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Efficacy of Diclofenac Sodium, Either Alone or Together with Cefotaxime Sodium, for Control of Postoperative Pain, in Dogs Undergoing Ovariohysterectomy

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ABSTRACT

There is not much data about diclofenac sodium as anti-inflammatory drug in veterinary practice, therefore the objectives of the present study were to assess the efficacy and adverse effects of diclofenac sodium on its own and together with cefotaxime Na as postoperative pain control in dogs. A prospective, randomized, blinded, clinical trial was carried out on twenty mongrel bitches undergoing elective ovariohysterectomy. The operated bitches were assigned to one of four groups according to postoperative injections: Group 1 (given diclofenac and cefotaxime), group 2 (control), group 3 (given cefatoxime only) and group 4 (given diclofenac only). Examinations were performed postoperatively using a pain scale modified from University of Melbourne at 0, 1, 2, 3, 4, 5, 6, 8, 12, 24 h. Statistical analysis of results was done. The results of the present study showed that groups (1 and 4) had mean pain score which were not significantly different from each other and different from groups (2 and 3) significantly. From three hours post-operative till twenty four hours post-operative, groups (2 and 3) recorded mean pain scores which were significantly higher than groups (1 and 4). On the other hand, groups 2 and 3 were not statistically different from each other. Also, groups 1 and 4 were not statistically different. In conclusion diclofenac sodium is an excellent analgesic for postoperative pain in healthy dogs undergoing ovariohysterectomy.

Key words: Diclofenac Na, cefotaxime Na, ovariohysterectomy, dogs, pain score

INTRODUCTION

Ovariohysterectomy is one of the routine laparotomies in small animals practice. This operation is a painful surgery that required postoperative anti-inflammatory drug (Lemke *et al*., 2002).

Several drugs were used as postoperative analgesics in dogs undergoing ovariohysterectomy including: carprofen (Lascelles *et al*., 1998), ketoprofen (Lemke *et al*., 2002), meloxicam (Frenso *et al*., 2005), morphine (Dzikiti *et al*., 2006), long acting sufentanil formulation (Slingsby *et al*., 2006).

Nonsteroidal anti-inflammatory drugs have been successfully used to control pain in dogs and cats by inhibition of cyclo-oxygenase and subsequent interference with prostanoid synthesis (Frenso *et al*., 2005).

Although diclofenac (DF) is a non-steroidal anti-inflammatory drug (NSAID) commonly used in human, its use in veterinary practice is relatively limited. It was used in cattle, pigs and horses for treatment of various inflammatory and degenerative post-trauma disorders and lameness, as well as pre-operative treatment for cataract extraction (Ku *et al*., 1986; Booth, 2001; Lascelles and Mair, 2001).

After muscle injury, accumulation of inflammatory cells, production of prostaglandins, cytokines and chemokines is rapidly occurred (Tidball, 1995; Summan *et al*., 2003) causing edema and soreness. It has been proposed that some components of the inflammatory response to injury are responsible for the increase in muscle function deficit (Hirose *et al*., 2001; Lapointe *et al*., 2002; Brickson *et al*., 2003). Early treatments of muscle injury have therefore been aimed at inhibiting the inflammatory response to alleviate the signs of inflammation and provide pain relief (Almekinders, 1993). Cefotaxime Na is one of the third generation cephalosporin commonly used as a strong broad spectrum antibiotic in dogs suffered serious and mixed infections (Trudel *et al*., 1994; Rebuelto *et al*., 2002).

University of Melbourne pain scale was developed to evaluate postoperative pain in dogs (Firth and Haldan, 1999). This scale based upon behavioral and physiologic measurements as reliable evaluation of degree of pain in dogs during the postoperative period and their response to analgesics.

The aim of the present study was to assess the efficacy and adverse effects of diclofenac sodium on its own and together with cefotaxime Na as postoperative pain control in dogs undergoing ovariohysterectomy.

MATERIALS AND METHODS

Animals: In the present study, a total of twenty mongrel bitches admitted to the surgery clinic at Faculty of Veterinary Medicine, Cairo University between January 2010 and December 2010, for elective ovariohysterectomy was used. The operated dogs aged 1-3 years and weighted 10-30 kg. None of the dogs had any clinically detectable concurrent diseases or were being given analgesic medications. Each dog was given a full physical examination on admission.

Anesthesia and surgical procedure: The same anesthetic protocol was used for all dogs including; Premedication with atropine sulphate (0.05 mg kg^{-1}, subcutaneously) and xylazine HCl (1 mg kg^{-1}, intramuscularly).

Induction of the general anesthesia was carried out by ketamine HCl (5 mg kg^{-1}, intravenously in the cephalic vein).

General anesthesia was maintained with thiopentone sodium (25 mg kg^{-1} 2.5%, intravenously).

Under aseptic condition, ovariohysterectomy was carried out as usual by the same surgeon and by using the same materials and method in all dogs.

Ovariohysterectomy was carried out through an incision on the ventral midline of the abdomen. Ovarian pedicles and uterine body were ligated with size -0 polyglactine before transaction. The linea alba was closed with size-0 polyglactine using simple interrupted pattern and subcutaneous tissues were opposed with 2-0 polyglactine using simple continuous pattern. The skin incision was close with size-0 nylon using simple interrupted pattern.

Postoperative medications: The operated bitches were randomly assigned to four groups according to the postoperative medications as follow:

Group 1: (Dcl+Ceft Group, 5 bitches): Dogs received a once-off diclofenac sodium at a dose of 1.1 mg kg^{-1} and a once-off cefotaxime Na at a dose of 10 mg kg^{-1} given intramuscularly just after surgery

Group 2: (Control Group, 5 bitches): Dogs received a once-off normal saline 1 mL given intramuscularly just after surgery

Group 3: (Ceft. Group, 5 bitches): Dogs received a once-off cefotaxime Na (Cefotax®, EIPICO) at a dose of 10 mg kg^{-1} given intramuscularly just after surgery

Group 4: (Dcl. Group, 5 bitches): Dogs received a once-off diclofenac sodium (Voltarine®, Novartis Co.) at a dose of 1.1 mg kg^{-1} given intramuscularly just after surgery

Assessment of postoperative pain: The dogs were scored for signs of pain under blind condition by another veterinarian at 0,1,2,3,4,5,6,8,12 and 24 h after surgery using a pain scale modified from University of Melbourne (Firth and Haldan, 1999).

Hematoma formation at the surgical site, persistent bleeding from the incision, or vomiting and diarrhea in the immediate postoperative period was recorded.

No provision was made for supplementary analgesia at any time. All bitches were constantly monitored and if a dog had been found to be in severe pain, it would have been excluded from the study and treated with potent analgesics.

Analysis of results: The results were expressed as the Mean±standard error of the mean (SEM). They were analyzed by using an analysis of variance for the scores recorded. SPSS 16 software was used for this statistical analysis. Significant differences ($p<0.05$) were further assessed by using Least Significant Difference (LSD) post hoc test.

RESULTS

None of the bitches was found to be in extreme discomfort and so none was excluded from the study. No pain score was≥9, therefore no supplemental analgesic was required.

Hematoma, persistent bleeding, or diarrhea was not seen in all bitches. Only one bitch from the Dcl group had vomition. The mean pain score in the different groups were collected in Table 1. Results of statistical analysis showed that there was no significant difference between all groups in mean pain score during the first hour post-operative. Two hours post-operative, the group 1 showed the significantly lowest mean pain score (2.67±0.67), while group 3 showed the highest mean (8±0.00) which was significantly higher than other groups. Groups (1 and 4) had mean pain score which were not significantly different from each other and different from groups (2 and 3) significantly.

Table 1: Mean±SEM of pain score in the studied group at different time intervals

	Group			
Time	1	2	3	4
Zero hour	2.33±0.33^{a}	3.67±1.67^{a}	3.67±0.33^{a}	3.33±0.33^{a}
1 hour post-operative	4.67±0.33^{a}	6.33±1.33^{a}	6.00±2.31^{a}	4.33±0.33^{a}
2 hours post-operative	2.67±0.67^{c}	5.33±0.33^{b}	8.00±0.00^{a}	3.00±0.58^{c}
3 hours post-operative	2.67±0.67^{b}	7.00±0.58^{a}	7.33±1.20^{a}	4.33±0.67^{b}
4 hours post-operative	2.67±0.67^{b}	6.67±0.67^{a}	7.33±0.33^{a}	2.00±0.58^{b}
5 hours post-operative	0.67±0.67^{b}	6.33±0.33^{a}	6.67±0.33^{a}	0.67±0.33^{b}
6 hours post-operative	0.67±0.67^{b}	7.33±0.67^{a}	7.00±0.00^{a}	0.67±0.33^{b}
8 hours post-operative	0.67±0.67^{b}	6.00±0.58^{a}	6.67±0.33^{a}	0.33±0.33^{b}
12 hours post-operative	1.67±0.88^{b}	7.00±1.15^{a}	6.33±0.33^{a}	0.67±0.33^{b}
24 hours post-operative	1.00±0.58^{b}	6.67±0.88^{a}	6.67±0.33^{a}	0.67±0.33^{b}

Means with different superscripts (a, b, c) within the saine raw are significantly different at p-value≤0.05

From three hours post-operative till twenty four hours post-operative, groups (2 and 3) recorded mean pain scores (ranged between 6.00± 0.58 and 7.33±0.33) which were significantly higher than groups (1 and 4) mean pain scores (ranged between 4.33±0.67 and 0.33±0.33), on the other hand groups (2 and 3) were not statistically different from each other. Groups (1 and 4) were not statistically different from each other (Table 1).

No significant difference was detected among the treated groups in regard to age and weight of the bitches or duration of surgery. The maximum main pain score after ovariohysterectomy was 8±0.00.

DISCUSSION

Opioids have long been the drugs of choice for control of postoperative pain. However, their potential adverse effects (bradycardia and hypo-ventilation) are not negligible (Grisneaux *et al.*, 1999).

In recent years, there have been significant advances in the control of pain in animals. One of the most important advances has been the development of new veterinary labeled NSIAD used for postoperative pain control.

Although, Diclofenac is an inhibitor of cyclooxygenase (Riendau *et al.*, 1997) and prostaglandin biosynthesis and reduces leukotriene formation (Kothari *et al.*, 2003), Information about Diclofenac sodium as postoperative pain control in dogs is scarce. Therefore the present study was designed to study the efficacy and adverse effects of this NSAID as postoperative pain control in dogs.

Absence of blood coagulation disorders and slight gastrointestinal disorders in the form of vomition during the postoperative period means that there are no severe adverse effects of Diclofenac sodium as postoperative care. This is in agreement with a previous study recorded that, in clinically normal dog's undergoing general anesthesia and elective surgery, the use of NSIAD as analgesic is not contraindicated (Lobetti and Joubert, 2000; Imagawa *et al.*, 2011).

Various pain scales have been developed, but none have gained widespread acceptance in veterinary medicine. The present study was depended upon University of Melbourne Pain Scale for assessment of post operative pain in all dogs and their response to analgesics because it is quite accurate pain scale as it is based on 6 categories of data associated with response to pain. These categories included; physiological data, response to palpation, activity, mental status, posture and vocalization (Firth and Haldan, 1999).

There was no significant difference between all groups in mean pain score during the first hour post-operative. Possible explanation for this was that recovery from anesthesia masked clinical signs of pain. Similar explanation was mentioned in a previous study (Pibarot *et al.*, 1997).

Cefotaxime Na is one of the most common used prophylactic antibiotics as post operative care in dogs. The present study was designed to study the effect of this antibiotic on pain control and if it has a synergistic action with diclofenac sodium or not. The results of the present study showed that the group 3 showed the highest mean pain score which was significantly higher than other groups and the mean pain scores of Groups (1 and 4) were not statistically different from each other. This means that there is neither direct analgesic nor synergistic action of cefotaxime Na as postoperative care.

From three hours post-operative till twenty four hours post-operative, groups received diclofenac sodium showed mean pain scores significantly lower than other groups. This means that the good action of diclofenac sodium starts at 3 h post administration and continues till 24 h.

On one hand, results of the present study are in disagreement with some studies (Jonhson, 1991; Gentry and Mann, 1993) that suggested that NSAID provide mild analgesia but

would not be adequate for immediate postoperative pain in orthopedic patients. This could be explained by the difference in the pain scores produced by different surgeries of soft and hard tissues.

On the other hand, this study is in agreement with recent studies (Nolan and Reid, 1993; Lascelles *et al*., 1994; Mathews *et al*., 1996) which demonstrated that some NSAID were more effective than opioids for relief of pain in dogs.

Postoperative pain was considered mild, moderate or severe if the total pain score was between 0 and 5, 6 and 9, or 10 and 13, respectively (Pibarot *et al*., 1997). The results of the present study recorded that the maximum mean pain score resulted from ovariohysterectomy was 8±0.00. This result means that ovariohysterectomy is a moderately painful surgery, therefore, anti-inflammatory drug as postoperative care is recommended.

CONCLUSION

At the dosage indicated above, diclofenac sodium on its own is an excellent analgesic for postoperative pain in healthy dogs undergoing moderately painful surgery, without compromising haemostasis or severe gastrointestinal disorders.

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