FULL PAPER *Surgery*

Efficacy and Safety of Firocoxib for the Treatment of Pain Associated with Soft Tissue Surgery in Dogs under Field Conditions in Japan

Yumi KONDO[1)]*, Kazuaki TAKASHIMA[2)], Satoshi MATSUMOTO[1)], Masahiro SHIBA[1)], Tomoko OTSUKI[1)], Gen KINOSHITA[1)], Joseph ROSENTEL[3)], Sheila J. GROSS[3)], Candis FLEISHMAN[3)] and Yoshihisa YAMANE[2)]

[1)]*Merial Japan, Tokyo Opera City Tower, 3–20–2 Nishi Shinjuku, Shinjuku, Tokyo 163–1488, Japan*
[2)]*Animal Clinical Research Foundation, 214–10 Yatsuya, Kurayoshi, Tottori 682–0025, Japan*
[3)]*Merial Limited, 3239 Satellite Blvd. Duluth, GA 30096, U.S.A.*

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ABSTRACT. Use of firocoxib in dogs for postoperative pain control has not been published in any of the journals in Japan. A field study was conducted to evaluate the efficacy and safety of firocoxib in dogs in controlling pain associated with soft tissue surgery in Japan. The study followed a negative control, double-blind, multicenter clinical efficacy study using a randomized block design. A total of 131 client-owned dogs presented to the clinical practices for soft tissue surgery were enrolled. Sixty-nine dogs were allocated to the firocoxib-treated group and received 5 mg/kg of firocoxib orally on Day 0 before the surgery and once daily through Day 2, while 62 dogs were allocated to the non-treated group handled in a similar manner only without the firocoxib administration. Pain assessment took place on Day 0 before the surgery through Day 2. The primary efficacy variable was a success/failure variable based on whether the dog needed rescue medication (based on pain assessment after the surgery or Investigator's judgment) and a significant difference between firocoxib-treated group (16.4%) and non-treated group (50.0%) (P=0.0031) was observed. There was no adverse event during the study that was considered to be related to the administration of firocoxib. This study indicated the clinical efficacy and safety profile of firocoxib administered to control pain associated with soft tissue surgery under field condition.

KEY WORDS: canine, efficacy, firocoxib, post-operative pain, safety.

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Many of the non-steroidal anti-inflammatory drugs (NSAIDs) have proven to be effective in controlling post-operative pain in dogs when used either alone or in combination with opioids [3, 5, 8, 10, 11, 13]. However, the administration of NSAIDs may induce gastrointestinal toxicity, compromise renal blood flow, and/or cause hemostatic abnormalities as the results of inhibition of cyclo-oxygenase (COX). There are at least two isoforms of COX that are responsible for synthesis of prostaglandins. COX-1 is usually a constitutive enzyme expressed in tissues. Prostaglandins, prostacyclin, and thromboxane synthesized by this enzyme are responsible for normal physiologic functions. COX-2 is induced and synthesized by macrophages and inflammatory cells after the stimulation by cytokines and other mediators of inflammation, although it may be a constitutive of some of the tissues [15]. Renal blood flow and hemostasis are the important factors especially for the safety of surgery, and it is desirable to minimize the effect on these functions.

Firocoxib was developed specifically for veterinary use, and it showed 350- to 430-fold selectivity for COX-2 in canine whole blood in *in vitro* assays [12, 14]. The efficacy of the drug has been demonstrated *in vivo* in the urate crystal model of acute synovitis [14]. Additionally, several clinical trials have shown that firocoxib is effective when used on dogs with osteoarthritis [6, 9, 16, 18]. Considering the physiological function of two isoforms and the fact that firocoxib has a high COX-2 selectivity, firocoxib has a possibility to be an optimal NSAID to be used for controlling post-operative pain. Firocoxib has been approved for the control of post-operative pain in many countries and one study using firocoxib, before surgery has been reported [1]. However, the type of surgery and anesthetic procedure was the same in the report. In actual clinical practice, surgical types and protocols and anesthetic procedures and drugs used in surgeries are various.

The purpose of this study was to evaluate the efficacy and safety of firocoxib in controlling post-operative pain associated with soft tissue surgery under field condition.

MATERIALS AND METHODS

Animals: Dogs presented to the clinical practices for soft tissue surgery were included in the study. Allowable procedures included: abdominal surgeries (e.g., ovariohysterectomy, abdominal cryptorchidectomy, splenectomy and cystotomy) or major external surgeries (e.g., mastectomy, skin tumor removal ≥8 cm). Castration was not included in the allowable procedures. Ovariohysterectomy did not present greater than 40% of the procedures for all sites. All dogs were in satisfactory general health other than the presenting condition. Animals that had been treated with non-steroidal anti-inflammatory drugs (NSAIDs), short acting

*CORRESPONDENCE TO: KONDO, Y., Merial Japan, Limited, Tokyo Opera City Tower, 3–20–2 Nishi Shinjuku, Shinjuku, Tokyo 163–1488, Japan.
e-mail: yumi.kondo@merial.com

steroids, and/or analgesics within the previous 14 days, or with long acting steroids, polysulfated glycosaminoglycans and/or other nutraceuticals within the previous 30 days, or were suffering from systemic disease, fractious or otherwise unsuitable for inclusion in the study, in the opinion of the Investigator, were excluded. According to the label instruction, dogs less than 3 kg of weight and 10 weeks of age were excluded. Animals with concurrent painful conditions other than the condition presented for surgery were considered unsuitable for inclusion in the study.

Study design: This study was a negative control, double-blinded, multicenter, clinical efficacy study using a randomized design, where blocks were the sites, and replicates were based on order of enrollment. The protocol was in compliance with and approved by the Merial Institutional Animal Care and Use Committee. Informed Consent and Agreement was obtained from the owner of each dog according to Japanese Good Clinical Practice Ministerial Ordinance, before dogs were enrolled in the study. At each site, Investigators who were veterinarians and by training and experience, capable of performing the procedures called for in the protocol were assigned. Investigators were blinded as to allocation and made assessments of the effect of the drug. Also, the owner of the animal was unaware of the treatment assignment. For each site, replicates of two dogs were formed based on order of enrollment for each surgery category (abdominal surgery or major external surgery). Within replicate, one dog was randomly allocated to the firocoxib-treated group and the other to the non-treated group. A unique allocation sequence generated by using a computer randomization list was provided to each site. Each dog was weighed for dosage calculation upon enrollment into the study on Day 0. The article was administered by the personnel different from the Investigators. The treatment administrator at the site administered firocoxib (5.0 mg/kg PO; PREVICOX®, Merial Japan Limited, Tokyo, Japan) to each dog in the firocoxib-treated group on Day 0 at 2 hr prior to the surgery, which was defined as the time from intubation to extubation, and repeated administration at 24-hr intervals on Days 1 and 2. In clinical practice, duration of treatment for pain relief and hospitalization after surgery varies depending on the type of surgery, condition of the animal (patient) or the practice of attending veterinarians. The treatment protocol until Day 2 in a clinic was considered to be possible for all targeted cases. Animals in the non-treated group were sham dosed and handled in a similar manner to the dogs in the firocoxib-treated group, but without administration of firocoxib. Day 0 was not the same calendar day for all participants.

Procedure: Pre-medications for scheduled surgeries were allowed except for NSAIDs, opioides or alpha-2 agonists. Dogs underwent general inhalant anesthesia for the surgical procedure. Standard anesthetic procedure already in use at each site was followed along with the intravenous fluid therapy during anesthesia or subcutaneous fluid administration before the surgery. Local anesthetics including nerve blocks, epidurals, etc. were excluded.

The short form of Glasgow Composite Measure Pain Scale (CMPS-SF) was used to quantify the level of pain in the dogs (Table 1) [17]. Measurements took place on Day 0 (baseline prior to the first treatment); on Day 0 at 90 min, 3, 5, 7, and 9 hr after the extubation; on Day 1 at 2 and 10 hr after the treatment; on Day 2, animals were observed for the final time-point at 2 hr after the treatment. For each case, the same Investigator recorded all observations, but was not granted access to previous assessments. Animals in the same replicate were not necessarily observed by the same Investigator.

Animals were treated according to normal surgical practice and with regard to their welfare. When the total CMPS-SF was 6 or greater, or if the Investigator considered additional pain medication was required, this was administered according to standard practice. This treatment was called a "rescue medication".

A physical examination was conducted by the Investigator generally on Day 0 (before the surgery), and once daily on Days 1 and 2 prior to the treatment. Blood and urine samples were generally obtained before the surgery prior to the treatment from each dog on Day 0 and again on Day 2 before the treatment. General hematology and chemistry profile were analyzed. Urine test (N-MUTISTICK® SG-L: Bayer Medical, Tokyo, Japan) and microscopic test of urine sediment were conducted.

Statistical analysis: The efficacy variable was the success/failure variable based on whether the dog needed rescue medication. If the total CMPS-SF was 6 or greater, or if the Investigator considered the dog to be in pain, then the dog needed rescue medication and was then considered a treatment failure, and a value of 1 was given for the success/failure variable. Otherwise, the success/failure variable was equal to zero. This variable was analyzed with a generalized linear mixed model, using the "glimmix" macro available in SAS® software version 8.2. The model included a binomial error function and a logit link function, consistent with analyzing a dichotomous response. Treatment was considered a fixed effect, while site and site-by-treatment interaction were considered random effects. CMPS-SF total score was analyzed using repeated measures analysis of variance. The model included site and all interactions with site as random effects, and treatment, time, and the interaction of treatment with time as fixed effects. Least-squares means by treatment and time were calculated. The individual CMPS-SF category scores also were evaluated using the Cochran-Mantel-Haenszel row mean scores test stratified by site.

All analyses utilized a two-sided significance level of α=0.05 and were performed using SAS software version 8.2.

RESULTS

A total of 131 client-owned dogs (71 females, 17 female neutered, 32 males, and 11 male neutered) of various breeds, 3.5 months to 16 years of age, weighing 2.6 to 36.0 kg, were enrolled across 19 sites in Japan. Among them, abdominal surgery was performed on 96 dogs, and 35 dogs underwent major external surgery. Sixty-nine dogs were assigned to the firocoxib-treated group and 62 dogs to the non-treated group (Table 2). Four dogs were excluded from the evalu-

Table 1. The short form of the Glasgow Composite Measure Pain Scale to quantify the level of pain in dogs

In the sections below please tick the appropriate score in each list and sum these to give the total score.

A. Look at dog in Kennel

(I) Vocalization		**(II) attention to wound area**	
Is the dog?		*Is the dog?*	
Quiet	0 ☐	Ignoring any wound or painful area	0 ☐
Crying or whimpering	1 ☐	Looking at wound or painful area	1 ☐
Groaning	2 ☐	Licking wound or painful area	2 ☐
Screaming	3 ☐	Rubbing wound or painful area	3 ☐
		Chewing wound or painful area	4 ☐

B. Put lead on dog and lead out of the kennel

C. If it has a wound or painful area including the abdomen, apply gentle pressure 5 cm around the site

(III) Mobility		**(IV) Response to touch**	
When dog rises/walks is it?		*Does it?*	
Normal	0 ☐	Do nothing	0 ☐
Lame	1 ☐	Look round	1 ☐
Slow or reluctant	2 ☐	Flinch	2 ☐
Stiff	3 ☐	Growl or guard area	3 ☐
It refuses to move	4 ☐	Snap	4 ☐
		Cry	5 ☐

D. Overall

(V) Demeanor		**(VI) Posture and activity**	
Is the dog?		*Is the dog?*	
Happy and content or happy and bouncy	0 ☐	Comfortable	0 ☐
Quiet	1 ☐	Unsettled	1 ☐
Indifferent or non-responsive to surroundings	2 ☐	Restless	2 ☐
Nervous or anxious or fearful	3 ☐	Hunched or tense	3 ☐
Depressed or non-responsive to stimulation	4 ☐	Rigid	4 ☐

Total Score (I + II + III + IV + V + VI)=_____

If the total score is equal to or exceed 6, than the dog should receive rescue medication.

ation of efficacy due to protocol deviation; one dog in the firocoxib-treated group was less than 3 kg (2.6 kg) and the other three dogs, one in the firocoxib-treated group and two in the non-treated group, received opioid or alpha-2 agonist inadvertently as the pre-medication for anesthesia.

The preoperative medications used in the study included acepromazine, ampicillin, atropine sulfate, carbazochrome sodium sulfonate, cefazolin sodium, cimetidine, droperidol, enrofloxacin, diazepam, glycopyrrolate, ketamine hydrochloride, midazolam, piperacillin sodium, ranitidine hydrochloride and vitaminB1. The induction and maintenance medications included diazepam, flunitrazepam, halothane, isoflurane, ketamine hydrochloride, propofol, suxamethonium chloride, thiamylal sodium and thiopental sodium. The postoperative medications included ampicillin, butylscopolamine bromide, carbazochrome sodium sulfonate, cefazolin sodium, dopamine hydrochloride, enrofloxacin, gentamicin, orbifloxacin, penicillin, ranitidine hydrochloride and streptomycin.

The efficacy variable was a success/failure variable based on whether the dog needed rescue medication (which was based on the total CMPS-SF score after surgery or Investigator's judgment) and a significant difference between the firocoxib-treated group (16.4%) and the non-treated group (50.0%) (P=0.0031) was observed (Fig. 1). Percentages of the dogs receiving rescue medication by major surgery types in firocoxib-treated group were 17, 25, 25, 20 and 0% for ovariohysterectomy, skin tumor removal, cystotomy, mastectomy and splenectomy.

The difference between the firocoxib-treated group and the non-treated group in the total CMPS-SF score (calculated as the sum of the 6 individual categories) was significant

Table 2. Demographic variables by treatment group

	Firocoxib-treated group	Non- treated group
N dogs (enrolled)	69	62
Age (years) mean	7.3	7.6
(age range)	(3.5 months–16 years)	(4.0 months–14 years)
Sex (n dogs) Female	38	33
Female spay	8	9
Male	17	15
Male castrate	6	5
Body weight (kg) mean	10.9	11.2
(weight range) (kg)	(2.6–36.0)	(3.0–28.6)
Breeds pure (n dogs)	48	40
Crossbreed (n dogs)	21	22
Surgery category		
Abdominal	53	43
Subtype		
Abdominal cryptorchidectomy	1	2
Cystotomy	8	5
Ovariohysterectomy	20 c)	17
Splenectomy	5 c)	2
Other a)	20	17
Major external	16	19
Subtype		
Mastectomy	5	10
Tumor	8	6
Other b)	3	3

a) Other: Pyometra, Perineocele, Gastrotomy, Cesarean section etc. b) Other: Orchidoncus, Perianal tumor removal, Perianal gland adenoma, etc. c) One dog had both an ovariohysterectomy and a splenectomy.

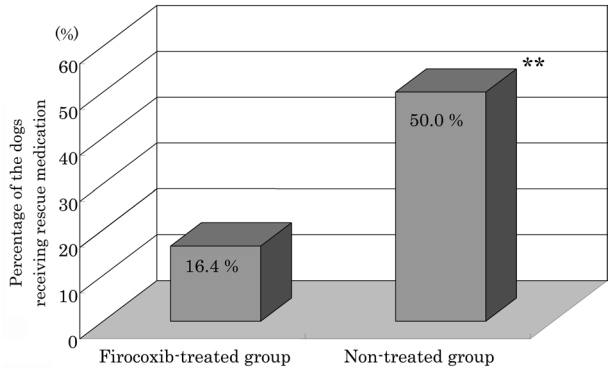

Fig. 1. Percentage of the dogs receiving rescue medication. Only 16.4% of the dogs in the firocoxib-treated group required rescue medication, while 50.0% of the dogs in the non-treated group required rescue medication. This difference was statistically significant (**P=0.0031).

(P=0.0012) (Fig. 2). Results indicated a significant difference between the groups for most of the individual CMPS-SF categories at each time point. Exceptions were seen in the A-i category (Vocalization), which was statistically significant only at 2 hr post treatment on Day 1 and Day 2; and the C-iv category (Response to touch), which was statistically significant at all time points except for Day 0 at 5 hr after the surgery. Total CMPS-SF score also differed significantly according to time (P=0.0009), but the interaction of treatment by time was not significant.

Most of the dogs were prescribed concomitant medications during the study period. Concomitant medications included, but were not limited to antibiotics, hemostatic agents, and vitamins according to normal surgical practice.

Two dogs in the firocoxib-treated group experienced adverse event; one experienced some hemorrhage from surgical incision after the surgery and the dog recovered by Day 2. The other experienced hematuria and recovered by Day 2. In the non-treated group, one dog experienced diarrhea. Analyses data of hematology, serum chemistry and urine specific gravity are shown in Table 3. On Day 2, globulin, potassium and total protein had a significant difference between groups ($0.10<P$). From the rest of urinary results for the firocoxib-treated group and the non-treated group, no remarkable problem was observed between before the surgery (Day 0 prior to the treatment) and after the surgery (Day 2).

DISCUSSION

NSAIDs have been used for the control of post-operative pain, and their efficacy and safety had been reported. Although NSAIDs have shown appropriate safety, theoretically there is still a potential risk of adverse effect on renal blood flow and/or hemostatic ability due mainly to inhibiting

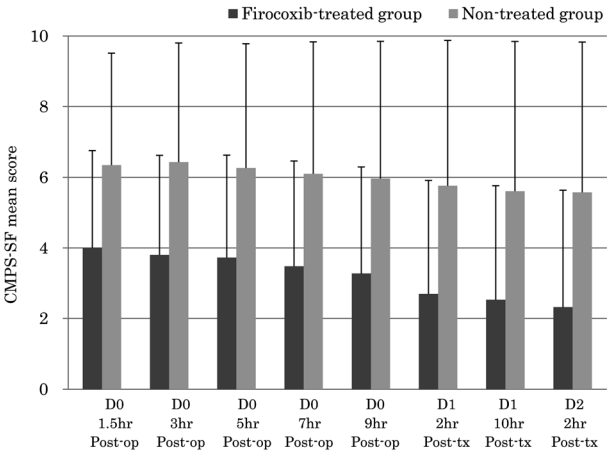

Fig. 2. Glasgow composite measure pain score (CMPS-SF) − Mean scores by treatment group and by time point. The mean scores for total were consistently lower (i.e., less pain) for the firocoxib-treated group than for the non-treated group. There was a significant difference between the groups in the total score (P=0.0012). D=Day. hr=hour. post-op=post-operatively. post-tx=post-treatment.

COX-1. Renal blood flow and hemostasis are important factors especially for the safety of surgery, and it is desirable to minimize the adverse effects on these functions. Firocoxib is expected to be free of the adverse effects caused by inhibition of COX-1, as therapeutic dose of firocoxib inhibits little to no COX-1 [14].

In most cases, it is better to start analgesic therapy before the potentially painful event rather than attempt to regain control of a pain, after it occurs [4]. Firocoxib was administered 2 hr before the surgery to be effective from the start of the procedure, because the time to peak plasma firocoxib concentration was 1.0 ± 0.5 hr [14].

In non-verbal patients, the difficulties of pain assessment are magnified because of the lack of effective communication. Therefore, the assessment relied on the recognition and interpretation of behavioral signs by an observer. There are several pain scales used to determine the level of pain, but they do not necessarily lead to an objective assessment [2, 7]. The pain score criteria used in this study, CMPS-SF, had been used on mixed population of dogs undergoing a variety of surgical procedures, scored by a large number of observers in the past. CMPS-SF was substantiated, because intervention level scores were similar across different clinics and different observers [17]. Additionally, CMPS-SF provides guidance with regard to analgesic requirement, i.e., rescue medication is required, if the total score is 6 or greater. It was considered that CMPS-SF would be an appropriate standard for the assessment of the efficacy of this test article.

The efficacy variable was the success/failure variable based on whether the dog needed rescue medication (which was based on the calculated total CMPS-SF scores after the surgery or Investigator's judgment) and treatment with firocoxib significantly reduced the number of dogs requiring rescue medication (P=0.0031).

The difference between the groups on the total CMPS-SF score (calculated as the sum of the 6 individual categories) was statistically significant (P=0.0012). Results also indicated a significant difference between the groups for most of the individual CMPS-SF categories at each time point. Exceptions were seen in the A-i category (Vocalization), which was statistically significant only at 2 hr post treatment on Day 1 and Day 2; and the C-iv category (Response to touch), which was significant at all time points except for Day 0 at 5 hr after the surgery. Generally, the firocoxib-treated group had lower scores (i.e., less pain and greater mobility), while the non-treated group had higher scores (i.e., greater pain and less mobility).

Total CMPS-SF score also differed significantly according to time (P=0.0009), but the interaction of treatment by time was not significant. Thus, the result indicates a relatively consistent treatment effect over the course of the study.

All results consistently indicated the efficacy of firocoxib treatment. Firocoxib significantly reduced the number of dogs requiring rescue medication (P=0.0031). CMPS-SF scores, representing the level of pain, were generally lower in the firocoxib-treated group than the non-treated group, resulting in a significant difference between the groups. Each category at each time point was generally lower in the firocoxib-treated group than the non-treated group, resulting in significant difference between the groups at most time points, indicating the continuous efficacy of the firocoxib treatment. The consistent treatment effect also was indicated by the total CMPS-SF score which differed significantly according to time (P=0.0009), while the interaction of treatment by time was not significant.

Firocoxib was used in this study with several different anesthetic and other drugs administered perioperatively. The major products used in the study were atropine sulfate, acepromazine, propofol, ketamine hydrochloride, isoflurane, and various antibiotics, and no safety impact suspected relation to firocoxib was reported. Therefore, the use of firocoxib with the commonly used perioperative drugs is very well tolerated.

Two dogs in the firocoxib-treated group experienced adverse event; one experienced some hemorrhage from the wound, after the surgery and the dog recovered by Day 2. The attending veterinarian considered that the hemorrhage was due to the low platelet levels (below normal range) at pre-surgery due to endometriosis and a follicular cyst and could be observed after other surgeries of ovarian and uterine diseases. The other experienced hematuria and recovered by Day 2. The attending veterinarian there considered that the hematuria was due to general stress caused by hospitalization. These observations can be seen after the surgery in the normal practice. Analyses data of hematology, serum chemistry, and urine specific gravity did not indicate clinically or biologically relevant changes in either the firocoxib-treated group or the non-treated group. From the rest of urinary results of the firocoxib-treated group and non-treated group, no remarkable problem was observed between before the surgery (Day 0 prior to the treatment) and after the surgery (Day 2). Those results demonstrated the safety profile of

Table 3. Summary of hematology, serum chemistry and urine specific gravity by treatment group

Variable	Visit	Firocoxib treatment		Untreated control		*P*-value	Reference range
		n	Mean ± SD	n	Mean ± SD		
Alanine aminotransferase (U/*l*)	Pre	68	54.43 ± 53.13	62	81.89 ± 174.84	0.2193	15–70
	Day 2	67	81.90 ± 107.13	62	91.31 ± 154.49	0.6865	
Albumin (g/*l*)	Pre	68	3.21 ± 0.44	62	3.14 ± 0.44	0.3881	2.8–4.0
	Day 2	67	2.91 ± 0.46	62	2.93 ± 0.45	0.7732	
Alkaline phosphatase (U/*l*)	Pre	68	183.31 ± 374.60	62	237.73 ± 740.52	0.5932	20–150
	Day 2	67	239.73 ± 378.08	62	261.84 ± 600.74	0.8014	
Aspartate aminotransferase (U/*l*)	Pre	69	52.01 ± 54.39	62	47.69 ± 41.87	0.6142	10–50
	Day 2	67	95.79 ± 206.38	62	78.69 ± 92.48	0.5503	
Calcium (mg/d*l*)	Pre	69	10.05 ± 0.92	62	10.07 ± 0.74	0.8579	9.0–11.3
	Day 2	67	9.75 ± 0.73	62	9.71 ± 0.70	0.7740	
Chloride (mEq/*l*)	Pre	69	113.96 ± 7.57	62	113.76 ± 5.06	0.8619	105–115
	Day 2	67	115.03 ± 8.56	62	114.65 ± 4.27	0.7503	
Cholesterol (mg/d*l*)	Pre	69	234.16 ± 75.73	62	223.42 ± 90.16	0.4603	100–265
	Day 2	67	217.96 ± 53.90	62	221.52 ± 75.59	0.7572	
Creatinine (mg/d*l*)	Pre	69	0.81 ± 0.27	62	0.77 ± 0.23	0.4287	0.5–1.5
	Day 2	67	0.75 ± 0.26	62	0.76 ± 0.36	0.8923	
Gamma glutamyl transferase (U/*l*)	Pre	68	13.38 ± 24.89	62	11.65 ± 20.93	0.6690	0–9.0
	Day 2	67	11.15 ± 19.17	62	10.71 ± 15.25	0.8862	
Globulin (g/d*l*)	Pre	68	3.08 ± 0.59	62	3.20 ± 0.55	0.2634	2.2–4.0
	Day 2	67	2.92 ± 0.47	62	3.11 ± 0.49	0.0229	
Glucose (mg/d*l*)	Pre	69	80.33 ± 23.96	62	83.69 ± 26.64	0.4486	65–118
	Day 2	67	82.43 ± 27.76	62	78.89 ± 31.13	0.4954	
Phosphorus (mg/d*l*)	Pre	69	4.14 ± 1.33	62	4.19 ± 1.02	0.8067	2.6–6.2
	Day 2	67	4.54 ± 1.22	62	4.60 ± 1.36	0.7883	
Potassium (mEq/*l*)	Pre	69	4.75 ± 0.46	62	4.57 ± 0.50	0.0339	4.4–5.4
	Day 2	66	4.72 ± 0.61[b)]	62	4.47 ± 0.52	0.0134	
Sodium (mEq/*l*)	Pre	69	144.88 ± 3.04	62	145.13 ± 4.13	0.6977	141–152
	Day 2	67	145.39 ± 3.07	62	146.31 ± 3.89	0.1376	
Total bilirubin (mg/d*l*)	Pre	69	0.62 ± 3.23	62	0.19 ± 0.13	0.2961	0.1–0.5
	Day 2	67	0.19 ± 0.16	62	0.21 ± 0.16	0.5947	
Total protein (g/d*l*)	Pre	68	6.29 ± 0.70	62	6.33 ± 0.73	0.7823	5.0–8.0
	Day 2	67	5.83 ± 0.66	62	6.05 ± 0.66	0.0629	
Triglycerides (mg/d*l*)	Pre	69	70.68 ± 50.10	62	62.53 ± 46.60	0.3385	23–57
	Day 2	67	64.99 ± 63.64	62	60.50 ± 29.37	0.6130	
Urea nitrogen (mg/d*l*)	Pre	69	13.93 ± 6.05	62	14.03 ± 5.46	0.9177	10–28
	Day 2	67	12.79 ± 7.11	62	13.00 ± 8.17	0.8768	
Neutrophils (K/μl)	Pre	67	8.62 ± 6.14	60	11.84 ± 15.03	0.1092	3.42–12.55
	Day 2	66	13.30 ± 11.05	62	16.64 ± 16.29	0.1750	
Basophils (K/μl)	Pre	67	0.05 ± 0.07	60	0.05 ± 0.08	0.8749	0–1.06
	Day 2	66	0.04 ± 0.05	62	0.06 ± 0.08	0.2796	
Eosinophils (K/μl)	Pre	67	0.33 ± 0.35	60	0.31 ± 0.34	0.7378	0.11–1.63
	Day 2	66	0.28 ± 0.27	62	0.22 ± 0.23	0.1566	
Lymphocytes (K/μl)	Pre	67	1.21 ± 0.55	60	1.13 ± 0.52	0.4314	0.68–4.89
	Day 2	66	1.14 ± 0.63	62	1.14 ± 0.81	0.9515	
Monocytes (K/μl)	Pre	67	0.59 ± 0.53	60	0.69 ± 0.73	0.3967	0.17–1.63
	Day 2	66	0.83 ± 0.58	62	0.85 ± 0.76	0.8903	
Hematocrit (%)	Pre	67	49.88 ± 8.16	60	48.26 ± 7.69	0.2508	37.0–55.0
	Day 2	66	46.71 ± 6.89	62	45.87 ± 8.20	0.5340	
Hemoglobin (g/d*l*)	Pre	67	16.08 ± 2.62	60	15.43 ± 2.79	0.1740	12.0–18.0
	Day 2	66	14.94 ± 2.49	62	14.61 ± 2.85	0.4890	
Mean corpuscular hemoglobin (*p*g)	Pre	67	23.10 ± 2.18	60	22.71 ± 2.08	0.3014	19.5–26.0
	Day 2	66	23.15 ± 1.87	62	22.77 ± 1.77	0.2433	
Mean corpuscular hemoglobin concentration (g/d*l*)	Pre	67	32.30 ± 2.35	60	31.92 ± 1.92	0.3212	32.0–36.0
	Day 2	66	31.89 ± 1.44	62	31.76 ± 1.29	0.5941	
Mean corpuscular volume (f*l*)	Pre	67	71.63 ± 5.02	60	71.27 ± 5.34	0.6960	60–70
	Day 2	66	72.67 ± 4.87	62	71.74 ± 5.02	0.2923	
Platelets (K/μl)	Pre	67	285.52 ± 119.38	60	283.86 ± 173.16	0.9493	164–510
	Day 2	66	257.90 ± 155.37	62	277.97 ± 157.65	0.4698	
Red blood cells (M/μl)	Pre	67	6.99 ± 1.16	60	6.81 ± 1.15	0.3783	5.50–8.50
	Day 2	66	6.46 ± 1.03	62	6.46 ± 1.07	0.9854	
White blood cells (K/μl)	Pre	67	10.79 ± 6.08	60	14.02 ± 15.20	0.1115	5.7–16.3
	Day 2	66	15.59 ± 11.10	62	18.90 ± 16.61	0.1846	
Urine specific gravity	Pre	53	1.027 ± 0.011	50	1.029 ± 0.012	0.2756	1.015–1.034
	Day 2	43	1.028 ± 0.016	39	1.023 ± 0.011	0.1070	

firocoxib when used on dogs undergoing surgeries.

This study indicated the clinical efficacy and the safety profile of firocoxib when administered orally at 5 mg/kg body weight once daily, starting approximately 2 hr prior to the surgery and continuing for 2 additional days, to control post-operative pain associated with soft tissue surgery under field condition.

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