

**Antinol[®]
Case Study
Contest**

2017



Case Report :
**Effect of PCSO-524[®] Supplement on
Inflammation and Pain Control and
Its Safety for Orthopedic Surgery
in Pregnant Cats**



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Abstract

Bone fracture is common in stray cats. It can cause severe pain and requires surgical treatment. Use of non-steroidal anti-inflammatory drugs (NSAIDs) or opioid drugs is common for control of pain from bone fracture. However, adverse effects are frequently reported for NSAIDs and opioid use. Objective of this study is to evaluate anti-inflammatory and pain-relieving effects and safety of PCSO-524[®] (Antinol[®]) for bone surgery in pregnant cats. Radiographic examination identified spiral fracture of femur of a cat. Orthopedic surgery, external skeleton fixation (ESF), was performed. Intramuscular injection of Tramadol 2 mg/kg was given before the operation. Post-operative medication included amoxicillin/clavulanic acid (Synulox[®], Zoetis) 8.75 mg/kg for 4 consecutive days to prevent infection and oral administration of PCSO-524[®] 50 mg (Antino[®], DKSH (Thailand)) 1 capsule sid throughout the treatment. Follow-up at 14 days after the operation found that the cat was able to bear weight, had increased appetite and gained body weight. Gestation was diagnosed on day 30 of the treatment and cesarean operation was performed on day 56. It took 67 days after external skeleton fixation operation that the fracture was completely healed. The cat was able to normally bear weight on hind limbs and nurturing kittens after the removal of ESF and the cesarean delivery, respectively. It was concluded that PCSO-524[®] (Antinol[®]) was effective for controlling of inflammation and pain of tissue surrounding the fracture following external skeleton fixation operation in cats without causing fetal malformation or irregular blood clotting during the operation.

Keywords: PCSO-524[®], gestation, spiral fracture, external skeleton fixation

Introduction

Cats often hide their pain and do not show clear symptoms of pain. Severe pain caused by bone fracture is usually found in stray cats hit in a car accident. This type of fracture must be treated immediately to restore normal function of the body.

Fifty percent of bone fracture occur at long bones, especially the leg bones (8). Surgical treatment for repairing bone fracture depends on type of fracture and severity of the fracture. Complications following bone surgery using plate or pin occur at 5.2% in cats (8). External skeleton fixation is a surgical technique that does not cause much damage to blood vessels and muscle surrounding the bone fracture. Cats underwent this surgical technique can bear weight rapidly (10) and there has never been a report of nonunion in cats.

Use of Non-steroidal anti-inflammatory drugs (NSAIDs) to reduce pain and inflammation in cats usually causes side effects including stomach ulcer, increased kidney function as indicated by blood parameters, and physiological change of maternal-placental unit in pregnant animals. Pregnant animals have less motility of gastrointestinal tract, and increase of total lipid, blood albumin, hepatic enzymes, and glomerular filtration. These physiological changes alter pharmacokinetics of drugs and their absorption. Therefore, NSAIDs are contradicted in pregnant animals due to transfer of the drugs to fetus that may cause fetal malformation. Another important side effect of NSAIDs is impaired platelet function causing prolonged or delayed blood coagulation during or after the delivery (2).

Nutraceutical PCSO-524[®] (Antinol[®]) is an alternative to NSAIDs, of which the use is limited, for controlling inflammation. PCSO-524[®] (Antinol[®]) is New Zealand green-lipped mussel extract consisting of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and over 90 essential fatty acids that are effective against the release of inflammatory mediators (5). Its safety for veterinary use has been reported. Objective of this study is to evaluate anti-inflammatory and pain-relieving effects and safety of PCSO-524[®] (Antinol[®]) use for bone surgery in pregnant cats.

Case history

A female intact, stray, domestic short hair cat was hit by a car approximately 1 week ago. The cat refused assistance after the accident by showing aggression and hiding so transferring to veterinary hospital was not possible until it was too weak to resist the capture.

Physical examination

On the first day of admission (28th of July 2017), the cat showed sign of depression and aggression. Physical examination found 10% dehydration, CRT higher than normal (>2 sec), normal body temperature (100.5 °F), normal heart sound, normal heart rate (120 bpm) and respiratory rate (26 bpm), fine crepitation lung sound, normal body condition score (BCS 3), and none of abdominal or urinary bladder distention. The cat's left hind leg was not able to bear weight at walk. Palpation at the leg found a closed fracture and swelling of tissues surrounding the fracture but deep pain was normal. Further examination using radiographic imaging and hematological test were performed. The cat was then admitted for surgical treatment.

Radiographic and laboratory examination prior to the operation

Radiographic images (Figure 1A and 1B) indicated a spiral fracture of the proximal femur that needed surgical treatment. Hematological examination found high white blood cell count from inflammation and infection and mild anemia. Blood chemistry test showed that ALT was slightly higher than normal.

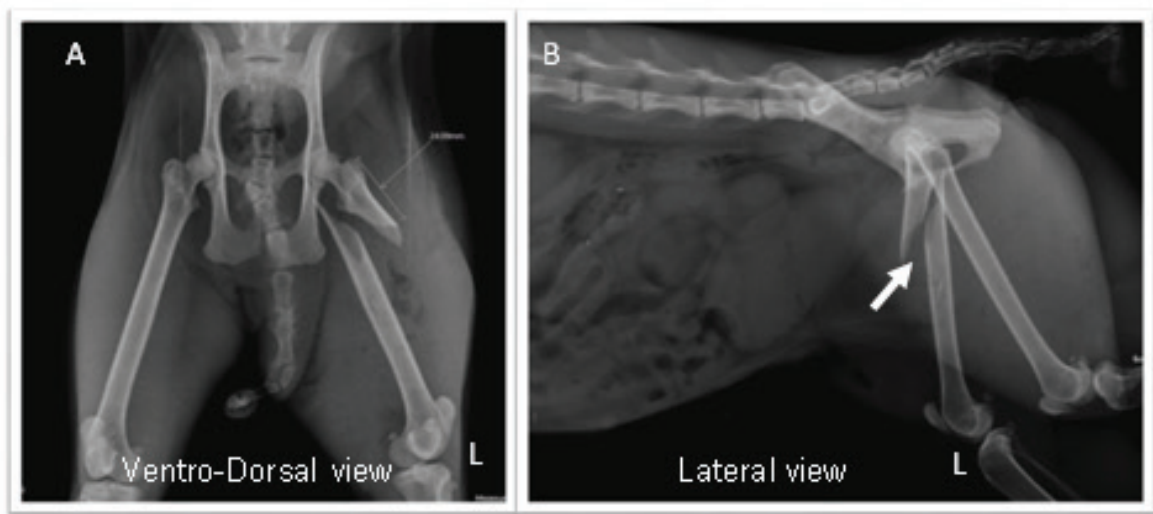


Figure 1. Radiographic images on day 0 (28th of July 2017) showing left spiral fracture at proximal femur (B) and the distance of 24 mm between Greater Trochanter and the fracture (A)

Table 1. Hematological and blood chemistry examination on day 0 (28th of July 2017)

Test (unit)	Normal range	Day 0
CBC		
RBC (x10 ⁶ per ul)	5.0-10.0	5.21
Hb (g/dl)	9.8-15.4	8.4
Hct (%)	26-47	27.5
Platelet (10 ³ per ul)	300-800	325
WBC (10 ³ per ul)	5.5-19.5	28.9
Neutrophils (%)	45-64	90.3
Eosinophils (%)	0-4	1.7
Lymphocyte (%)	1.5-7.0	7.3
Monocyte (%)	0-5	2.4
Serum chemistry test		
BUN (mg%)	19-34	24
Creatinine (mg%)	0.9-2.2	0.8
ALT (u/l)	25-97	490
ALK (u/l)	0-45	23

Treatment and treatment outcome

Medication provided to restore body condition prior to surgical treatment consisted of amoxicillin/clavulanic acid (Synulox[®], Zoetis) 8.75 mg/kg, PCSO-524[®] (50 mg, DKSH (Thailand)) 1 capsule sid and Samarin(Samarin 70[®], Berlin Pharmaceutical Industry) ½ tablet bid.

The cat body condition was ready for the orthopedic surgery on day2 (30th of July 2017) of the treatment. The distance between the fracture at the proximal femur and the greater trochanter was 24 mm, which was not sufficient for installing 3 plates and screws. Additionally, the cat was diagnosed as mild anemia, which was a concern for surgical treatment. Non-invasive technique, external skeleton fixation, therefore was selected for the operation. Pre-medication for the operation included intramuscular injection of atropine-xylazine, amoxicillin/clavulanic acid (Synulox[®], Zoetis) 8.75 mg/kg and Tramadol 2 mg/kg for pain control. Anesthesia induction, Zoletil[®], was used before inhalation of anesthetic drug, isoflurane. The operation took approximately 45 minutes. Recovery after the operation was normal and the cat was admitted at the veterinary hospital until cesarean delivery and removal of the fixation.

Post-operation medication consisted of amoxicillin/clavulanic acid (Synulox®) and oral administration of 1 capsule of PCSO-524® (Antinol®) sid. Cold compression was applied for 3 days consecutively after the operation. Wound dressing was scheduled daily to minimize the chance of getting infection around the external pin.

Nine days after the operation, the cat showed less panic attack, starting self-grooming, less isolation, increased water and diet appetite and body weight gain.

Thirty days after the operation (27th of August 2017), weight bearing of hind limbs was improved, and the cat's body weight was drastically increased. Physical examination found abdominal enlargement and fixation instruments remained steady in place. There was no loosen pins and no signs of infection around the pins. X-ray examination found that the bone healing was promising and no signs of infection (Figure 3). The x-ray images also showed skeletal structure of 4 kittens, of which heart beat was confirmed later by ultrasound examination (Table 3). Gestation was diagnosed and PCSO-524® (Antinol®) 1 capsule sid was continued for inflammation and pain control during the gestation period.

Fifty-six days after the operation (23rd of July 2017), the cat was restless, lost appetite, and was showing sign of pushing for delivery. The veterinarian decided to perform cesarean section to avoid chance of dystocia due to malfunctioned hind limbs of the cat. Spaying was performed in the same operation. Premedication included intramuscular injection of amoxicillin/clavulanic acid (Synulox®) and Tramadol. Anesthesia induction medication was Zoletil®, and the inhalation anesthetic drug was isoflurane. The operation used midline incision technique and gave satisfied outcomewhich 3 out of 4 kittens survived. Hematological and blood chemistry test showed normal values (Table 2). There was no excessive hemorrhage or delayed blood coagulation during and after the operation. Administration of nutraceutical supplement, PCSO-524® (Antinol®), 1 capsule sid was continued after the operation.

Sixty-seven days after the operation (4th of October 2017), weight bearing of the hind limbs was improved. X-ray examination showed sufficient bone healing (Figure 5). An operation for removal of fixators was done using Zoletil® as anesthetic drug. After the operation, weight bearing was normal.

Radiographic and laboratory examination after surgical treatment

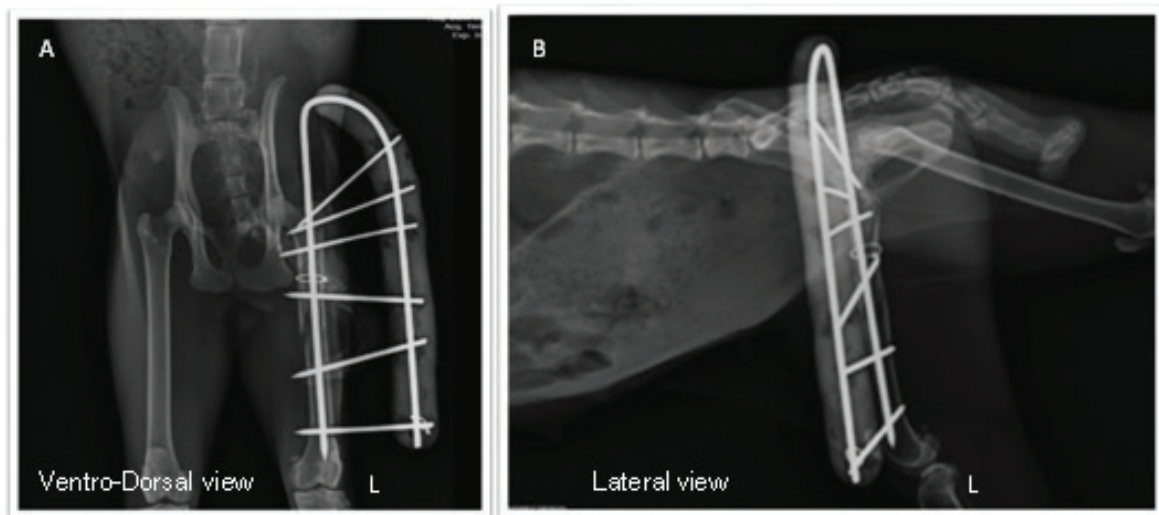


Figure 2. Radiographic images 2 days after operation (30th of July 2017)

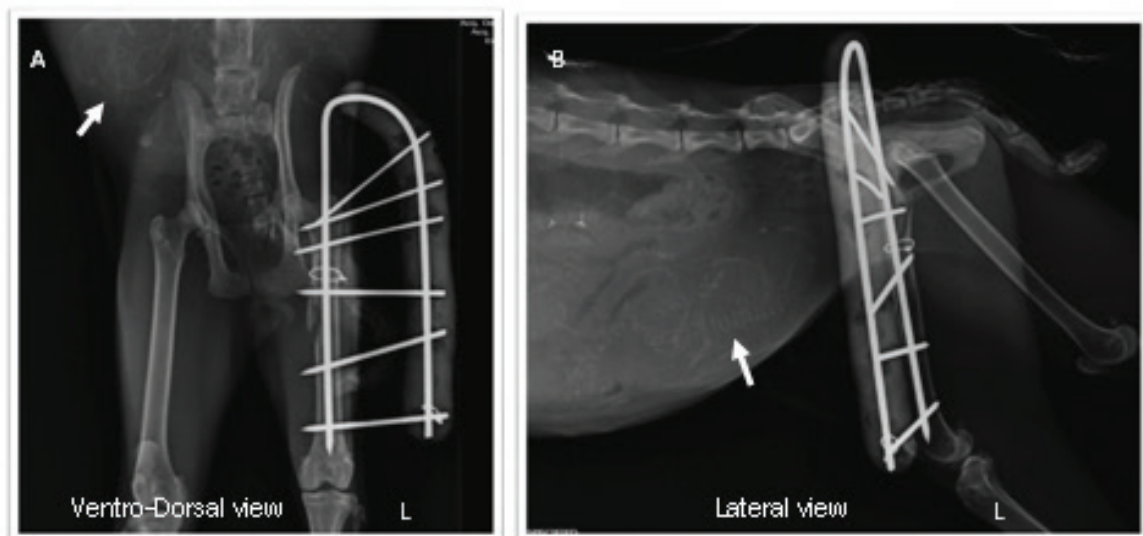


Figure 3. Radiographic images 30 days after operation (27th of August 2017) showing bone healing at the fracture and skeleton of fetuses (arrow)



Figure 4. Radiographic image 67 days after operation (4th of October 2017) showing secondary bone healing at the fracture line

Table 2. Hematological test results

CBC (unit)	Normal range	Day 0 (28/7/17)	Day 35 (1/9/17)	Day 56 (23/9/17)
RBC ($\times 10^6$ per ul)	5.0-10.0	5.21	5.22	6.70
Hb (g/dl)	9.8-15.4	8.4	7.9	10.1
Hct (%)	26-47	27.5	26.1	32.4
Platelet (10^3 per ul)	300-800	325	634	551
WBC (10^3 per ul)	5.5-19.5	28.9	15.1	17.3
Neutrophils (%)	45-64	90.3	77.9	60.6
Eosinophils (%)	0-4	1.7	9.1	4.3
Lymphocyte (%)	15-7.0	7.3	8.3	5.2
Monocyte (%)	0-5	2.4	3.8	4.4

Table 3. X-ray and ultrasound examination results

Diagnostic method	Day 0 (28/7/17)	Day 30 (27/8/17)	Day 56 (23/9/17)
X-ray	Left Spiral fracture at proximal femur	Secondary bone healing at fracture line	Bone union
Ultrasound		Found fetus	

Discussion

External fixation was appropriate for nearly all types of bone fracture. A study of Worth (2007) showed that the average time for bone healing that fixator could be removed was 7 weeks (5-12 weeks) in cats depending on type of fracture, damage of blood vessels and complications. In this case study, we were able to remove the fixator 9 weeks after the operation, which was within normal time range reported by the paper.

Non-steroidal anti-inflammatory drugs (NSAIDs) and drugs in opioid group are effective for pain control before and after operation. Tramadol, an opioid drug, is effective pain control in cats and not costly. Adverse effects of Tramadol are reported in cats, for example, dilated pupil, vomiting, and excessive saliva. Use of Tramadol during early gestation can increase the risk of having cardiovascular disorders by 1.56 times (2). However, there is no report on adverse effects of Tramadol in animals. Since the gestation was diagnosed during the hospital admission, NSAIDs use for pain and inflammatory control was limited. Diet supplement containing omega 3 was an appropriate alternative for controlling inflammation. Omega 3 is safe for use in pregnant animals and contains fatty acid essential for cats during gestation and lactation by enhancing neurological system and visibility of the fetus (6). Oil extract from New Zealand Green-lipped mussel (*Perna canaliculus*); PCSO-524[®] (Antinol[®]), was used throughout the treatment to control inflammation and support the pregnancy. A study of PCSO-524[®] (Antinol[®]) safety in cats used the supplement at double and triple size of what recommended for 28 days and found that hematological and blood chemistry values and physiological functions were normal (7).

A comparison study of fish oil and PCSO-524[®] for treatment of osteoarthritis in 66 dogs that received the supplement for 24 weeks found that serum WF6, biological marker for osteoarthritis, was significantly decreased in dogs received PCSO-524[®] when compared to dogs received fish oil since the second week of the treatment (9). The dog that received PCSO-524[®] also showed better weight bearing while there were no changes observed after 12 weeks of treatment in dogs received fish oil (9). In this study, the cat was able to bear weight since the second week of the operation.

Self-healing of the bone occurs after bone trauma by a mechanism similar to embryogenesis of infants. At the early stage after bone fracture, there is an inflammatory mechanism called cyclooxygenase activity that can be affected by use of NSAIDs resulting in delayed fracture healing process (1). Mechanism of bone healing is complicated and consists of a process that needs lipid mediators to regulate bone homeostasis and regeneration. A lipid mediator derived from omega 3 is Resolvin E1 (RvE1), which has anti-inflammatory effect and inhibits osteolysis during the inflammation (1, 8). Our study showed that PCSO-524[®] (Antinol[®]) is effective for bone healing and safe for use in pregnant cats without causing any malformation of fetus or other adverse effects after the operation.

Conclusion

Diet supplementation with PCSO-524[®] (Antinol[®]) is effective against inflammation of the tissues surrounding bone fracture after the external fixation operation in cats. It is safe for use in pregnant cats without causing any malformation of fetus or blood clotting disorder.

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