

Efficacy of postoperative oral tepoxalin after decompressive surgery in dogs with degenerative lumbosacral stenosis

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Abstract

Twenty-three client-owned dogs with degenerative lumbosacral stenosis (DLS) treated by decompressive surgery were included in this study. The dogs were assigned to postoperative medication protocols of tepoxalin (10 mg/kg, SID) for 2 weeks (8 dogs, group 1), of tepoxalin (10 mg/kg, SID) for 6 weeks (7 dogs, group 2), and of carprofen (2 mg/kg, BID) for 2 weeks (8 dogs, group 3). Gait function after decompressive surgery of the dogs was evaluated by force plate analysis (FPA) and questionnaires filled out by their owners. FPA was performed before surgery, and at 4 days, 6 weeks, and 6 months after surgery. Peak vertical (F_z^+), braking (F_y^+), and propulsive forces (F_y^-), and also pelvic/thoracic (P/T) limb ratio of F_z^+ (P/TF z^+), F_y^+ (P/TF y^+), and F_y^- (P/TF y^-) were determined. Questionnaires were completed by the owners before surgery, and at 6 weeks and 6 months after surgery. During the period of the study, the F_z^+ , F_y^+ and F_y^- of the most affected pelvic limb were not different among the groups. The P/TF y^- decreased at 4 days after surgery in all groups, but the difference was not significant. At 6 weeks and 6 months after surgery, there was no significant difference in the P/TF y^- of the dogs in groups 1, 2, and 3. From the questionnaires, the majority of owners were moderately to very satisfied with the result of surgery. In conclusion, tepoxalin has similar postoperative anti-inflammatory and analgesic efficacy to carprofen in dogs with DLS that undergo decompressive spinal surgery.

Keywords: degenerative lumbosacral stenosis, decompressive surgery, force plate, tepoxalin, dogs

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Introduction

Degenerative lumbosacral stenosis (DLS) is a degenerative disorder including Hansen type II disc protrusion, hypertrophy of ligaments, osteophyte formation, and lumbosacral instability (Palmer and Chambers, 1991; Sharp and Wheeler, 2005). These changes contribute to the narrowing of the vertebral canal and the intervertebral foramina, which result in cauda equina compression and inflammation of the nerve roots. The most common signs consist of low back pain, difficulty rising up, reluctance to jump or climb stairs, and unilateral or bilateral pelvic limb lameness (Palmer and Chambers, 1991; Sharp and Wheeler, 2005; Suwankong et al., 2008; Worth et al., 2010). Preliminary diagnosis is based on history, clinical signs, and results of physical examination; the diagnosis is then confirmed by (contrast) radiography, computed tomography (CT), and/or magnetic resonance imaging (MRI) (Sharp and Wheeler, 2005). Nonsurgical treatment comprises exercise restriction and anti-inflammatory medication, using nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids (Sjöström, 2003). Surgical treatment is recommended when pain is severe and unresponsive to medical treatment. Surgical decompression of the cauda equina can be accomplished by dorsal laminectomy. Dorsal fenestration and partial discectomy (Sjöström, 2003; Meij and Bergnut, 2010), or lateral foraminotomy (Gödde and Steffen, 2007) can be performed, if indicated. A surgical success rate of 41 to 78% has been demonstrated (Danielsson and Sjöström, 1999; Janssens et al., 2000; Jones et al., 2000; de Risio et al., 2001; Linn et al., 2003; Suwankong et al., 2007; Suwankong et al., 2008).

Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used for postoperative pain control. Tepoxalin is a potent new NSAID that inhibits the pathways of cyclooxygenase (both COX-1 and COX-2) and 5-lipoxygenase (5-LOX) enzymes in rats and dogs (Wallace et al., 1993; Knight et al., 1996). Tepoxalin has *in vivo* inhibitory activity against COX-1, COX-2, and 5-LOX in dogs with osteoarthritis at the current approved recommended dosage (Agnello et al., 2005). Tepoxalin is available in oral form and its bioavailability is improved by feeding (Homer et al., 2005). Carprofen is a propionic-acid derivative, inhibitor of cyclooxygenase which has well-demonstrated analgesic properties (McKellar et al., 1990). Carprofen is available in oral and injectable forms (Fox and Johnston, 1997). Tepoxalin and carprofen provide effective anti-inflammatory control and pain relief in dogs with osteoarthritis and results have been reported in separate *in vitro* and *in vivo* studies (McKellar et al., 1990; Wallace et al., 1991; Holtsinger et al., 1992; Wallace et al., 1993; Argentieri et al., 1994; Vasseur et al., 1995; Knight et al., 1996; Fox and Johnston, 1997; Kirchner et al., 1997; Lipscomb et al., 2002; Agnello et al., 2005; Homer et al., 2005). However, there are no studies that compare the efficacy of tepoxalin and carprofen *in vivo* for postoperative pain medication in a spontaneous disease animal model.

Following decompressive spinal surgery, the most common complication is recurrence of spinal pain

due to chronic local inflammation and fibrotic adhesions between muscles, nerves and dura mater. Autogenous fat transplantation in the laminar slot is an effective mechanical barrier to prevent the formation of fibrotic adhesions (Quist et al., 1998) but it does not prevent local inflammation. Limb function can be improved if postoperative pain is minimized (Millis, 2004). It is hypothesized that prolonged use of NSAIDs after spinal surgery reduces postoperative spinal pain and improves long-term outcome.

In clinical evaluation, the degree of postoperative pain is difficult to assess objectively in dogs. Veterinarians may subjectively assess the degree of pain in dogs by interviewing the owners, observe and examine the degree of lameness in the dogs, and assess the evoked pain or discomfort by manipulation of the spine.

Force plate analysis (FPA) is a noninvasive, objective assessment of the locomotion in humans and animals (Anderson and Mann, 1994; DeCamp, 1997; McLaughlin, 2001). It has been used to study normal gait (Budsberg et al., 1987; Budsberg et al., 1993) and to evaluate gait in lame dogs, before and after medical and surgical treatments (Dueland et al., 1977; McLaughlin et al., 1991; Budsberg et al., 1996; Jevens et al., 1996; Cross et al., 1997; Rumph and Steiss, 1998; Theyse et al., 2000; Budsberg, 2001; Borer et al., 2003; Grisneaux et al., 2003; Hazewinkel et al., 2003; Horstman et al., 2004; van Klaveren et al., 2005; Suwankong et al., 2007). FPA can provide accurate and reproducible information on the function of each limb and an objective assessment of the efficacy of treatment. In previous studies in dogs with DLS (van Klaveren et al., 2005; Suwankong et al., 2007), ground reaction forces (GRFs) revealed that surgical treatment partially restored the propulsive force of the pelvic limbs in a 6-month postoperative period.

The objective of this study was to evaluate the efficacy of short-term (i.e. 2 weeks) administration of tepoxalin in comparison with a positive control (i.e. carprofen) after decompressive surgery in dogs with DLS. Also, it was hypothesized that prolonged (i.e. 6 weeks) administration of a NSAID might result in decreased spinal pain and improved limb function for a long period (i.e. 6 months) after surgery. Therefore, tepoxalin (2 weeks) was compared to carprofen (2 weeks) and short-term tepoxalin (2 weeks) was compared to long-term (6 weeks) tepoxalin postoperative administration. Outcomes were evaluated using force plate analysis and questionnaires completed by dogs' owners.

Materials and Methods

Animals: Twenty-three client-owned dogs with DLS, referred to the Department of Clinical Sciences of Companion Animals, Utrecht University, and treated by decompressive surgery, were included in the study. The dogs were assigned to three protocols of postoperative oral anti-inflammatory pain medication. The dogs in groups 1, 2 and 3 matched in gender, breed, age, and body weight. The dogs in group 1 (n=8) were 6 male dogs (4 intact, 2 neutered) and 2 female dogs (1 intact, 1 neutered) with a mean age ($\pm$ SD) of 4.3 ± 2.2 years and a mean body weight ($\pm$ SD) of $40.8 \pm$

19.3 kg. The dogs in group 2 (n=7) were 6 male dogs (2 intact, 4 neutered) and 1 intact female dog with a mean age of 5.3 ± 3.1 years and a mean body weight of 33.4 ± 3.6 kg. The dogs in group 3 (n=8) were 6 male dogs (5 intact, 1 neutered) and 2 female dogs (1 intact, 1 neutered) with a mean age of 4.7 ± 1.9 years and a mean body weight of 33.6 ± 7.8 kg.

Dog breeds included Labrador retriever, Great dane, Border collie, German shepherd dog and other shepherd dogs, equally divided in all groups. The majority of dogs in each group were kept as companion animals. Dogs with other lumbosacral disorders, e.g. neoplasia, discospondylitis, and traumatic injuries, were excluded from this study.

Imaging: Survey radiography of the lumbosacral region was performed in the dogs under sedation. Ventrodorsal and lateral views were set with the neutral position of the lumbosacral spine. CT and/or MRI of the L6-S1 region was made in the dogs under anesthesia with sternal recumbency and pelvic limbs extended caudally.

CT was performed using a single slice helical CT scanner (Philips CT Secura, Philips Medical Systems, Eindhoven, The Netherlands) with the exposure settings of 360 mA, 120 kV and with 1 second scanning time. Contiguous transverse 2-mm-thick CT slices were obtained from the region of the last lumbar to the caudal sacral vertebrae. Transverse images were assessed using both bone and soft tissue window settings. Sagittal images were reconstructed from the transverse images.

MRI was performed using a 0.2 Tesla open magnet (Magnetom Open Viva, Siemens AG, Germany). The dogs were put in the position as for CT. T1-weighted transverse and sagittal images were conducted with a repetition time of 510-624 ms and an echo time of 26 ms. T2-weighted sagittal images were conducted with a repetition time of 3835-4450 ms and an echo time of 117 ms. Pixel sizes of 0.95×0.71 mm and 0.86×0.59 mm were used for the sagittal and transverse planes, respectively. Contiguous slice thickness was 3 mm.

Surgical Procedure: Decompressive surgery was performed in all dogs by the same surgeon (BM) with the anesthetized dogs in the position of sternal recumbency. The caudal lumbar and lumbosacral spine was in neutral position. The pelvic limbs were in frog position with both tarsal joints level with the ischiatic tuberosities. Dorsal laminectomy was performed with a motorized burr and Kerrison bone rongeurs in all dogs. The cauda equina nerve roots was determined and investigated for swelling and adhesion. Dorsal fenestration and partial discectomy were carried out to further relieve compression when needed. An autogenous fat graft was obtained from the subcutis and transplanted to the laminectomy site to prevent dural adhesion (Quist et al., 1998).

Postoperative medication and care: Postoperative treatment consisted of amoxicillin/clavulanic acid (12.5 mg/kg every 12 hours, orally) for 2 weeks in all dogs. For postoperative NSAID medication, the dogs were assigned to three protocols. Dogs in group 1 (n=8)

were administered tepoxalin (10 mg/kg every 24 hours) for 2 weeks, dogs in group 2 (n=7) were administered tepoxalin (10 mg/kg every 24 hours) for 6 weeks, and dogs in group 3 (n=8) were administered carprofen (2 mg/kg every 12 hours, orally) for 2 weeks.

Restriction on short walks with a leash was recommended in all dogs for the first six weeks postoperatively, followed by gradual increase in an exercise activity during postoperative weeks 7 through 12.

FPA: FPA was performed before surgery, and repeated at 4 days, 6 weeks, and 6 months postoperatively. The force plate was a quartz crystal piezoelectric Kistler force plate (Kistler type 9261, Kistler Instrumente AG, Winterthur, Switzerland) together with the Kistler 9865E charge amplifiers. Dimension of the force plate was 60 cm wide and 40 cm long. It was built mounted flush with the surface in the center of an 11 m long walkway. A 50 cm high fence was installed in the middle of the runway (5 m) to guide the dogs over the force plate. GRFs were quantified by force transducers which were installed in every corner of the plate. The amplifiers were connected to an Analog-Digital converter, interfaced with a computer that stored the signals. The sampling rate was 100 Hz, and recordings were saved on a computer for further processing. The signals corresponded with the GRFs in the mediolateral (Fx), craniocaudal (Fy), and vertical (Fz) direction. Fz calibration was performed with a standard weight before each recording session. Forward velocity of the dog was quantified during FPA, using two photoelectric switches spaced 3 meters apart and centered on the force plate and computer timing. The FPA recordings were automatically started and stopped by these photoelectric switches.

All dogs were controlled over the force plate with a leash at a walking gait with speed of 1.1 ± 0.2 m/s. Data recorded from runs in which a thoracic limb and, after a short interval, the ipsilateral pelvic limb contacted the plate were determined valid. Each pass across the plate was assessed by an observer, to confirm foot strikes and gait. A minimum of 8 recordings were used for data processing. All forces were normalized for body weight.

Questionnaire: Owners of the dogs (n=23) were asked to fill in the questionnaires for evaluation at different time points (i.e. before surgery, and at 6 weeks and 6 months after surgery). The questionnaire was composed of questions regarding history and clinical symptoms before surgery, and progress in neuro-orthopedic functioning after surgery. The questionnaire consisted of questions answered in YES or NO format, free text answers, a choice of pre-set answers, and answers on a 10-point frequency scale (i.e. 1-10: ranging from "always" to "never") or a 10-point qualitative scale (i.e. 1-10: ranging from "very bad" to "very good").

Calculations and Statistical Analysis: The following parameters were used in the analysis: the peak vertical force (Fz⁺), the peak braking force (Fy⁺), and the peak propulsive force (Fy⁻) of the most affected pelvic limb, i.e.

the limb with the smallest propulsive force. The forces were expressed as N/kg body weight. The pelvic/thoracic (P/T) limb ratio for Fz^+ (P/TFz^+) was identified as the ratio of the sum of the peak vertical forces of the pelvic limbs to the sum of the peak vertical forces of the thoracic limbs.¹³ The P/T ratio for Fy^+ (P/TFy^+) and the P/T ratio for Fy^- (P/TFy^-) were identified in the same way.

Analysis of force plate measurements and evaluation of the questionnaires were performed without prior knowledge about the treatment group to which the dog was assigned. The efficacy of tepoxalin was assessed using a linear mixed model. Three effects were analyzed: 1) the effect of 2 weeks of tepoxalin (group 1) versus 2 weeks of carprofen (group 3), 2) the effect of 2 weeks of tepoxalin (group 1) versus 6 weeks of tepoxalin (group 2), and 3) for all groups, the effect of treatments by comparing force plate measurements before surgery, and at 4 days, 6 weeks, and 6 months after surgery.

Reliability of the responses to the questionnaires was tested by calculation of Cronbach's alpha. A Cronbach's alpha value of 0.70 or higher was determined to be reliable. Comparison of the mean scores of the questionnaires before surgery, and at 6

weeks and 6 months after surgery was performed using the Wilcoxon signed-rank test. All data were expressed as mean $\pm$ SD. The level of significance was set at $P < 0.05$.

Results

Clinical Signs: The clinical signs prior to surgery were similar in all 3 groups (Table 1). The dogs with DLS in all groups refused to perform specific movements (i.e. getting up, jumping into the car, walking stairs, squatting during urination or defecation). The dogs with DLS in each group showed pelvic limb lameness and caudal lumbar pain, and the lumbosacral pressure test evoked a pain reaction (Table 1).

Imaging Findings: The imaging findings were similar in all 3 groups (Table 2). The imaging findings on radiography, CT, and MRI included step formation at the lumbosacral junction, spondylosis deformans, sclerosis of the sacral end plate, elongation of the cranial sacral lamina into the caudal spinal canal of L7 (telescoping), and transitional lumbosacral vertebra (Table 2).

Table 1 Clinical signs in 23 dogs with degenerative lumbosacral stenosis that were divided into 3 groups for postoperative medication after decompressive surgery

Clinical signs	Tepoxalin 2 wks (n=8) N (%)	Tepoxalin 6 wks (n=7) N (%)	Carprofen 2 wks (n=8) N (%)
Pelvic limb lameness	7 (87.5)	6 (85.7)	6 (75)
Caudal lumbar pain	7 (87.5)	6 (85.7)	5 (62.5)
Hypersensitive caudal lumbar spine	1 (12.5)	1 (14.3)	4 (50)
Pain evoked by lumbosacral pressure	7 (87.5)	6 (85.7)	8 (100)
Pain on hyperextension of caudal lumbar spine	6 (75)	5 (71.4)	6 (75)
Pain on tail extension	1 (12.5)	2 (28.6)	1 (12.5)
Atrophy of the thigh muscles	4 (50)	3 (42.9)	3 (37.5)
Difficulty sitting down	5 (62.5)	3 (42.9)	6 (75)
Reluctance to get up	6 (75)	6 (85.7)	8 (100)
Difficulty climbing stairs	5 (62.5)	4 (57.2)	4 (50)
Difficulty jumping	5 (62.5)	3 (42.9)	5 (62.5)

Table 2 Imaging (radiography, CT and MRI) findings and surgical findings in 23 dogs with degenerative lumbosacral stenosis that were divided into 3 groups for postoperative medication after decompressive surgery

Imaging findings	Tepoxalin 2 wks (n=8) N (%)	Tepoxalin 6 wks (n=7) N (%)	Carprofen 2 wks (n=8) N (%)
Disc protrusion	8 (100)	7 (100)	8 (100)
Step formation at L7-S1	5 (62.5)	5 (71.4)	6 (75)
Swelling of spinal nerve roots	3 (37.5)	3 (42.9)	6 (75)
Loss of epidural fat dorsal to the dural sac	2 (25)	1 (14.3)	2 (25)
Transitional vertebra segment	1 (12.5)	-	1 (12.5)
Loss of NP signal intensity on T2 at LS (MRI)	6 (75)	5 (71.5)	6 (75)
Surgical findings			
Disc protrusion	8 (100)	7 (100)	8 (100)
Loss of epidural fat dorsal to the dural sac	2 (25)	1 (14.3)	3 (37.5)
Swelling of spinal nerve roots	3 (37.5)	3 (42.9)	5 (62.5)
Hypertrophy of ligamentum flavum	1 (12.5)	2 (28.6)	1 (12.5)

Surgical Findings: The surgical findings were similar in all 3 groups (Table 2) and included protrusion of the lumbosacral intervertebral disc, loss of epidural fat covering the dural sac dorsally, swelling of the spinal nerve roots, and bulging of the ligamentum flavum.

FPA: The Fz^+ , Fy^+ and Fy^- of the most affected pelvic limb (i.e. the limb with the smallest Fy^-) were not

different among the groups at the start of the study or at 4 days, 6 weeks, and 6 months after surgery (Fig. 1, 2, and 3). At 6 months after surgery, there were no significant differences in the Fy^- of the dogs between group 1 and groups 2 and 3 ($P=0.24$ and $P=0.15$, respectively) (Fig. 3).

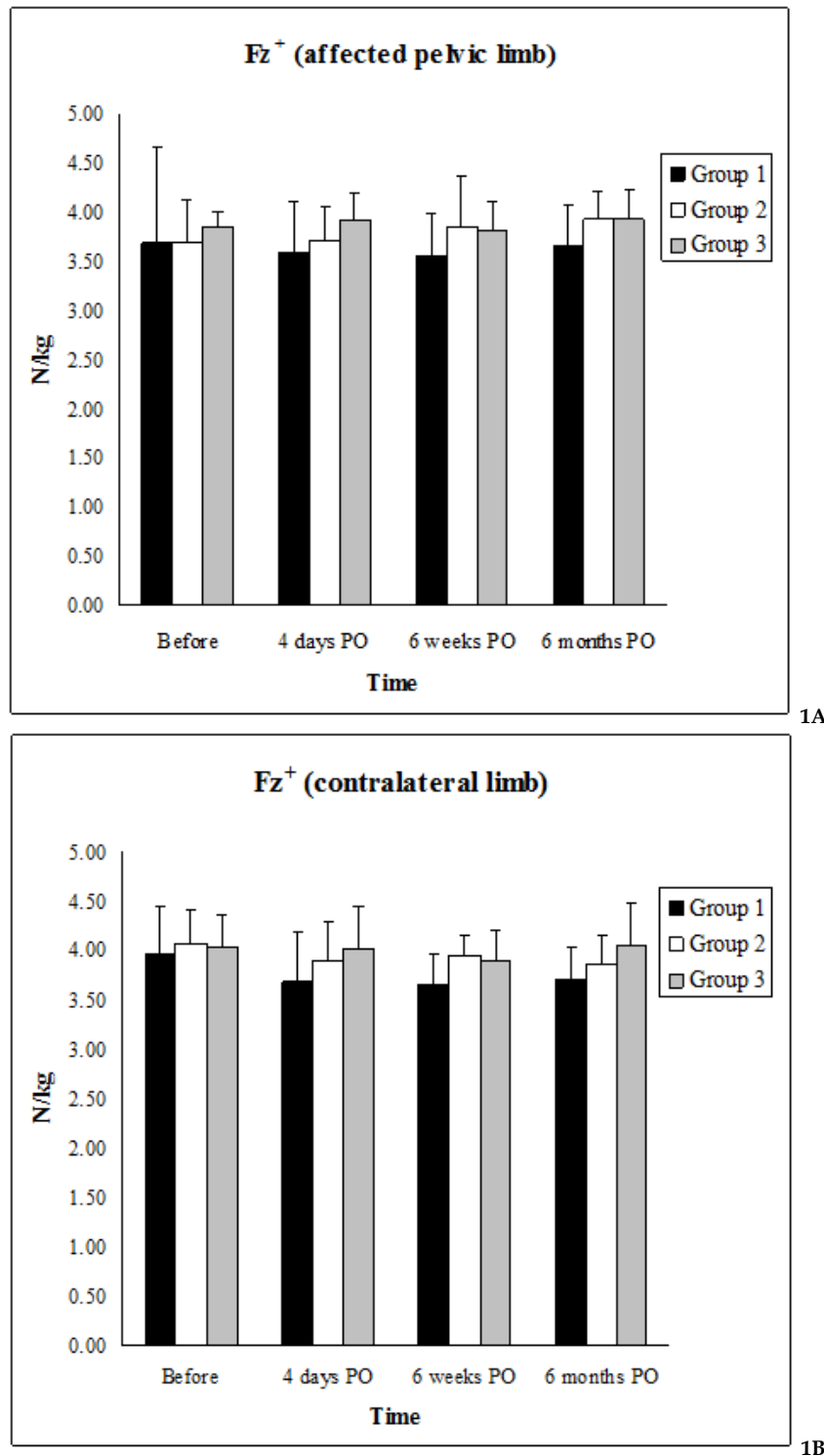


Figure 1 The mean $\pm$ SD peak vertical force (Fz^+) of the affected pelvic limb (1A) and contralateral limb (1B) in dogs with degenerative lumbosacral stenosis before surgery, and at 4 days, 6 weeks, and 6 months postoperatively (PO). Forces are expressed as Newton per kg body weight (N/kg). The postoperative oral medication protocol consisted of 2 weeks of tepoxalin (10 mg/kg SID, group 1), 6 weeks of tepoxalin (10 mg/kg SID, group 2), or 2 weeks of carprofen (2 mg/kg BID, group 3).

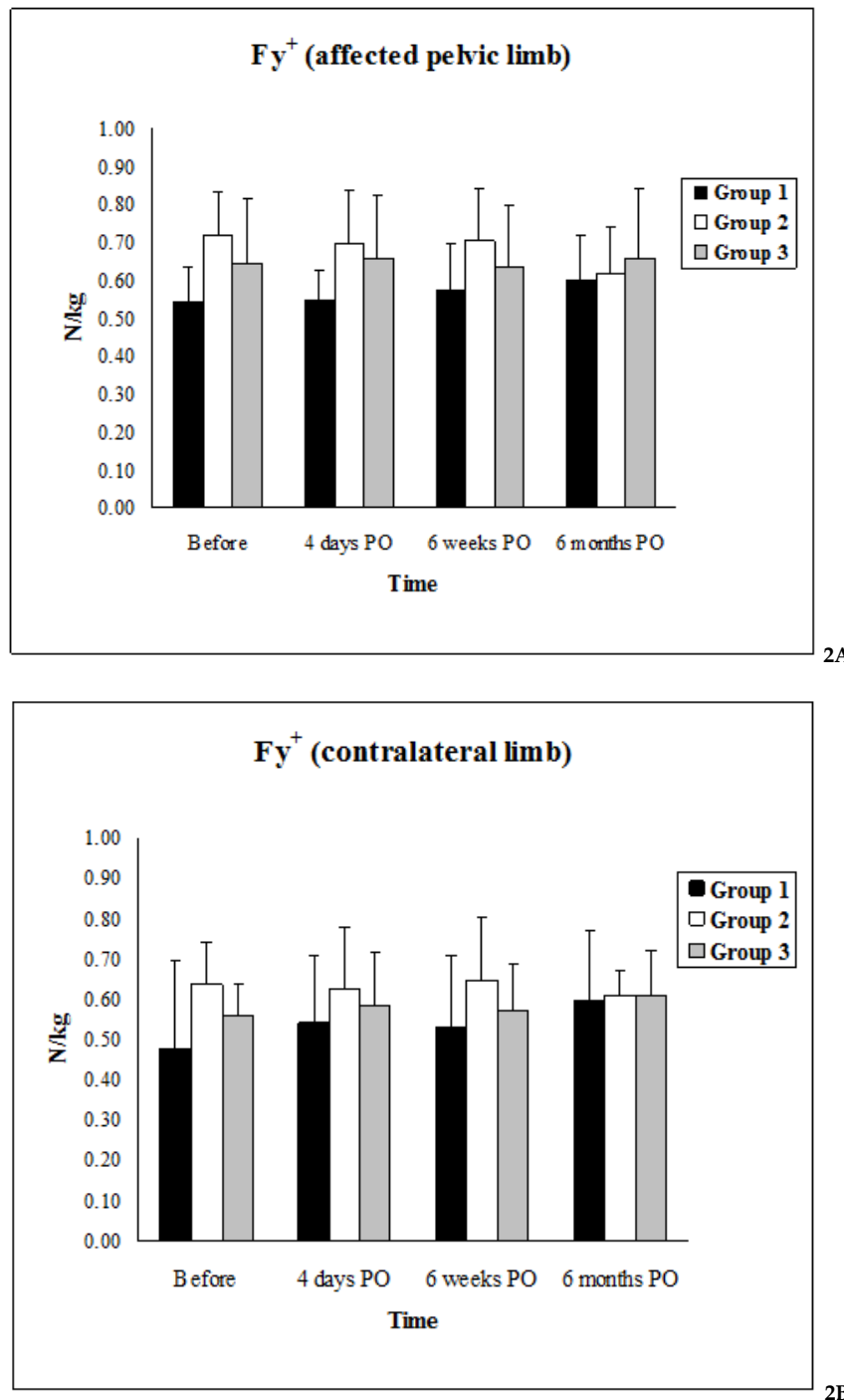


Figure 2 The mean $\pm$ SD peak vertical force (Fz^+) of the affected pelvic limb (**1A**) and contralateral limb (**1B**) in dogs with degenerative lumbosacral stenosis before surgery, and at 4 days, 6 weeks, and 6 months postoperatively (PO). Forces are expressed as Newton per kg body weight (N/kg). The postoperative oral medication protocol consisted of 2 weeks of tepoxalin (10 mg/kg SID, group 1), 6 weeks of tepoxalin (10 mg/kg SID, group 2), or 2 weeks of carprofen (2 mg/kg BID, group 3).

The mean ($\pm$ SD) of P/TFy⁻ for groups 1, 2, and 3 before surgery was 0.67 ± 0.20 , 0.67 ± 0.10 , and 0.65 ± 0.10 , respectively. The mean P/TFy⁻ for groups 1, 2, and 3 at 6 months after surgery was 0.70 ± 0.17 , 0.68 ± 0.1 , and 0.61 ± 0.13 , respectively. The P/TFy⁻ was decreased at 4 days after surgery in all groups compared to the ratio before surgery and that at 6 weeks and 6 months after surgery. However, the difference was not significant. At 6 weeks and 6 months after surgery, the P/TFy⁻ of the dogs in group 1 was not significantly different from the P/TFy⁻ of the dogs in groups 2 and 3 (Fig. 4). Also, there was no

significant difference in the P/TFz⁺ and P/TFy⁺ among the groups of dogs.

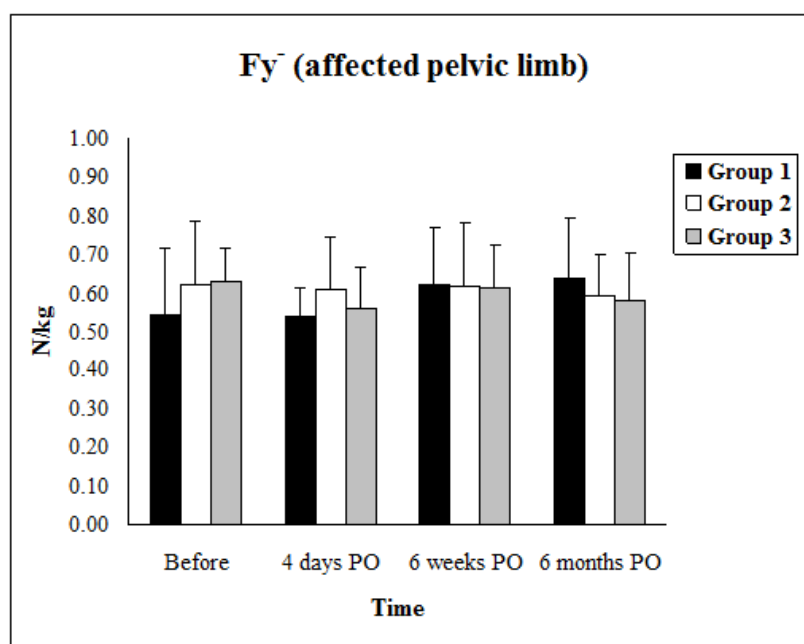
Questionnaires: Responses to the questionnaires were received from all owners in each group. The Cronbach's alpha values of the responses to the questionnaires were 0.70-0.80, indicating that the answers were reliable.

After surgery, the dogs were restrained and walked with a leash for 9.3 ± 4.4 , 7.5 ± 2.4 , and 9.3 ± 3.4 weeks for groups 1, 2 and 3, respectively. At 6 months after surgery, 6 dogs (6/8, 75%) in group 1, 4 dogs (4/7,

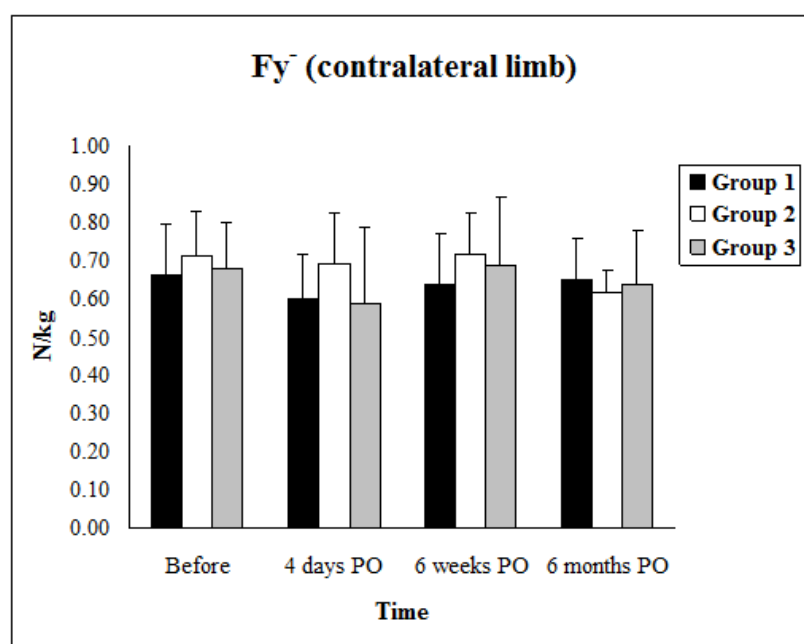
57.1%) in group 2, and 5 dogs (5/8, 62.5%) in group 3 functioned normally. Recurrence of clinical signs occurred in 2 dogs (2/8, 25%) in group 1, 2 dogs (2/7, 28.6%) in group 2, and 2 dogs (2/8, 25%) in group 3.

Improvement in complaints of pelvic limb(s), caudal lumbar pain, difficulty rising, difficulty lying down, and pelvic limb lameness was significantly higher at 6 weeks and 6 months after surgery compared to before surgery ($P < 0.05$) (Fig. 5).

The majority of owners were moderately to very satisfied with the result of surgery and gave a mean score of 7.5 ± 1.8 , 6.8 ± 2.9 , and 7.1 ± 2.8 for the dogs in groups 1, 2 and 3, respectively. The owners were very satisfied with the information supplied before the surgery and gave a mean score of 9.2 ± 0.6 , 7.4 ± 1.5 , and 6.9 ± 1.7 for the dogs in groups 1, 2 and 3, respectively.



3A



3B

Figure 3 The peak propulsive force (Fy) of the affected pelvic limb (3A) and contralateral limb (3B) in dogs with degenerative lumbosacral stenosis before surgery, and at 4 days, 6 weeks, and 6 months postoperatively (PO). Forces are expressed as Newton per kg body weight (N/kg). The postoperative oral medication protocol consisted of 2 weeks of tepoxalin (10 mg/kg SID, group 1), 6 weeks of tepoxalin (10 mg/kg SID, group 2), or 2 weeks of carprofen (2 mg/kg BID, group 3).

One dog in group 1 developed a transient gingivitis during the first days of treatment. One dog in group 2 vomited but had a similar history when treated with carprofen for a previous unrelated orthopaedic problem. The vomiting disappeared when

tepoxalin was administered in combination with a gastro-mucosal protective agent. No other side effects were reported.

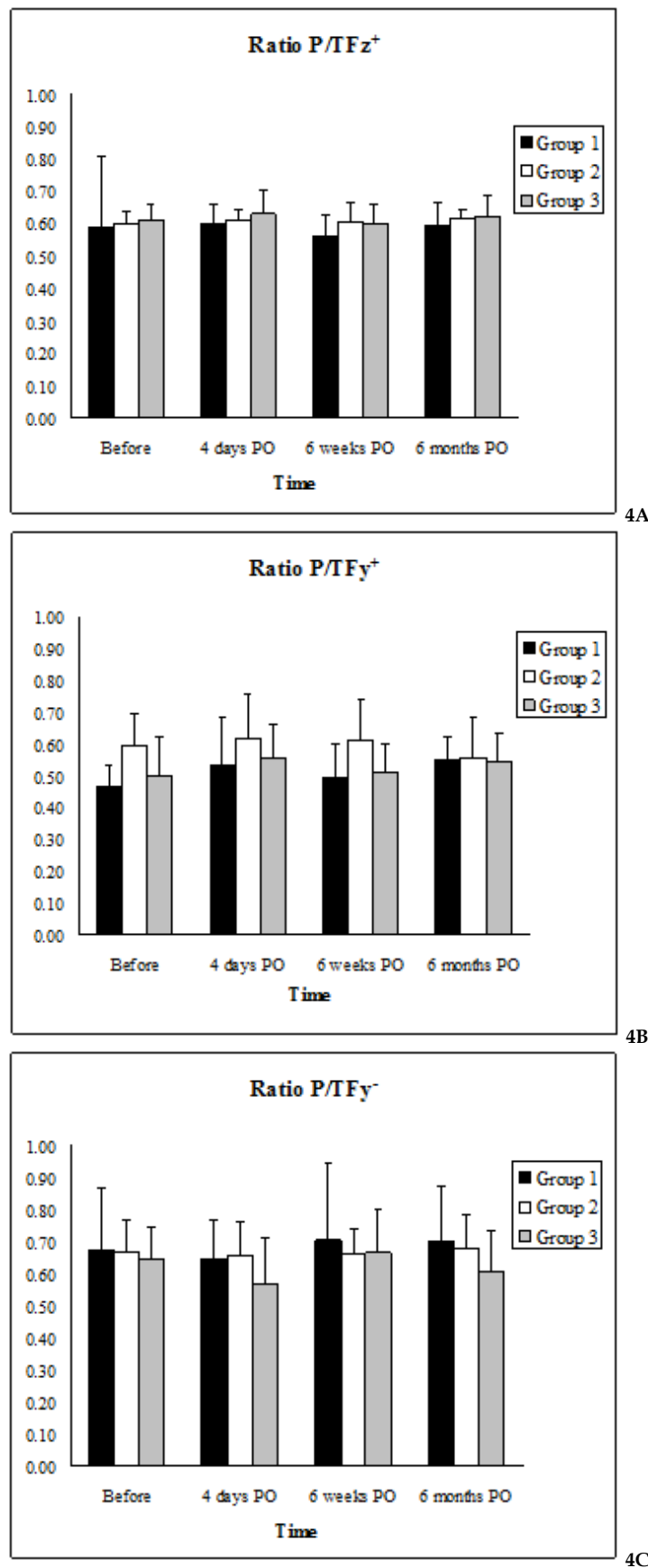
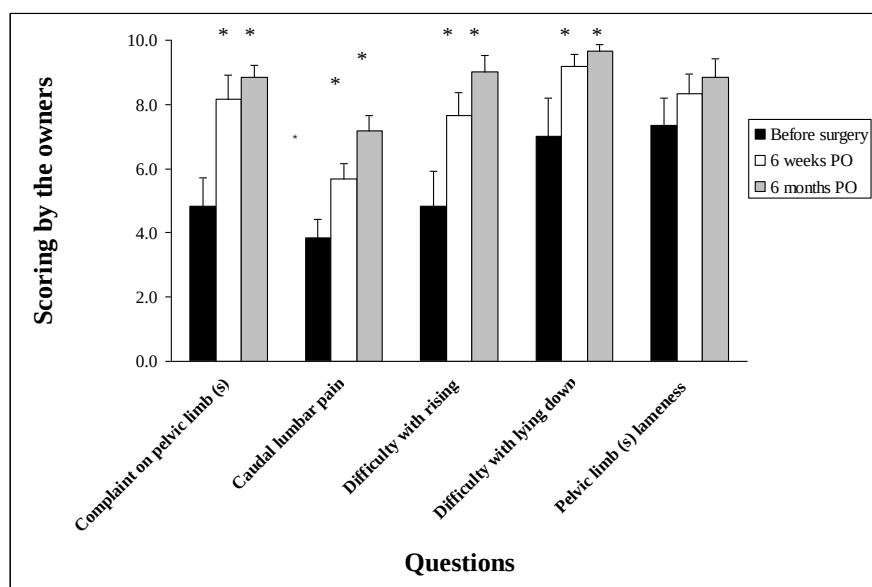
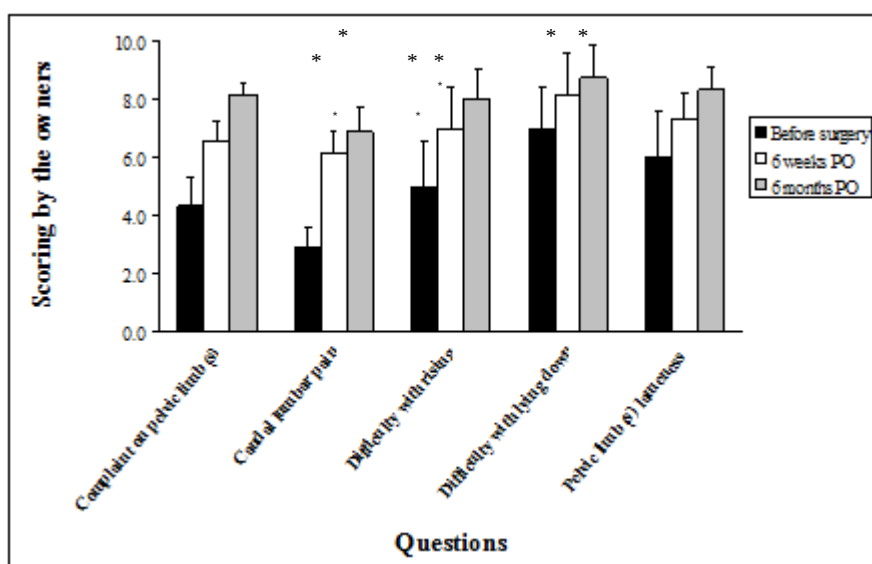


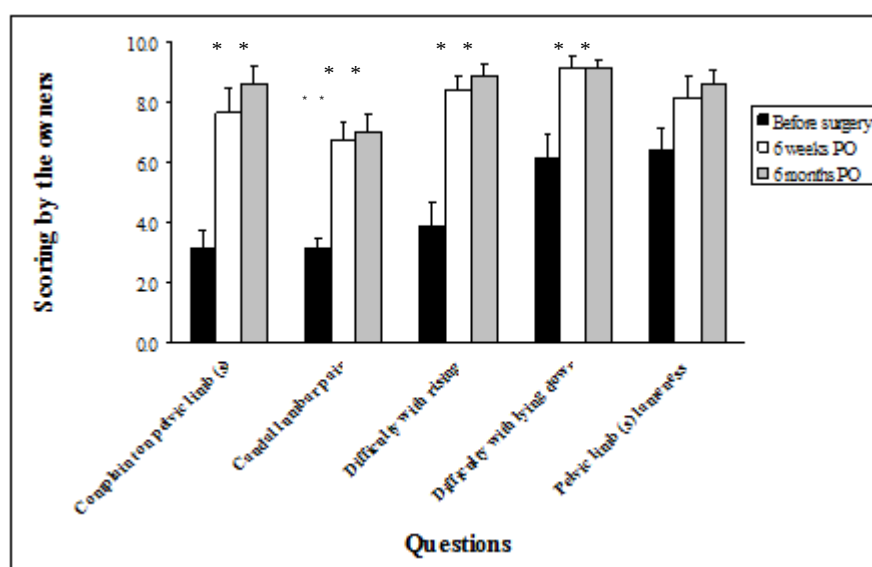
Figure 4 The pelvic/thoracic (P/T) limb ratio for Fz⁺ (4A), Fy⁺ (4B) and Fy⁻ (4C) in dogs with DLS before surgery, and at 4 days, 6 weeks, and 6 month postoperatively. The postoperative oral medication protocol consisted of 2 weeks of tepoxalin (10 mg/kg SID, group 1), 6 weeks of tepoxalin (10 mg/kg SID, group 2), or 2 weeks of carprofen (2 mg/kg BID, group 3).



5A



5B



5C

Figure 5 Results (mean $\pm$ SEM) of responses to the questionnaires completed by owners of the dogs with degenerative lumbosacral stenosis (DLS) before surgery, at 6 weeks and 6 months after surgery. The postoperative oral medication protocol consisted of 2 weeks of tepoxalin (10 mg/kg SID, group 1, **5A**), 6 weeks of tepoxalin (10 mg/kg SID, group 2, **5B**), or 2 weeks of carprofen (2 mg/kg BID, group 3, **5C**). SEM, standard error of mean, * $P < 0.05$, Friedman test, compared with value before surgery.

Discussion

Studies in humans showed that the postoperative period following spinal surgery was very painful. Previous studies in dogs showed that the force plate analysis objectively reflected lameness due to pain (Anderson and Mann, 1994; DeCamp, 1997; McLaughlin, 2001), and was therefore a reliable tool to evaluate and compare the efficacy of analgesic drugs (Cross et al., 1997; Borer et al., 2003; Grisneaux et al., 2003; Hazewinkel et al., 2003; Horstman et al., 2004).

Corticosteroids are widely used as anti-inflammatory drugs in case of diseases of the spine despite their limited efficacy in nerve injuries and severe side effects when used for longer duration (Toombs et al., 1986; Hinton et al., 2002). Tepoxalin is a novel NSAID which inhibits both COX and LOX pathways, resulting in a corticosteroid-like effect without causing corticoid-like side effects in long-term treatment (Wallace et al., 1993; Argentieri et al., 1994). Preclinical toxicity studies in rats and beagle dogs with tepoxalin at 30 times the therapeutic dosage of 10 mg/kg once daily for 6 months showed that, especially in dogs, tepoxalin had a wide safety margin (Knight et al., 1996). Studies in lab animals demonstrated less gastrointestinal ulcerogenic activity with tepoxalin than that with other NSAIDs. The mechanism of this benefit is uncertain. However, tissue-selective prostaglandin inhibition or a protective effect caused by 5-lipoxygenase inhibition has been suggested. The relative lack of gastrointestinal side effects, within the estimated therapeutic dose range, distinguishes tepoxalin from most marketed anti-inflammatory drugs (Knight et al., 1996). Tepoxalin has been described as an effective analgesic drug giving pain relief for conditions in the appendicular skeleton, but has not been described for treatment of pain originating from the spine. It was hypothesized that dogs treated with tepoxalin following spinal surgery would have decreased pain, better limb function and recovery from spinal surgery.

The efficacy of tepoxalin was compared with that of carprofen, which has been a routinely used method for postoperative pain control and is usually administered for 2 weeks postoperatively (Horstman et al., 2004; Pollmeier et al., 2006). Previous studies in dogs with DLS showed that locomotion, especially the propulsive force (F_y) of the pelvic limbs, would decrease slightly in the long run at 6 months after decompressive surgery in comparison with earlier improvement at 6 weeks after spinal surgery (de Risio et al., 2001; van Klaveren et al., 2005). Scar tissue formation, adhesions, residual spinal pain, progressive degenerative changes and increasing lumbosacral instability have been suggested as the causes of long-term decrease in locomotor function (Meij et al., 2007; Suwankong et al., 2007; Smolder et al., 2012). Therefore, the aim of the present study was to investigate the benefits of long-term anti-inflammatory and analgesic effects of tepoxalin administered during a 6-week period in comparison with the routine use of a NSAID (tepoxalin or carprofen) administered during the initial 2 weeks postoperatively.

The investigation was performed in a group of dogs with clinical signs related to lumbosacral

stenosis, including pelvic lameness, caudal lumbar pain and pain evoked by lumbosacral pressure (Suwankong et al., 2007; Suwankong et al., 2008; Worth et al., 2009). Lateralization of the clinical signs in dogs with DLS has been reported by several authors (Denny et al., 1982; Lenehan, 1983; Chambers, 1989; Palmer and Chambers, 1991; Janssens et al., 2000; Linn et al., 2003; Sjöström, 2003; Sharp and Wheeler, 2005; Gödde and Steffen, 2007), and explained by the eccentric location of the disc protrusion and unilateral entrapment of L7 and/or S1 nerve roots (Jones et al., 2000; Suwankong et al., 2006). Midcenter or eccentric disc protrusion and spinal nerve root swelling, evident on imaging studies, and bilateral and unilateral lameness were also common findings in this study. The weight bearing of the pelvic limbs, as reflected by the peak vertical ground reaction force (F_z^+) showed variation between both sides before surgery in all three groups, and became more homogeneous for both pelvic limbs in the postoperative period for all groups.

At 6 months after surgery, each pelvic limb carried approximately 3.7-4.0 N per kg body weight, which corresponds with the value of dogs without disturbance of locomotion (reference value of $F_z^+ = 3.9$ -4.0 N per kg body weight in normal dogs) reported previously (Suwankong et al., 2007; van Klaveren et al., 2005). The force necessary for braking the forward velocity increased during the postoperative period in both groups treated with tepoxalin (2 weeks and 6 weeks, respectively). The propulsive force (F_y), being the most significant force for pelvic limbs in the normal gait in dogs, and often the most sensitive parameter in case of pelvic limb lameness, revealed no significant difference before surgery between the most affected limb and the contralateral limb. Small variable changes can be explained by eccentric involvement of the cauda equina nerve roots, or by compensating mechanisms of the contralateral pelvic limb. At 6 weeks after surgery, the mean value of F_y in group 1 and group 3 (2-week tepoxalin and carprofen group), but not in group 2 (6-week tepoxalin), decreased slightly, followed by improvement later in the study in the originally most affected limb.

The P/T ratio reflects the ground reaction forces of both pelvic limbs in relation to the ground reaction forces of both thoracic limbs. Changes in the P/T ratio reflect the compensatory mechanisms or shift that may occur in the use of pelvic limbs versus thoracic limbs (van Klaveren et al., 2005). The P/TF z^+ ratio was not different among the groups at measure points before and after surgery. The P/TF y^+ ratio reached the same value for all 3 groups by the end of the study. In the present study, all 3 groups of dogs with DLS had similar P/TF y^- ratios, reflecting the ratio of the propulsive forces of the pelvic limbs in relation to those of the thoracic limbs. The P/TF y^- ratios before surgery were similar to the P/TF y^- ratios in dogs with DLS in our previous studies, which were significantly smaller than the corresponding values in healthy dogs (van Klaveren et al., 2005; Suwankong et al., 2007). The P/TF y^- ratio was not different between groups 1 and 2 (2 and 6 weeks of tepoxalin groups) and group 3 (the carprofen group) at every time point of the study, reflecting similar gait. Also, there was no increase in the P/TF y^- ratio during the course of the study in both

tepoxalin groups and the carprofen group. There were no groups with decreased ground reaction forces at 6 months when compared with 6 weeks after surgery, indicating the benefit of surgery in all cases with DLS, which is in accord with previous reports (van Klaveren et al., 2005; Suwankong et al., 2007).

The dogs in group 2 (6 weeks of tepoxalin) had similar ground reaction forces to the dogs in group 1 (2 weeks of tepoxalin) and in group 3 (2 weeks of carprofen). Based on this finding, it may be concluded that between 2 and 6 weeks after surgery the dogs did not suffer from significant spinal pain. The gradual improvement after the time point of 6 weeks cannot be subscribed to the prolonged use of a NSAID but may be attributed to the improvement in muscle strength.

A questionnaire is a subjective tool for evaluation of treatment. It may be difficult for the owners to evaluate their dogs especially when asked to grade abnormalities on a 10-point qualitative scale. The results of questionnaires in this study showed that the improvement at 6 weeks and 6 months after surgery was attributed to complaint on pelvic limb, caudal lumbar pain, difficulty rising, difficulty lying down, and pelvic limb lameness in all groups. The results of questionnaires indicate that the dogs functioned normally in 75% (group 1), 57.1% (group 2), and 62.5% (group 3) at 6 months after surgery compared to before surgery. The combination of the use of force plate analysis and questionnaires resulted in valuable information on the surgical outcome in dogs with DLS.

In our study, an adverse effect such as vomiting occurred in one dog, which might be caused by the decreased level of prostaglandin E₂ (the prostaglandin essential for normal gastric integrity). However, a previous study showed that oral administration of tepoxalin spared the level of prostaglandin E₂, which was relatively unchanged in the gastric mucosa in treated rats (Wallace et al., 1993; Kirchner et al., 1997). Tepoxalin significantly reduced prostaglandin E₂ levels at sites of experimentally-induced inflammation (Wallace et al., 1993). There is no convincing evidence that the administration of tepoxalin is associated with gastrointestinal side effects in dogs when given at the recommended dosage (Bosmans et al., 2007), which is in accord with findings in our study. Since spinal pain may have several origins (e.g. discogenic, meningeal and radicular pain), it is recommended to control pain at several levels and not only treat inflammation with NSAIDs but also treat meningeal and radicular (neuropathic) pain with gabapentin (Willems et al., 2016).

From this study, it can be concluded that, after a 6-month follow-up period, tepoxalin has similar postoperative anti-inflammatory and analgesic efficacy to carprofen in dogs with DLS that undergo decompressive surgery, as assessed by force plate analysis and questionnaires. This study could not demonstrate an added value for prolonged administration of tepoxalin up to 6 weeks after decompressive surgery. To avoid undesirable side effects of NSAIDs, the administration of NSAIDs for 2 weeks seemed to be an appropriate duration for postoperative pain management in dog with DLS undergoing decompressive surgery.

Acknowledgements

We gratefully acknowledge animal patients and their owners for the results, and would like to thank Ank van Wees, Monique Schwencke and Salisa Klinhom for their help.

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บทคัดย่อ

ประสิทธิภาพของการกินยาที่พอกซาลินหลังการศัลยกรรมเพื่อลดการกดทับในสุนัขที่มีภาวะเสื่อมและตีบแคบของกระดูกสันหลังช่วงเอวและกระดูกใต้กระเบนเหน็บ

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ศึกษาสุนัขจำนวน 23 ตัวที่มีภาวะเสื่อมและตีบแคบของกระดูกสันหลังช่วงเอวและกระดูกใต้กระเบนเหน็บที่ได้รับการรักษาด้วยวิธีศัลยกรรมเพื่อลดการกดทับ โดยแบ่งสุนัขเป็น 3 กลุ่มตามการรักษาที่ให้หลังการทำศัลยกรรม คือ สุนัขกลุ่ม 1 ได้รับยาที่พอกซาลิน (ขนาด 10 มิลลิกรัม/กิโลกรัม) วันละ 1 ครั้ง เป็นเวลา 2 สัปดาห์ (สุนัข 8 ตัว) สุนัขกลุ่มที่ 2 ได้รับยาที่พอกซาลิน (ขนาด 10 มิลลิกรัม/กิโลกรัม) วันละ 1 ครั้ง เป็นเวลา 6 สัปดาห์ (สุนัข 7 ตัว) และสุนัขกลุ่มที่ 3 ได้รับยาคาร์โปรเฟน (ขนาด 2 มิลลิกรัม/กิโลกรัม) วันละ 2 ครั้ง เป็นเวลา 2 สัปดาห์ (สุนัข 8 ตัว) ประเมินผลการรักษาโดยการวิเคราะห์แรงที่กระทำลงบนพื้นและการตอบแบบสอบถามโดยเจ้าของสุนัข โดยทำการประเมินก่อนการทำศัลยกรรมและที่ 4 วัน 6 สัปดาห์ และ 6 เดือนหลังการทำศัลยกรรม ทั้งนี้ ได้วิเคราะห์แรงที่กระทำในแนวตั้งฉากกับพื้น (Fz^+), แรงที่ใช้เพื่อหยุดการเคลื่อนไหว (Fy^+) และแรงที่ใช้ในการผลักดันไปข้างหน้า (Fy^-) รวมทั้งสัดส่วนของแรงที่ขาหลังต่อขาหน้าของแรงทั้งสามดังกล่าว (P/TFz^+ , P/TFy^+ และ P/TFy^-) การศึกษาพบว่า Fz^+ , Fy^+ และ Fy^- ของขาหลังข้างที่เจ็บของแต่ละกลุ่มไม่มีความแตกต่างกัน ค่า P/TFy^- ที่เวลา 4 วันหลังทำศัลยกรรมมีค่าลดลงในสุนัขทุกกลุ่ม แต่ไม่พบความแตกต่างอย่างมีนัยสำคัญ และพบว่าค่า P/TFy^- ที่เวลา 6 สัปดาห์และ 6 เดือนหลังทำศัลยกรรมในสุนัขกลุ่มที่ 1 มีค่าสูงกว่า ในสุนัขกลุ่มที่ 2 และ 3 อย่างไรก็ตาม ไม่พบความแตกต่างอย่างมีนัยสำคัญ จากการตอบแบบสอบถาม พบว่าเจ้าของสุนัขส่วนใหญ่มีความพึงพอใจในระดับปานกลางถึงระดับมากต่อผลของการทำศัลยกรรม ผู้วิจัยสรุปว่า ยาที่พอกซาลินสามารถให้ผลในการต้านการอักเสบและบรรเทาปวดหลังการทำศัลยกรรมเพื่อลดการกดทับในสุนัขที่มีการเสื่อมและตีบแคบของกระดูกสันหลังช่วงเอวและกระดูกใต้กระเบนเหน็บได้เทียบเท่ากับคาร์โปรเฟน

คำสำคัญ: การเสื่อมและตีบแคบของกระดูกสันหลังช่วงเอวและกระดูกใต้กระเบนเหน็บ ศัลยกรรมเพื่อลดการกดทับ การวิเคราะห์แรงที่กระทำลงบนพื้น ที่พอกซาลิน สุนัข

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