J Vet Clin 20(3) : 278-285(2003)

The Efficacy of Conjugated Linoleic Acid and Carprofen in Progression of Early Stage of Experimentally Induced Osteoarthritis in Dogs

Se-il Park, Jae-sung Bae, Young-sam Kwon, Hwan-soo Jang, Wen-xue Li, Jae-hyun Lim, Ki-dong Eom, Jung-eun Kim and Kwang-ho Jang[1]

Department of Veterinary Medicine Kyungpook National University

Abstract : This study was performed to compare early stage changes following the administrations of Conjugated Linoleic Acid (CLA), Carprofen and their combinations in the experimental canine cranial cruciate ligament rupture. Twenty five mongrel dogs were divided into five groups; Groups 1, 2, and 3 received a sectioning the cranial cruciate ligament (CCL) of the right stifle joint, and were administered CLA (250 mg/kg/day/orally), carprofen (4.4 mg/kg/day/orally), and their combinations for 4 weeks beginning 4 weeks postsurgery, respectively. Group 4 received sectioning CCL and no treatment. Group 5 was composed of unoperated normal dogs. The macroscopic observation of cartilage erosions on both the condyles and plateaus were evaluated, and the severity of the cartilage lesions and synovial inflammation was examined histologically at eight weeks after surgery. Histological examinations including hematoxylin and eosin stain, standard toluidine blue method, PAS technique and Masson trichrome technique, hematologic and radiographic evaluation were performed after experimental surgery. Slight yellowish discoloration of the surface was found in some of the experimental dogs. However macroscopic findings showed no significant differences among the groups. In radiographic findings, cranial displacement of the proximal tibia relative to the femoral condyles in all groups was observed but no significant differences among the groups was seen. This study showed that oral administration of CLA, carprofen and their combinations revealed no early stage change in the canine stifle joint following experimental rupture of the cranial cruciate ligament.

Key words **:** Conjugated Linoleic Acid (CLA), Carprofen, Cranial cruciate ligament, Dog

Introduction

The cranial cruciate ligament (CCL) is critical for the congruent anatomy and function of the canine stifle. The function of the CCL is to constrain the stifle joint so as to limit internal rotation and cranial displacement of the tibia relative to the femur[5,17]. The CCL prevents stifle hyperextention, internal rotation of the tibia, and cranial translation of the tibia relative to the femoral condyles[18].

The first report of canine cranial cruciate ligament rupture was in 1926; since then much has been learned about this ligament yet the optimum mode of treatment remains controversial[30]. The ligament is injured when the stifle is rotated rapidly with the joint in 20-50 degrees of flexion. Injury can also occur when the joint is forcefully hyperextended[1,2]. Injury and rupture of the CCL is the major cause of degenerative joint disease (osteoarthritis) in the stifle and one of the most common injuries in the dog[24].

Osteoarthritis (OA) is a chronic, noninflammatory joint disease characterized by slowly developing joint pain, stiffness, deformity, and limitation of motion and the most common form of all articular disorder[26]. The etiology of OA is unknown. But it appears to be the result of a complex system of interacting mechanical, biological, biochemical, and enzymatic feedback loops. When one or more of these systems fails, the clinical events follow. Many mechanisms can initiate the cellular and tissue events that constitute a final common pathway. Such mechanisms include: congenital joint abnormalities; genetic defects; infectious, metobolic, endocrine, and neuropathic disease; virtually any disease process that alters the normal structure and function of hyaline cartilage; and acute or chronic trauma to the hyaline cartilage or tissue surrounding same[19].

Conjugated Linoleic Acid (CLA) refers to a group of di- and tri-enoic derivatives of linoleic acid that occur naturally in milk and meat of ruminating animals. It can be synthesized chemically in the laboratory and is available commercially as a dietary supplement and has been shown to be nontoxic[16]. It appears to modulate the immune system under conditions where COX-2 enzyme is induced by suppressing PGE2 production. Excess production of PGE2 is linked to osteoporosis and arthritis and is associated with bone and proteoglycan loss[16]. The mechanism for the observed anti-inflammatory effects of CLA in various animal models has been associated with reduced arachidonic acid, a precursor for PGE2, accumulation in cell membranes[29]. Any effect CLA on the synthesis of eicosanoids should correlate with the uptake of CLA into neutral phospholipids by cells. CLA can be readily incorporated in a dose-dependant manner into the tissues of animals consuming diets containing CLA and a concomitant reduction of arachidonic acid. Recent investigations with growing rats given butter fat and supplements of CLA demonstrated an increased rate of bone formation and reduced vivo bone PGE2 production, respectively. Furthermore, the supplements of CLA resulted in their enrichment in

[1]Corresponding author.
E-mail : khojang@knu.ac.kr

This research was supported by Kyungpook National University Research Fund, 2002

lipids of various bone compartments of animals.

Carprofen((±)-6-chloro-a-methylcarbazole-2-aceticacid) is a non-steroidal antiinflammatory drug (NSAID) of the propionic acid class that includes ibuprofen, naproxen, and ketoprofen. The mechanism is believed to be associated with the inhibition of cyclooxygenase activity. Two unique cyclooxygenases have been described in mammals[25]. The constitutive cyclooxygenase, COX-1, synthesizes prostaglandins necessary for normal gastrointestinal and renal function. The inducible cyclooxygenase, COX-2, generates prostaglandins involved in inflammation. Inhibition of COX-1 is thought to be associated with gastrointestinal and renal toxicity while inhibition of COX-2 provides anti-inflammatory activity. The specificity of a particular NSAID for COX-2 versus COX-1 may vary from species to species[13]. In an in vitro study using canine cell cultures, carprofen demonstrated selective inhibition of COX-2 versus COX-122.

Ceuppens *et al* demonstrated that carprofen had modulatory effect on humoral and cellular immune responses in 1982[7,8]. Data also indicated that carprofen inhibited the production of osteoclast-activating factor, PGE1, and PGE2 by its inhibitory effect in prostaglandin biosynthesis. Nowadays, Pelletier *et al*[20] reported that carprofen reduced the progression of early cartilage loss/degradation. It based on analysis of the subchondral morphologic and biochemical changes.

The canine cranial cruciate ligament transection model was used in our study because it was well characterized and clinically relevant, and it permited longitudinal studies of synovial fluid composition[10,15,21,23,28]. And it also allowed the study of the early changes of the disease as well as several of the pathophysiological pathways. Dedrick *et al*[9] reported that in this model the subchondral bone is the site of important morphological changes. The report also showed that, as early as 2 or 3 months after surgery, the subchondral bone plate was osteopenic and that this phenomenon reversed and bone sclerosis appeared between 18 and 54 months after ligament transection. These findings suggested that in this model, the subchondral bone changes might be linked to the progression of cartilage lesions. Therefore, this study was performed to compare early stage changes in the cartilaginous surface of the canine stifle joint following the administrations of CLA, carprofen and their combinations in the experimental canine cranial cruciate ligament rupture.

Materials and Methods

Experimental Groups & Drug Administration

Twenty five mongrel dogs of either sex, weighing 4.5 ± 0.6 kg each, with no clinical or radiographic evidence of joint disease were used for this study. They were vaccinated with DHPPL, dewormed with febantel (Rintal®, Bayer Korea Ltd., Korea). Experiments were started after an initial adaption for about two weeks. The experimental animals were randomly divided into five groups; Group 1 (CLA group, n = 5), CCL rupture dogs given CLA (250 mg/kg/day/orally) (Biochemistry Lab. of Applied Life Sciences Gyeongsang National University, Korea); Group 2 (Car group, n = 5), CCL rupture dogs given carprofen(4.4 mg/kg/day/orally) (RIMADYL®, Pfizer Animal Health); Group 3 (CC group, n = 5), CCL rupture dogs given their combinations, for four weeks starting four weeks after surgery; Group 4 (Con group, n = 5), CCL rupture dogs with no treatment; Group 5 (Nor group, n = 5), unoperated normal dogs. All dogs were killed at eight weeks after surgery. CLA was composed of CLA mixture (72.8%), oleic acid (15.6%), palmitic acid (7.6%), stearic acid (2.8%), and linoleic acid (1.2%).

Surgical Procedures

Surgical sectioning of the CCL of the right stifle joint was performed on twenty dogs through a stab wound, lateral arthrotomy. Prior to surgery, the animals were anesthetized with 0.05 mg/kg of atropine sulfate (Atropine®, Dai Han Pharm. Co. Ltd., Korea) subcutaneously and 1.1 mg/kg of xylazine (Rompun®, Bayer Korea Ltd., Korea) intramuscularly followed by 22 mg/kg of ketamine HCl (Ketamin®, Yuhan Co., Korea) intramuscularly. The dogs were placed in lateral recumbency and the entire right hindlimb was clipped. The skin was prepared with povidone-iodine solution and 70% alcohol for aseptic surgery, sterile surgical instruments and supplies were used in all surgical procedures (Fig 1A). For a lateral approach to the stifle joint made a lateral skin incision beginning the patella and extending tibial crest. Subcutaneous tissue was incised along the same line. Joint capsule was identified, it was incised approximately 2 cm in length (Fig 1B). After cranial cruciate ligament was identified, it was incised in middle part by No. 11 scalpel blade(Fig 1C. D). Joint capsule was perfused by saline. It was closed using a simple continuous suture of 2-0 catgut and the skin was closed by a simple interrupted suture of 3-0 nylon (Fig 1E. F). To convict for cranial cruciate ligament rupture, drawer movement was performed after surgery.

Post-surgical Management

The dogs were kept in animal care facilities, maintained in a soft bandage (Tegaderm®, 3M Health Care, USA) for one week, at a housing farm where they were free to exercise in a large pen for seven weeks. Each animal was monitored for sign of pain, lameness, swelling, palpable crepitus during motion, and joint instability. Antibiotic (Baytril®, Bayer Korea Ltd., Korea, 5 mg/kg/day) was injected subcutaneously to reduce the risk of postoperative infection for three days.

Macroscopic Evaluations

Immediately after sacrifice, the right knee of each dog was dissected and each knee was examined by 2 independent, blinded observers for gross morphologic changes, including the presence of osteophyte formation and cartilage lesions as previously described. The depth of erosion was graded on a scale of 0-4, as follows: 0 = surface appears normal; 1 = minimal fibrillation or a slight yellowish discoloration of

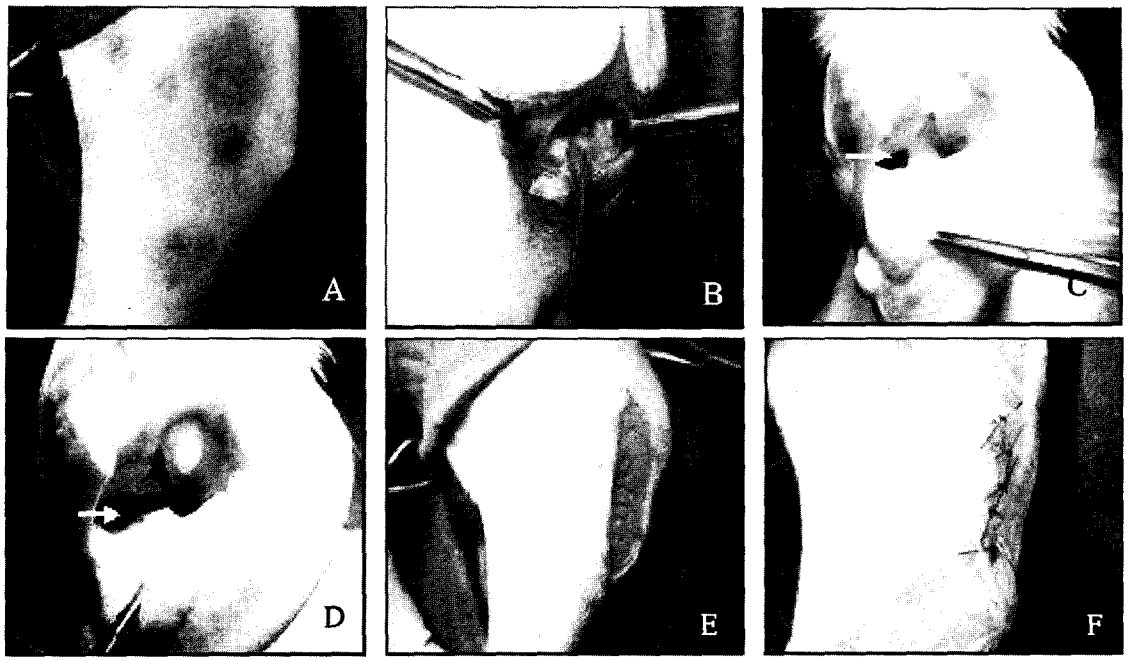

Fig 1. A, The dogs were placed in lateral recumbency and the skin was prepared with povidone-iodine solution and 70% alcohol for aseptic surgery. B. Joint capsule was identified, it was incised approximately 2cm in length. C, Arrows indicate cranial cruciate ligament. D, Arrows indicate rupture of the cranial cruciate ligament by No. 11 scalpel blade. E, Joint capsule was closed using a simple continuous suture of 2-0 catgut. F, The skin was closed by a simple interrupted suture of 3-0 nylon.

the surface; 2 = erosion extended into superficial or middle layers; 3 = erosion extended into deep layers; and 4 = erosion extended to the subchondral bone.

Histologic Evaluations

1) Cartilage. Histologic evaluation was performed on sagittal sections of cartilage from the lesional areas of each femoral condyle and tibial plateau as described. Specimens were dissected, fixed in 10% bufferd formalin, and embedded in paraffin for histologic evaluation. Serial sections (5 μm) were stained with hematoxylin and eosin stain, Standard Toluidine Blue method, PAS technique and Masson trichrome technique.

2) Synovial membrane. Representative specimens of synovial membrane from the gutters of the medial and lateral knee compartments were also dissected from underlying tissue. The specimens were fixed in 10% bufferd formalin, embedded in paraffin, sectioned (5 μm), and stained with hematoxylin and eosin. Two synovial membrane specimens from each compartment were examined, serial selections were made throughout the specimens.

Hematological and Radiological Evaluations

Hematologic and biochemical values were evaluated before the operation, on day 1, 3, 5, 7, 14 and 28 after the operation, and on day 14 and 28 after the administration of drugs; WBC, RBC, PCV, AST, ALT, BUN, creatinine and T-protein. Radiographic findings were evaluated on day -1, 14 and 28 after the operation, and on day 14 and 28 after the administration of drugs.

Results

Macroscopic Findings

The earliest changes of patients with cranial cruciate ligament rupture are characterized by disruption and loss of the collagen fibrils and proteoglycans. This eventually leads to gross changes ranging from fibrillation and fissures to complete loss of surface cartilage, exposing underlying bone. Despite these facts, we could not find fibrillation of surface cartilage and it appeared normally in all groups. Slight yellowish discoloration of the surface found some of the experimental dogs. But macroscopic findings showed no significant differences among the groups (Fig 2).

Histologic Findings

On microscopic examination, focal swelling and fibrillation of the cartilaginous surface did not make progress to extensive splitting and cracking of superficial and deeper layers of the cartilage and cartilage surface, and synovium are normal in all groups. Histologic findings showed no significant differences among the groups (Fig 3).

Laboratory Findings

1) WBC. The changes of WBC values ($10^3/\mu l$) were increased from 14.86 ± 4.23 on day 0 to 23.24 ± 6.33 on day 1 in Group 1, from 17.93 ± 7.36 to 22.05 ± 7.36 in Group 2,

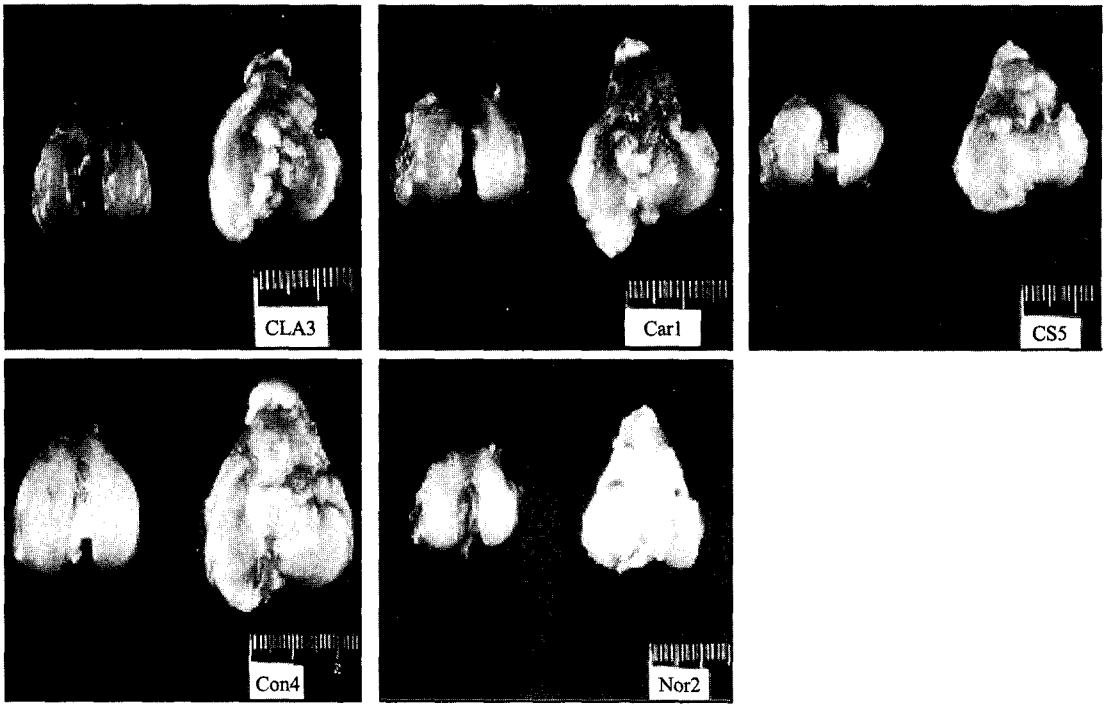

Fig 2. Macroscopic appearance, at 8 weeks, cartilage from the femoral condyles and tibial plateaus in each group. Slight yellowish discoloration of the cartilage surface found some of the experimental dogs. But, macroscopic findings showed no significant differences among the Groups.

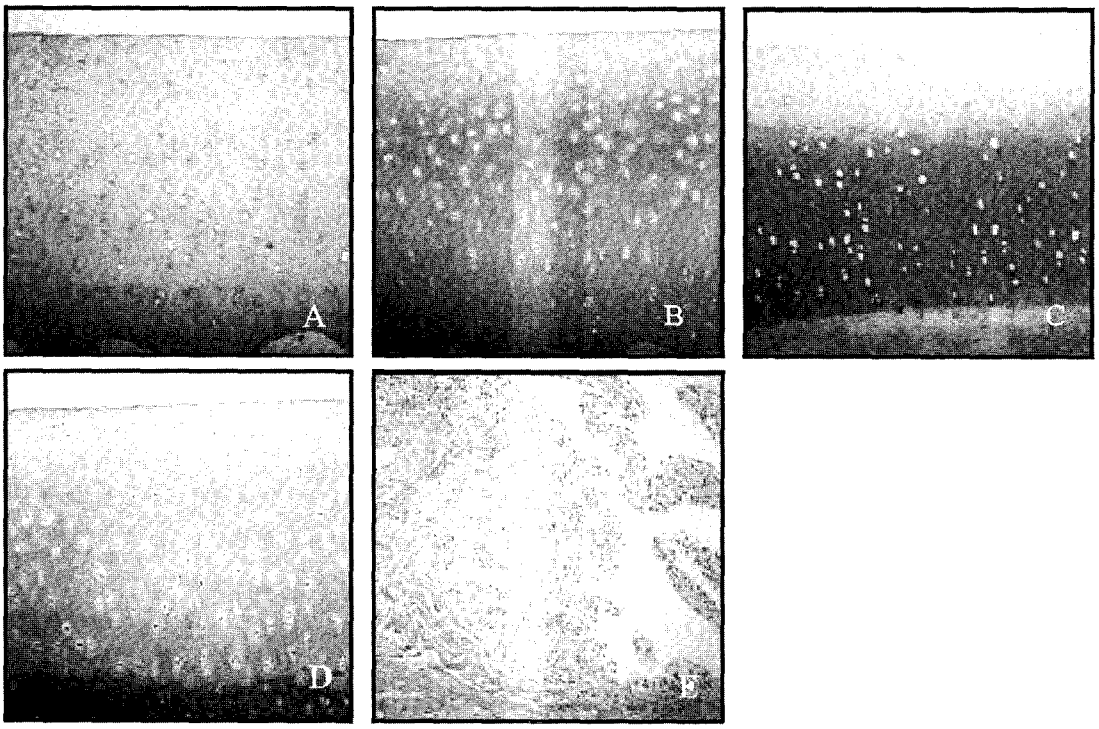

Fig 3. Representation sections of articular cartilage in Control group. Chodrocytes are flattened, and collagen fibrils are mostly parallel to the surface in the tangential zone. Fibrils decussate in the intermediate zone and lie more perpendicular to the surface in the radial zone. A, H&E B, PAS C, standard toluidine blue method D, Masson trichrome technique E, synovium (H&E) × 100

from 15.02± 3.34 to 21.18± 1.12 in Group 3 and from 21.82 ± 2.97 to 24.87± 4.62 in Group 4.

The WBC values of Group 1, 2, 3 and 4 were 12.07± 2.01, 12.84± 1.29, 14.21± 4.49 and 18.67± 3.38 on day 14, respectively. These values decreased gradually from day 5, and recovered from normal ranges on day 56 (Table 1).

2) RBC. The ranges of RBC counts (10^6/μl) were from 6.39± 7.09 to 7.72± 6.76 in Group 1, from 5.94± 4.62 to 7.52± 9.61 in Group 2, from 5.10± 2.49 to 7.46± 8.04 in Group 3 and from 5.82± 5.69 to 7.44± 8.14 in Group 4. The values showed no significant differences among the Groups (Table 2).

3) PCV. The PCV values (%) were from 38.56± 4.96 to 45.34± 6.36 in Group 1, from 37.56± 2.58 to 43.65± 2.99 in Group 2, from 39.97± 1.54 to 46.69± 1.32 in Group 3 and from 38.56± 1.23 to 43.56± 3.11 in Group 4. The values showed no significant differences among the groups (Table 3).

Radiographic Findings

Radiographic findings in patients with cranial cruciate lig-

Table 1. Changes of total WBC counts in dogs with experimental cruciate ligament rupture (Mean± SD, 10^3/μl)

Groups	1 (CLA)	2 (Car)	3 (CC)	4 (Con)
Pre-operation	14.86± 4.23	17.93± 7.36	15.02± 3.34	21.82± 2.97
day 1	23.24± 6.33	22.05± 7.36	21.18± 1.12	24.87± 4.62
day 3	16.75± 7.90	16.95± 5.88	18.27± 7.84	17.05± 5.39
day 5	15.14± 4.19	16.51± 5.96	19.87± 7.34	16.41± 5.05
day 7	16.03± 7.89	15.43± 7.75	16.28± 8.41	17.52± 6.14
day 14	15.42± 3.13	17.11± 7.08	22.19± 1.04	18.74± 5.83
day 28	15.83± 3.13	24.64± 2.26	19.80± 1.04	15.53± 1.26
day 42	11.85± 2.88	16.60± 7.32	18.92± 6.36	16.92± 6.18
day 56	12.07± 2.01	12.84± 1.29	14.21± 4.49	18.67± 3.38

*CLA; conjugated linoleic acid, Car; carprofen, CC; CLA+Car, Con; control

Table 2. Changes of total RBC counts in dogs with experimental cranial cruciate ligament rupture (Mean± SD, 10^6/μl)

Groups	1 (CLA)	2 (Car)	3 (CC)	4 (Con)
Pre-operation	7.27± 6.27	6.03± 9.63	5.10± 2.49	6.88± 1.06
day 1	6.66± 5.01	6.23± 6.84	5.53± 1.75	5.82± 5.69
day 3	6.39± 7.09	6.17± 5.13	5.68± 1.15	5.94± 1.06
day 5	6.50± 7.08	6.45± 1.33	5.94± 8.55	5.89± 7.24
day 7	6.70± 4.85	6.16± 5.30	5.44± 6.69	5.75± 7.70
day 14	6.84± 4.94	5.94± 4.62	5.89± 6.94	6.21± 1.07
day 28	7.72± 6.76	7.01± 9.23	7.08± 8.38	7.11± 4.23
day 42	7.27± 7.37	6.32± 1.85	7.19± 1.03	7.44± 8.14
day 56	6.46± 1.03	7.52± 9.61	7.46± 8.04	5.82± 5.69

*CLA; conjugated linoleic acid, Car; carprofen, CC; CLA+Car, Con; control

Table 3. Changes of total PCV in dogs with experimental cranial cruciate ligament rupture (Mean± SD, %)

Groups	1 (CLA)	2 (Car)	3 (CC)	4 (Con)
Pre-operation	40.56± 1.25	42.35± 2.32	41.23± 2.36	43.56± 3.11
day 1	39.56± 1.89	43.65± 2.99	42.36± 1.99	40.65± 2.11
day 3	42.36± 1.85	43.35± 4.63	41.23± 1.45	42.35± 3.25
day 5	41.33± 3.64	40.65± 1.56	44.84± 3.87	40.56± 1.23
day 7	43.56± 2.56	39.65± 4.56	45.55± 2.10	42.23± 4.22
day 14	45.34± 6.36	42.34± 2.54	46.69± 1.32	40.23± 1.23
day 28	43.56± 2.98	40.51± 2.65	41.32± 2.54	42.53± 5.33
day 42	40.86± 2.76	39.86± 3.64	39.98± 2.31	39.23± 2.33
day 56	38.56± 4.96	37.56± 2.58	39.97± 1.54	38.56± 1.23

*CLA; conjugated linoleic acid, Car; carprofen, CC; CLA+Car, Con; control

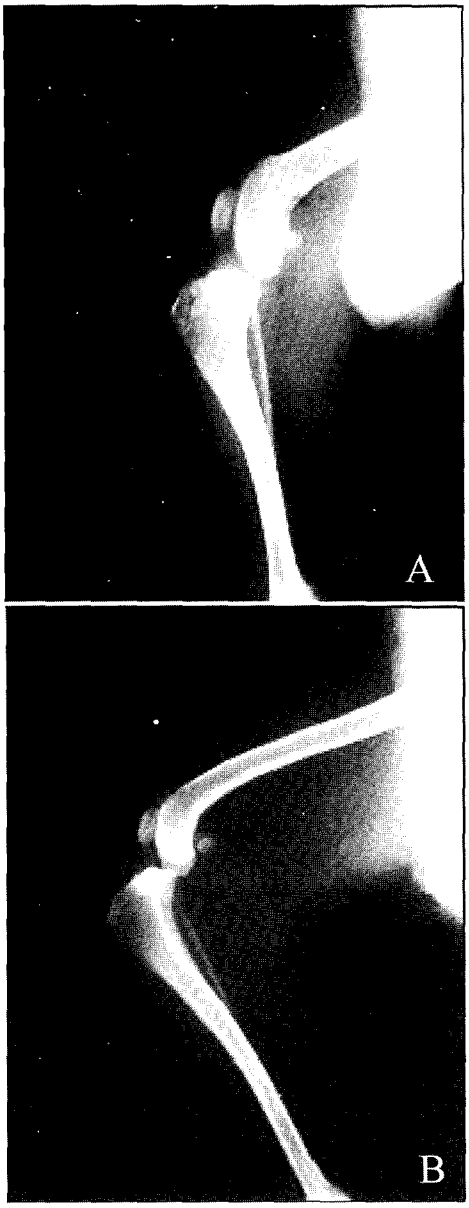

Fig 4. Lateral radiographs of the stifle in a dog with cranial cruciate ligament rupture. A; Cranial displacement of tibia B; Joint effusion.

ament rupture include osteophyte formation along the trochlear ridge, caudal surface of the tibial plateau, and inferior pole of the patella. Thickening of the medial fibrous joint capsule and subchondral sclerosis are also evident. Despite these facts, we could not find articular and periarticular osteophyte formation, subchondral bone sclerosis in our study. But, there were cranial displacement of the proximal tibia relative to the femoral condyles in all groups. The popliteal sesamoid were normal in position in all groups, but appeared relatively more caudal in position because of cranial displacement of tibia. There were also observed joint effusion. Radiographic findings showed no significant differences among the Groups (Fig 4).

Discussion

The most common mechanism of CCL rupture is usually associated with a sudden rotation of the stifle with the joint in 20° to 50° of flexion. In this position the cruciate ligaments begin to twist on each other and on themselves to limit the normal internal rotation of the tibia on the femur. With excessive internal rotation of the tibia, the CCL becomes wound very tightly and is subject to trauma from the lateral femoral condyle as it rotates against it[1]. This may cause the CCL to rupture in its midpoint or, in the case of younger animals, to avulse a portion of its bony attachment. Another mechanism of injury to the CCL is hyperextension. The CCL is the primary check against hyperextension of the stifle.

Rupture of either or both cruciate ligaments produces marked instability of the stifle joint, resulting in pain and lameness[3]. This instability also leads to progressive degenerative changes within the joint. Clinical[31] and experimental[3,4,12,14], observations have demonstrated that these changes consist of periarticular osteophyte formation, capsular thickening, and meniscal degeneration. Our study produced marked pain and lameness. However, we could not find lesions of surface cartilage and it appeared normally in our study. We thought that because it was a short time after CCL rupture in our study relative to others study. So, these changes did not occur in our study. Histologic survey also showed that by CCL of 5 years of age showed overall loss of fibroblasts, metaplasia of surviving fibroblasts to chondrocytes, the structural organization of collagen fibers and primary collagen bundles. And these degenerative changes progressed in severity with age[11]. These developments have been associated with the aging process and may explain the fact that the majority of cruciate injuries are seen in dogs over 5 years of age[27]. We do not exactly know age of our experimental dogs. But, We used to experimental dogs of under 5 years in ages. So, we thought that histological changes did not occur in our study.

In obese animals, stresses are increased and the possibility of degenerative joint changes is greater. As joint changes develop, the cruciate ligaments undergo alteration in their micro-structure and synovium[27]. In dogs weighing less than 15 kg, the degenerative changes were less severe and started several years later. The maximum stress and strain energy of the ligament decreased, and this decrease was significantly greater in dogs weighing more than 15 kg than in those weighing less[2].

So, we thought that degeneration and rupture of the CCL initiated osteoarthritis within the stifle as a result of instability. Therefore, much research was focused on finding a possible link between loss of the CCL and initiation of osteoarthritis. We suggest, however, that osteoarthritis is the primary lesion within the stifle, preceding and contributing to rupture of the CCL.

So, we thought that no early stage change in the canine stifle joint following experimental rupture of the cranial cruciate ligament in this study.

References

1. Arnoczky SP. Marshall JL. Pathomechanics of cruciate and meniscal injuries. In Bojrab MJ(ed); Pathophysiology of Small Animal Surgery. Philadelphia: Lea & Febiger. 1981: 590-603.
2. Arnoczky SP. Pathomechanics of cruciate ligament and meniscal injuries. In Bojrab MJ(ed): Disease Mechanisms in Small Animal Surgery, 2nd ed. Philadelphia: Lea & Febiger. 1993: 764-777.
3. Arnoczky SP, Rubin RM, Marshall JL. Microvasculature of the cruciate ligaments and its response to injury. J Bone Joint Surg 1979; 61: 1221-1229.
4. Bentley G, Kreutner A, Ferguson AB. Synovial regeneration and articular cartilage changes after synovectomy in normal and steroid-treated rabbits. J Bone Joint Surg 1975; 57: 454.
5. Brinker WO, Piermattei DL, Flo GL. Diagnosis and treatment of orthopedic conditions of the hindlimb. In: Handbook of Small Animal Orthopedics and Fracture Treatment, 2nd ed. Philadelphia: W.B. Saunders. 1990: 341-470.
6. Carney SL, Billinggham MEJ, Muir H. Sandy JD. Demonstration of increased proteoglycan turnover in cartilage explants from dogs with experimental arthritis. J Orthop Res 1984; 2: 201-206.
7. Ceuppens JL. Endogenous prostaglandin E2 enhances polyclonal immunoglobulin production by ionically inhibiting T suppressor cell activity. Cell Immunol 1982; 70: 41.
8. Ceuppens JL. Non-steroidal anti-inflammatory agents inhibit the synthesis of IgM rheumatoid factor in vitro. Lancet 1982; 1: 528.
9. Dedrick DK, Goldstein SA, Brandt KD. A longitudinal study of subchondral plate and trabecular bone in cruciate-deficient dogs with osteoarthritis followed up for 54 months. Arthritis Rheum. 1993; 36: 1460-1467.
10. Eyre DR, McDevitt CA, Billinggham MEJ, Muir H. Biosynthesis of collagen and other matrix components by articular cartilage in experimental osteoarthritis. Biochem J 1980; 188: 823-837.
11. Gabbiani G, Hirschel BJ, Ryan GB, Statkov PR, Majno G. Granulation tissue as a contractile organ. A study of structure and function. J Exp Med 1972; 135: 719.
12. Glazer I, Kol R, Lavis. Penetrating membrane interaction in communicative systems of cells. In: Electron Microscopy, Vol 2. New York: Elsevier. 1981: 32-33.
13. Grossman CJ, Wiseman J, Lucas FS. Inhibition of constitutive and inducible cyclooxygenase activity in human platelets and mononuclear cells by NSAIDs and COX-2 inhibitors. Inflammation Reserch 1995; 44: 253-257.
14. Hohn RB, Newton CD. Surgical repair of ligamentous structures of the stifle joint. In: Current Techniques in Small Animal Surgery, Philadelphia: Lea & Febiger. 1975: 470-479.
15. Howell DS, Muller F, Manicourt DH. A mini review: Proteoglycan aggregate profiles in the Pond-Nuki dog model of osteoarthritis and in canine disuse atrphy. Br J Rheumatol 1992; 32(suppl. 1): 7-11.
16. Hugh E, Glucosamine, conjugated linoleic acid, and ascorbic acid compositions for the prevention and treatment of inflammation, osteoarthritis, and their degenerative joint disease. PCT int 2002: 16-19.
17. Hulse DA, Johnson AL. Management of joint disease. In: Small Animal Surgery. St Louis: Mosby. 1997: 957-986.
18. McLaughlin RM. Hind limb lameness in the young patient. Vet Clin North Am Small Anim Pract 2001; 23: 106-107.
19. Merck. Methods and compositions for the prevention and treatment of inflammation, osteoarthritis, and other degenerative joint disease. PCT int 2002; 16-22.
20. Pelletier JP, Lajeunesse D, Hilal G, Jovanovic D. Carprofen reduces the structural changes and abnormal subchondral bone metabolism of experimental osteoarthritis. Osteoarthritis and cartilage 1999; 7: 327-328.
21. Pelletier JP, Martel-Pelletier J, Altman RD, Ghandur-Mnaymneh L, Howell DS, Woessner JF. Collagenolytic activity and collagen matrix breakdown of the articular cartilage in the Pond-Nuki dog model of osteoarthritis. Arthritis Rheum 1983; 26: 866-874.
22. Ricketts AP, Lundy KM. Evaluation of selective inhibition of canine cyclooxygenase 1 and 2 by carprofen and other nonsteroidal anti-inflammatory drugs. Am J Vet Res 1998; 59: 1441-1446.
23. Sandy JD, Adams ME, Billinggham MEJ, Plaas A, Muir H. In vivo and in vitro simulation of chondrocyte biosynthetic activity in early experimental osteoarthritis. Arthritis Rheum 1984; 27: 388-397.
24. Stone EA, Betta CW, Rudy RL. Folding of the caudal horn of the medial meniscus secondary to the severance of the cranial cruciate ligament. Vet Surg 1980; 9: 121.
25. Vane JR, Botting RM. Mechanism of action of anti-inflammatory drugs. Scand J Rheumatol 1996; 102: 9-21.
26. Vasseur PB, Johnson AL, Budsberg SC, Lincoln JD, Toombs JP. Randomized, controlled trial of the efficacy of carprofen, a nonsteroidal anti-imflammatory drug, in the treatment of osteoarthritis in dogs. J Am Vet Med Assoc 1995; 206: 807-811.
27. Vasseur PB, Pool RR, Arnoczky SP, Lau RE. Correlative biomechanical and histological study of the cranial cruciate ligament in dogs. Am J Vet Res 1985; 46: 1842-1854.
28. Venn G, Billinggham MEJ, Hardingham TE. Increased proteoglycan synthesis in cartilage in experimental canine osteoarthritis does not reflect a permanent change in condrocyte phenotype. 1995; 38: 525-532.
29. Watkins BA, Li Y, Lippman HE, Seifert MF. Biochemical and molecular actions of fatty acids in bone modeling. World Rev Nutr Diet 2001; 88:126-140.
30. Weinberger A, Schumacher HR. Experimental joint trauma: synovial response to blunt trauma and inflammatory reaction to intraarticular injection of fat. J Rheumatol. 1981; 8: 380-389.
31. Zahm H. Surgical treatment of rupture of the crucial ligament in dogs with the use of synthetic materials. Berl Munch Tierarztl Wochenschr 1966; 79: 1-4.

개에서 Conjugated Linoleic Acid와 Carprofen이 실험적 골관절염 초기 진행에 미치는 효능

박세일 · 배재성 · 권영삼 · 장환수 · 李文學 · 임재현 · 엄기동 · 김정은 · 장광호[1]
경북대학교 수의과대학

요 약 : 개에서 실험적으로 앞쪽 십자인대 중간부를 절단한 다음 초기 병변을 관찰하고 그 초기 병변에 대한 conjugated linoleic acid (CLA), carprofen 그리고 두 약물의 병용에 따른 효과를 비교하고자 본 실험이 수행되었다. 실험견은 앞쪽 십자인대를 파열한 CLA 처치군, Carprofen 처치군, CLA와 Carprofen 병용처치군 그리고 양성대조군과 파열하지 않은 정상견으로 구성된 음성대조군으로 총 5개군으로 분류하고 각 군에 5두씩 배치하였다. 실험견의 무릎관절 외측 피부를 절개하고 관절낭 외측을 절개한 다음 앞쪽 십자인대 중간부로 판단되는 부위를 절단하였다. Carprofen과 CLA는 수술 후 4주부터 4주 동안 경구 투여하였다. 술후 8주 후에 육안적, 조직학적 평가를 실시하였다. 조직학적 검사로는 hematoxylin and eosin 염색, standard toluidine blue, PAS 그리고 Masson trichrome 염색법을 이용하였으며 혈액학적, 그리고 방사선학적 검사를 실시하였다. 조직학적 검사와 혈액학적 검사에서 유의적인 변화는 나타나지 않았다. 방사선 검사에서는 앞쪽 십자인대 파열에 따른 대퇴골과 경골의 정렬이상과 부종이 모든 군에서 나타났으며 육안적 검사에서는 대부분 실험견의 대퇴 연골 표면상이 엷은 황색을 보였다. 이상의 결과를 통하여 실험적으로 유발된 개의 앞쪽 십자인대 파열에 대해 CLA, carprofen 그리고 이들의 합제는 초기 변화상에서 뚜렷한 변화를 나타내지 않았다.

주요어 : Conjugated Linoleic Acid, carprofen, 앞쪽십자인대, 개