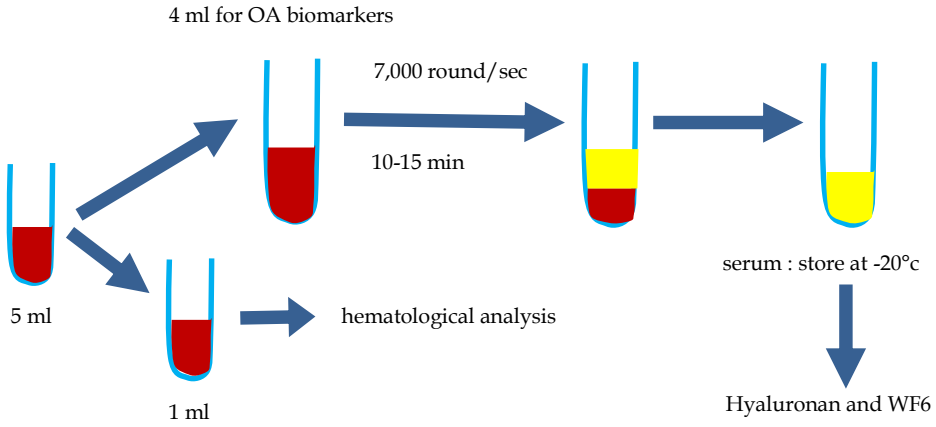


Figure 1 Process of blood collection: 5 ml of blood sample was divided into 2 parts, 4 ml for serum OA biomarker analysis and 1 ml for hematological analysis.

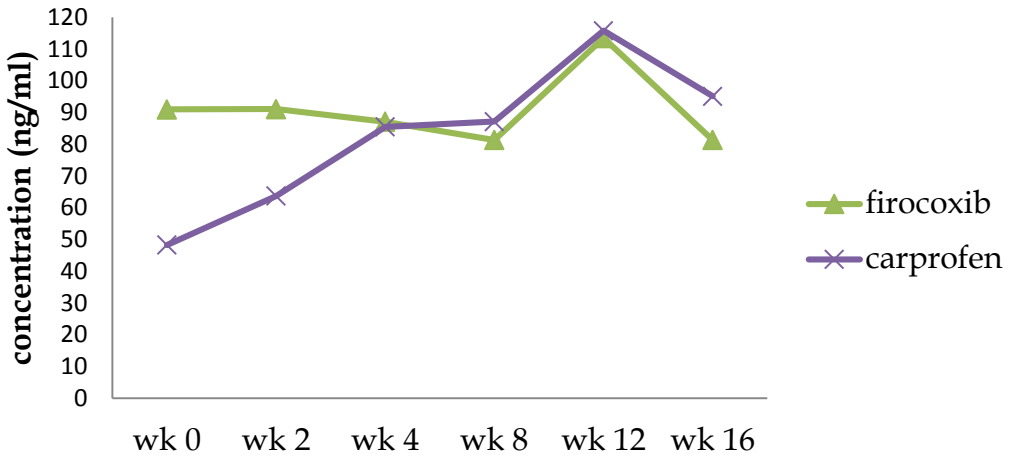
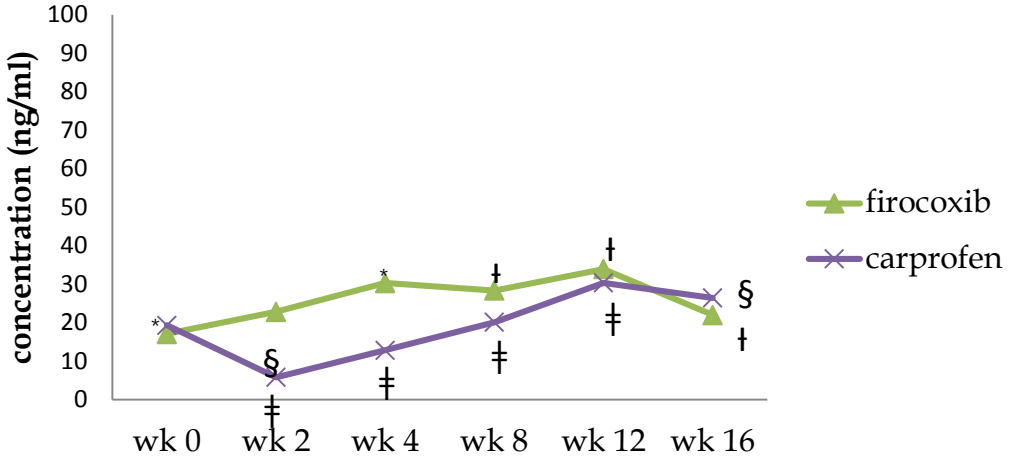
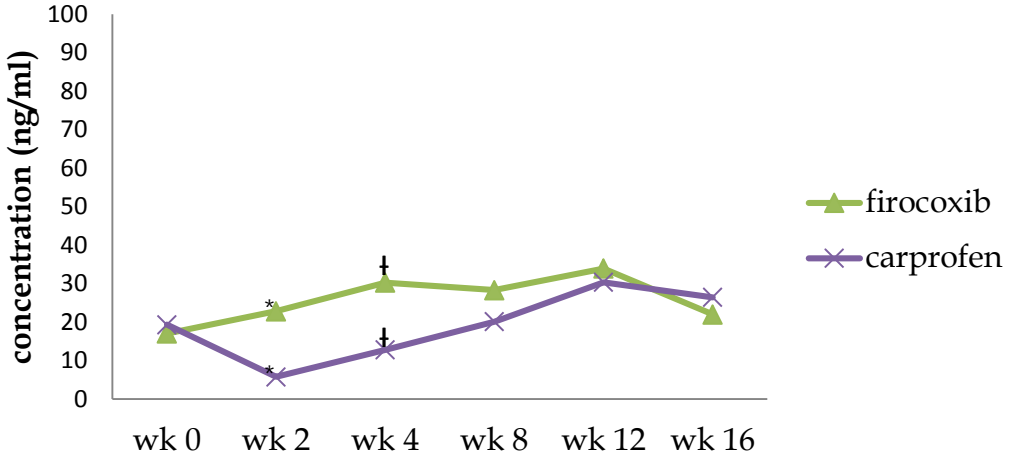


Figure 2 Mean of serum hyaluronan levels of dogs in firocoxib and carprofen groups revealed no statistically significant difference within and between groups.



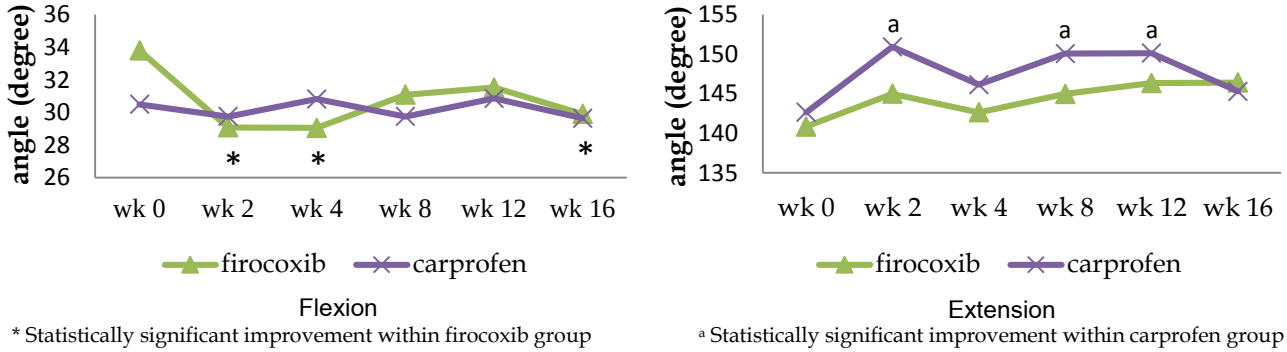
Firocoxib group: *significant difference between weeks 0 and 4, ǂ week 16 significantly less than weeks 8 and 12
Carprofen group: ǂ week 12 significantly greater than weeks 2, 4 and 8, § significant difference between weeks 2 and 16

Figure 3 Comparison of mean of serum chondroitin sulfate epitope WF6 levels of dogs within each groups



* significant difference at week 2, ǂ significant difference at week 4

Figure 4 Comparison of mean of serum chondroitin sulfate epitope WF6 levels of dogs between firocoxib and carprofen groups



* Statistically significant improvement within firocoxib group
[a] Statistically significant improvement within carprofen group

Figure 5 Passive range of motion of coxofemoral joints on flexion and extension

Although there was no statistically significant improvement in the pain and lameness scores of both groups (Fig 6), there were evidences of clinical improvement found on the physical examination and overall clinical assessments at weeks 2, 4, 8 and 16 after treatment.

The radiographic examination compared within and between both groups revealed no statistically significant change after treatment (Fig 7).

The radiographic lesion did not relate to clinical improvement.

The owners' scores after treatment were better but without statistical significance. The improvement scores revealed that the dogs in firocoxib group showed greater improvement than those in the carprofen group even though they were not statistically significantly different after treatment (Fig 8).

In this study, there was no adverse effect found on monitoring hematological analysis. The complete blood count and biochemistry profile of all dogs showed that all factors were within the normal range (Table 5) and there was no significant change in all factors after the treatment. The urinalysis monitoring revealed no sign of abnormality after treatment. The fecal examination by fresh smear showed normal finding residue and no sign of hemorrhage. There was no client complaint about adverse effects such as anorexia, lethargy, vomiting, diarrhea, hematuria, etc.

Table 5 Hematological profile of the samples

Blood profile	Normal value (units)	Group \ Week		0	2	4	8	12	16
RBC	5.2-8.06 ($X10^6$ cells/µl)	Firocoxib	mean	6.478889	5.81	6.16625	6.088889	6.05	6.1125
			SD	0.751539	0.959635	0.45635	0.817686	1.00995	1.171614
		Carprofen	mean	6.78	6.657143	6.428571	6.657143	6.671429	6.86
			SD	0.446356	0.472077	1.02423	0.761265	0.555921	0.268328
Hb	12.4-19.1 (g/dl)	Firocoxib	mean	14.22222	13.77778	13.8875	13.76667	13.8375	14.1875
			SD	1.563472	2.108185	1.461347	1.786057	2.002811	2.294364
		Carprofen	mean	15	15.28571	14.37143	15.28571	14.78571	15.16667
			SD	0.816497	1.112697	2.407429	1.496026	0.805044	0.983192
Hct	29.8-57.5 (%)	Firocoxib	mean	46.44444	44.11111	44.625	44.77778	44.75	44.5
			SD	5.126185	7.007932	3.814914	4.57651	5.650537	6.141196
		Carprofen	mean	48.42857	48.42857	46	48.42857	47.85714	47.33333
			SD	2.225395	2.992053	7.72442	4.353433	2.609506	2.875181
Platelet	160-525 ($x10^3$ cells/µl)	Firocoxib	mean	202.5556	232.6667	261.25	198.7778	271.5	277.25
			SD	117.9153	80.96141	135.6263	137.0062	72	57.85141
		Carprofen	mean	249.5714	276	209.4286	228.8571	207.8571	259
			SD	99.79956	94.07975	114.4507	80.09043	72.81353	154.1506
WBC	5400-15300 (cells/µl)	Firocoxib	mean	8,959	8,720	9,160	8,706	9,188	9,579
			SD	2264.732	1984.244	2669.666	1242.589	2134.477	1764.495
		Carprofen	mean	8,203	8,956	8,440	8,929	9,044	8,970
			SD	1448.091	1415.767	2946.348	2327.885	2526.274	2244.237
SGPT	4.0-91.0 (Units)	Firocoxib	mean	29.88889	30.33333	33.66667	32.88889	31.375	29.25
			SD	7.94425	9.63068	14.59452	9.18483	8.601287	9.176834
		Carprofen	mean	42.14286	44.42857	44.85714	42	43.28571	24.14286
			SD	13.54534	17.8499	21.96534	16.94107	14.31449	20.22728
ALP	3.0-60.0 (IU/Ls)	Firocoxib	mean	36.22222	36.44444	28.88889	34.22222	36.625	34.5
			SD	16.26943	15.88325	10.65885	15.62672	11.53798	10.3923
		Carprofen	mean	69.14286	54.14286	55	72.57143	61.42857	88.42857
			SD	52.25715	45.8455	56.03868	91.74758	38.94807	33.27089
BUN	7.0-26.0 (g%)	Firocoxib	mean	11.92222	13.88889	15.67778	15.74444	17.275	17.8625
			SD	2.894727	4.166667	6.845396	7.361235	4.575322	5.8172
		Carprofen	mean	18.28571	16.65714	13.42857	14.61429	17.85714	13.5
			SD	3.988077	4.599586	3.457222	4.390303	4.413184	4.046809
Creatinine	0.6-1.4 (mg%)	Firocoxib	mean	0.9875	0.977778	1.1	1.088889	1.077778	1.125
			SD	0.188509	0.17873	0.141421	0.169148	0.148137	0.212132
		Carprofen	mean	0.885714	0.9	0.828571	0.857143	0.9	0.728571
			SD	0.267261	0.238048	0.249762	0.190238	0.23094	0.205866
Total protein	5.8-7.9 (mg%)	Firocoxib	mean	6.683333	6.4375	6.055556	6.155556	5.95	6.4875
			SD	0.381663	0.620915	2.277121	0.441902	0.495696	0.804341
		Carprofen	mean	7.65	6.533333	6.6	6.357143	6.371429	6.45
			SD	1.767767	0.778888	0.822598	0.84628	0.771825	0.928978

Discussion

In this study, the HA levels of both firocoxib and carprofen groups were not significantly different within and between groups. Although hyaluronan or HA is one of the components of articular cartilage, HA is also found in many organs such as skin, umbilical cord, vitreous body, muscle, lung, brain and kidney (Arican et al., 1994; Fraser et al., 1997; Nganvongpanit et al., 2008). Moreover, in human, increased serum HA levels were affected by activities and eating after more than 1-hour arising in the morning (Criscione et al., 2005) and chronic joint instabilities probably conduced to articular cartilage change that affected HA levels (Pruksakorn et al., 2009). According to these evidences, serum HA may not be an appropriate biomarker for the detection of osteoarthritis as there are several factors inducing serum HA level change. However, further studies may confirm the alteration of serum HA levels of dogs over 24 hr.

Chondroitin sulfate epitope WF6 is a monoclonal antibody that is specific to chondroitin-6-sulfate and chondroitin 2,6 sulfate in articular cartilage. Elevation of serum WF6 levels revealed increase in both articular cartilage catabolism and destruction of chondroitin that released to bloodstream (Nganvongpanit and Ong-Chai 2004b; Nganvongpanit et al., 2008; Trakulsantirat et al., 2010). The present study revealed that the serum WF6 levels in the firocoxib group gradually increased until week 12 and decreased at week 16. This evidence might indicate that the catabolism of articular cartilage continuously progressed until week 12 and after that the process was diminished. In the carprofen group, the reduction in serum WF6 levels in week 2 and their gradual increase until week 16 might indicate the lessened cartilage catabolism until week 2 followed by its gradual progression. A previous study of De Boer et al. (2009) of the effect of NSAIDs on articular cartilage reported the effect of celecoxib, selective COX-2 NSAID, on osteoarthritic articular cartilage of human and found that celecoxib not only improved proteoglycan structure and synthesis but also decreased destroyed proteoglycan release. Pelletier et al. (2000) revealed that carprofen could slow the alteration of structure and the abnormal metabolism of subchondral bone. The authors of these two studies used histopathology to confirm their hypotheses. Besides serum OA biomarker evaluation, further studies of the chondroprotective effect of firocoxib and carprofen should place importance on histopathologic examination of pre- and post-treatment osteoarthritic articular cartilage and subchondral bone to confirm the action of these NSAIDs on joints. In addition, 24-hour monitoring of serum WF6 levels may be performed in order to observe changes in levels and factors that influence the biomarker.

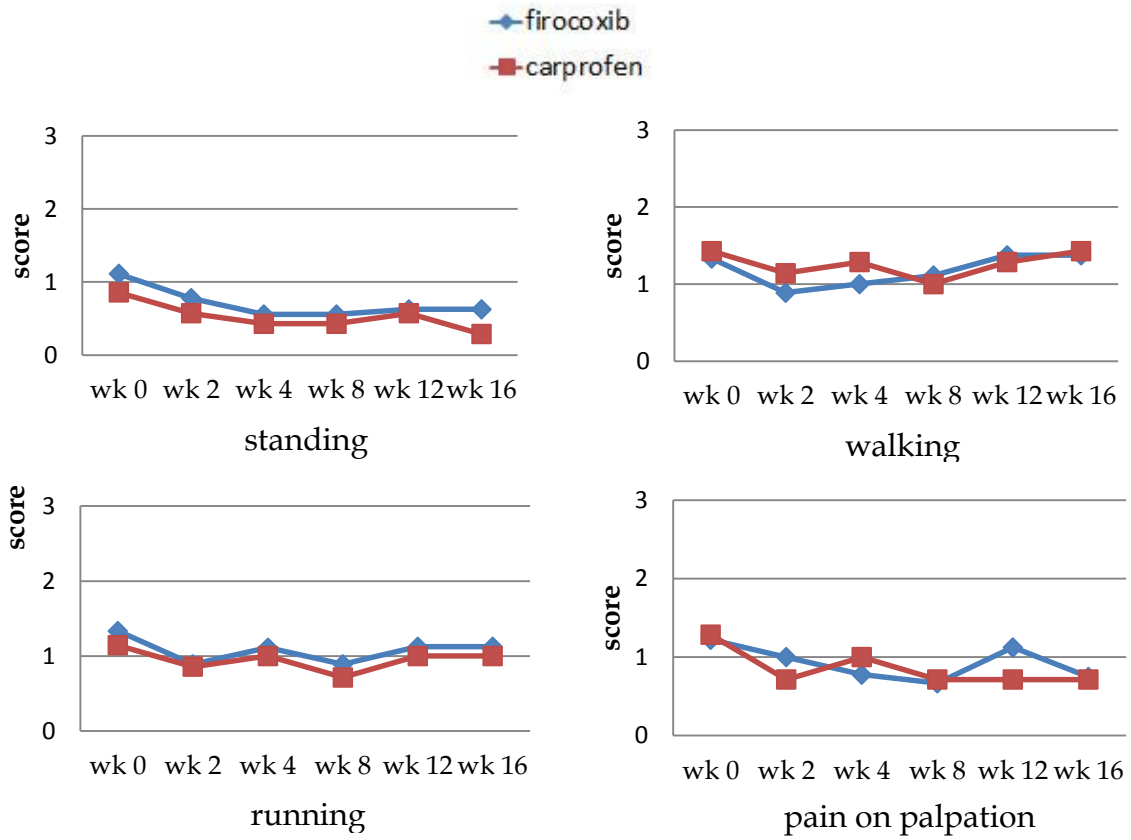


Figure 6 Pain and lameness scores: There was no statistically significant difference within and between groups.

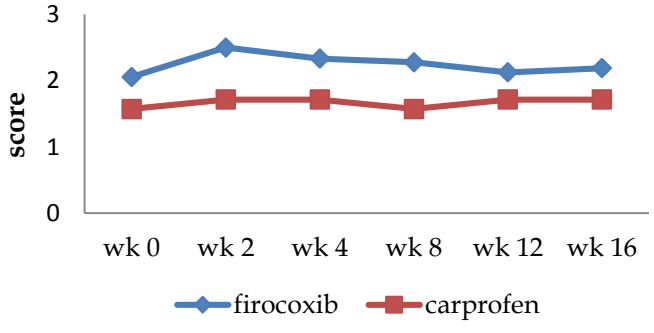


Figure 7 Radiographic scores: There was no statistically significant difference in radiographic lesion score before and after treatment.

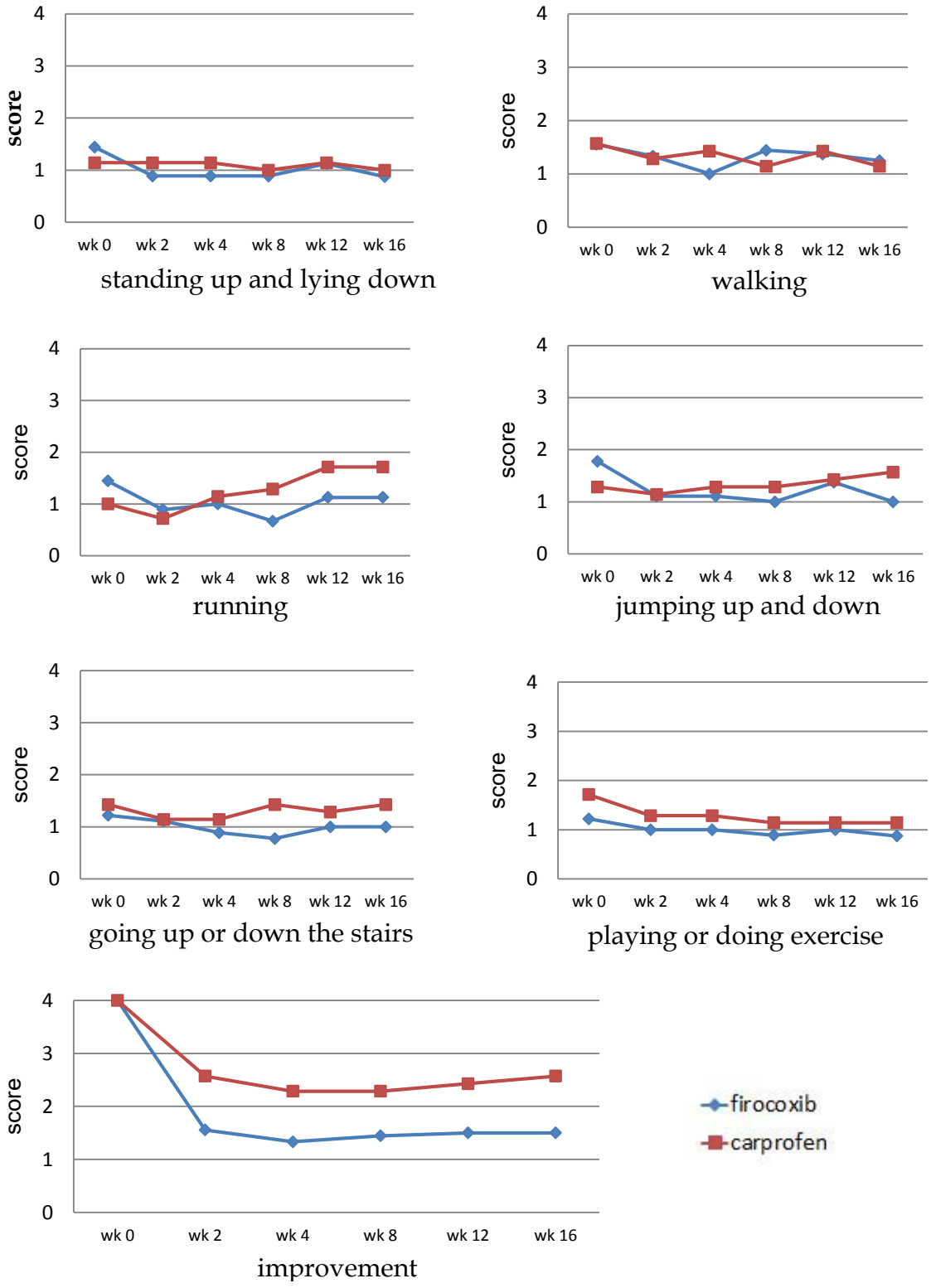


Figure 8 Owner assessment and preference scores: There was no statistically significant difference within and between groups.

Even though the samples in this study were affected by the variation of breed, age, severity of the lesions and experience of pain, which are factors that may cause difference in pain expression of dogs (Lipscomb et al., 2002; Hansen, 2003; Hellyer et al., 2007; Lockhead, 2010), all dogs in this research revealed the clinical improvement as shown by the improved passive ROM and owners' observation.

Although passive ROM measurement in conscious OA dogs could cause pain and resistance, this assessment might represent the maximum ROM that did not cause pain on flexion and extension (Jaegger et al., 2002). The improvement in passive ROM in this study reflected the efficacy of both firocoxib and carprofen to relief pain and inflammation and enhance the use of affected limbs within 2 weeks after treatment.

In this research, there was no significant difference in the radiographic lesions of both groups after treatment while the clinical signs improved. This

evidence might reveal that the radiographic lesions were not associated with the clinical signs. Allan (2007) explained that some structures formed in an early stage of OA, such as cartilaginous osteophyte, were not found by radiography so there were some samples showing severe radiographic lesion scores with mild lameness.

The passive ROM improvement after treatment and the no life-threatening adverse effect found in this study are the evidences that firocoxib and carprofen are appropriate for long-term treatment of canine osteoarthritis. Additionally, from week 2 to week 8, alternate-day firocoxib and carprofen administration revealed clinical improvements although without statistical significance. This study provides useful information for the treatment of OA with firocoxib or carprofen in weak patients. Besides, weight control or reduction, rehabilitation and nutraceutical administration may reduce lameness and promote greater improvements (Impellizeri et al., 2000; Lascelles et al., 2005; Mansa et al., 2007; Marshall et al., 2010). Further studies may include gait analysis to improve objective reliability of the studies of OA.

In summary, firocoxib and carprofen could improve the clinical outcome revealed by passive range of motion enhancement. Serum hyaluronan was not the specific biomarker for identifying osteoarthritis. The chondroprotective effect of both NSAIDs is still obscure even though the serum WF6 levels decreased after treatment. Histopathology of articular cartilage and other OA biomarkers such as 3B3 in further studies may indicate the chondroprotection of these NSAIDs. The owners tended to prefer firocoxib for the treatment of canine osteoarthritis.

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บทคัดย่อ

การเปรียบเทียบประสิทธิภาพของฟิโรคอกซิบและคาร์โปรเฟนในการรักษาภาวะข้อกระดูกสะโพกเสื่อมในสุนัขทางคลินิก

ณัฐวรรณ ตั้งมหากุล[1] กัมปนาท สุนทรวิภาต[1] กรกฎ งานวงศ์พาณิชย์[2]*

ฟิโรคอกซิบและคาร์โปรเฟนเป็นยาระงับปวดและบรรเทาการอักเสบชนิดไม่ใช่สเตียรอยด์ที่ถูกนำมาใช้ในการรักษาภาวะข้อกระดูกเสื่อมในสุนัข การศึกษานี้ทำการประเมินประสิทธิภาพของยาทั้ง 2 ชนิดนี้เพื่อเป็นข้อมูลประกอบการใช้ยาในการรักษาภาวะข้อกระดูกเสื่อมทางคลินิก โดยทำการศึกษาในสุนัขพันธุ์ใหญ่ อายุ 5 ปีขึ้นไป ซึ่งพบภาวะข้อกระดูกสะโพกเสื่อม และปราศจากโรคทางระบบอื่นๆในร่างกาย รวมทั้งไม่พบการตั้งครรภ์ จำนวน 16 ตัว โดยแบ่งเป็น 2 กลุ่ม คือ กลุ่มที่ได้รับฟิโรคอกซิบ 5 มิลลิกรัมต่อน้ำหนักตัว 1 กิโลกรัม จำนวน 9 ตัว และกลุ่มที่ได้รับคาร์โปรเฟน 4.4 มิลลิกรัมต่อน้ำหนักตัว 1 กิโลกรัม จำนวน 7 ตัว ให้ยาแต่ละชนิดเป็นเวลา 16 สัปดาห์ แบ่งเป็น 2 สัปดาห์แรกให้ยาทุกวัน สัปดาห์ที่ 3 ถึง 8 ให้ยาวันเว้นวัน และสัปดาห์ที่ 9 ถึง 16 ให้ยาวันเว้น 2 วัน ประเมินการศึกษาในสัปดาห์ที่ 0, 2, 4, 8, 12 และ 16 หลังได้รับยา โดยการตรวจระดับตัวชี้วัดทางชีวภาพของภาวะข้อกระดูกเสื่อมในซีรั่ม ได้แก่ ไฮยาลูโรแนน และคอนดรอยตินซัลเฟตอิพิโทปชนิด WF6 การตรวจทางโลหิตวิทยาและชีวเคมี ร่วมกับการตรวจร่างกาย การวัดพิสัยการเคลื่อนไหวของข้อต่อ การให้คะแนนความเจ็บปวด การถ่ายภาพรังสีข้อสะโพก การตรวจปัสสาวะและอุจจาระ และการประเมินอาการและความพึงพอใจของเจ้าของสุนัข จากการศึกษาพบว่า ระดับ WF6 ในซีรั่มของกลุ่มที่ได้รับฟิโรคอกซิบมีแนวโน้มเพิ่มสูงขึ้นถึงสัปดาห์ที่ 12 ก่อนจะลดลงในสัปดาห์ที่ 16 ส่วนกลุ่มที่ได้รับคาร์โปรเฟนมีแนวโน้มลดลงในสัปดาห์ที่ 2 และเพิ่มสูงขึ้นอย่างต่อเนื่องถึงสัปดาห์ที่ 16 แม้ว่าจะมีการเปลี่ยนแปลงของระดับ WF6 ในซีรั่ม แต่คุณสมบัติในการปกป้องกระดูกอ่อนข้อต่อของฟิโรคอกซิบและคาร์โปรเฟนยังคงไม่แน่ชัด จากการศึกษาพิสัยการเคลื่อนไหวข้อต่อพบว่า สุนัขในกลุ่มที่ได้รับฟิโรคอกซิบสามารถงอข้อสะโพกได้มากขึ้นในสัปดาห์ที่ 2, 4 และ 16 ($p<0.05$) และกลุ่มที่ได้รับคาร์โปรเฟนสามารถเหยียดข้อสะโพกได้มากขึ้นในสัปดาห์ที่ 2, 8 และ 12 ($p<0.05$) พิสัยการเคลื่อนไหวข้อต่อที่ดีขึ้นนี้แสดงให้เห็นว่าทั้งฟิโรคอกซิบและคาร์โปรเฟนสามารถบรรเทาอาการของภาวะข้อกระดูกเสื่อมในสุนัขได้เป็นอย่างดี

คำสำคัญ: ภาวะข้อกระดูกเสื่อมในสุนัข คาร์โปรเฟน ฟิโรคอกซิบ ยาระงับปวดและบรรเทาการอักเสบชนิดไม่ใช่สเตียรอยด์

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