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Anti-nociceptive Efficacy of Carprofen and Meloxicam in Ovario-hysterectomized Dogs

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ABSTRACT

Anti-nociceptive efficacy of carprofen and meloxicam was evaluated in twelve female dogs brought for elective ovario-hysterectomy randomly assigned to Group A and Group B. In Group A Carprofen was administered @ 4 mg/kg i.v, whereas in Group B, Meloxicam was administered @ 0.2 mg/ kg i.v, immediately after completion of surgery. Pain scores decreased significantly following analgesia with carprofen and meloxicam. Carprofen was found to be better analgesic than meloxicam in terms of its effect in reducing the behavioural pain responses post-operatively.

Keywords: Anti-nociceptive, carprofen, meloxicam, dog

Uncontrolled pain in animals can result in complications, including cardiovascular stress, immune-suppression, anorexia and cachexia (Mathews, 2000). Pain scoring, using a validated behavioural pain scales enables identification of subjects that are in pain and guides the use of drugs to mitigate it. Many of the methods used in evaluating veterinary patients with pain have been taken from similar assessment methods used in human paediatrics (Jensen *et al*., 1986 and Firth and Haldane, 1999). Physiological indices such as heart rate, respiratory rate, temperature and biochemical biomarkers like serum cortisol and glucose are commonly used as objective, indirect measure of pain (Fox *et al*., 1994 and Hansen *et al*., 1997). These indices when used alone to evaluate pain have shown inconsistent results in many studies in animals (Fernandez *et al*., 2007). Nonetheless, an identified behaviour or set of behaviours that correlate with pain provides a means to monitor response to pain treatment. Numerous pain assessment scoring systems have been developed in veterinary medicine, which includes Visual analogue scale, Numerical rating scales, Simple descriptive scales and Behavioural and Physiologic response scales (Dar *et al*., 2010). The paper records the post-operative anti-nociceptive efficacy of two non-steroidal anti-inflammatory drugs, carprofen and meloxicam, based on behavioural pain scores.

MATERIALS AND METHODS

Twelve clinically healthy female dogs weighing between 8-15 kg brought for elective ovario-hysterectomy were randomly divided into two groups comprising six animals each. All the procedures were done only after the animals got acclimatized to the hospital environment. All the animals were pre-medicated with atropine sulphate @ 0.04 mg/kg administered intramuscularly (i.m). After pre-medication, the animals were kept in a quite environment for approximately 30 minutes. A catheter was placed in the cephalic vein and diazepam was administered @0.5 mg/kg intravenously (i.v). Five minutes later anaesthesia was induced with 5% solution of Thiopentone sodium given "till effect" as bolus i.v administration. The anaesthesia was maintained by repeated increments of thiopentone sodium as and when required.

On the day of surgery, the animals were randomly assigned to Group A and Group B. In Group A Carprofen was administered @ 4 mg/kg i.v, whereas in Group B, Meloxicam was administered @ 0.2 mg/kg i.v, immediately after completion of surgery.

Surgical procedure

Mid-ventral area from xiphoid to pubis was prepared aseptically for surgery according to the standard procedure described by Bojrab, 1997. The same surgical procedure was followed in all the animals with regard to the site and length of incision (2.5-4.0 centimetres).

At all the stages of the trial, pain levels were measured first, followed by recording of the other parameters. The pain level was measured on the basis of Melbourne Pain Scale (MPS) (Lascelles *et al*., 1998), Glassgow Composite Pain scale (GCPS) (Firth and Haldane, 1999) and Dynamic and Interactive Visual Analog Scale (DIVAS) (Hansen, 2003) at 2,4,8,12 and 24 hr post-operatively.

The MPS consisted of six broad categories: physiological data, such as respiration rate, heart rate, rectal temperature, salivation and dilatation of pupil and behavioural data such as response to palpation, activity, mental status, posture and vocalization, each of which was divided into three or more levels and assigned a different numerical weight. For example, the category mental status consisted of four levels; submissive, overtly friendly, wary and aggressive; and these levels were accorded scores of 0, 1, 2 and 3 respectively. In total, the maximum number of possible points for pain awarded by scale was 27.

In DIVAS, animals were first observed undisturbed from a distance and then approached, handled and encouraged to walk. Next, the surgical site and surrounding area was palpated and a final overall pain score was recorded. At each assessment with the DIVAS pain scoring system, a mark was made on a 100 mm scale, anchored on the left by either the number "0" or wording such as "no pain" (Reid and Nolan,1991; Mathews *et al*., 2001 and Slingsby and Water-Pearson, 2002). Each animal was observed for a pre-determined time period, using clinical judgement about the severity of pain, and a line was drawn that intersected the 100 mm DIVAS. The distance from the left end of the line to the point of intersection was then measured in millimetres giving the DIVAS pain score.

Under GCP scale animals were first observed undisturbed in kennel and their behaviour was recorded and then a leash was put on dogs and lead out of the kennel and their rising and walking activities were noted. Gentle pressure was applied 2 inches around the surgical incision and the dog's response was noted and assigned a score accordingly. At the end, overall behaviour of dog was noted and marks were assigned for their different activities (Holton *et al*., 2001).

Kolmogorov-Smirnov-test was performed to assess normality of variables. For parametric variables split plot design was used and if the data yielded significant difference ($P<0.05$), then least significant difference (LSD) test as post hoc test was used in order to compare difference between treatment groups at different time intervals. For all parametric analysis, values of ($P<0.05$) were considered significant.

For non parametric variables Kruskal- Wallis test was used to compare difference between treatment groups at different time interval and when the test yielded a significant difference ($P<0.05$), Bonferoni test was used as post hoc test. For all non-parameteric analysis, values of ($P<0.05$) were considered significant. For each treatment group, the Duncan test was used to compare values obtained at each time interval after surgery with values obtained before surgery.

RESULTS AND DISCUSSION

In the present study the maximum average MPS score at 2 hr post-operatively for group A was 5.50±0.24, whereas in group B it was 7.33±0.23. Since all the values were below MPS 8, it suggests that both the drugs were effective in controlling post-operative pain. In subsequent assessment periods there was a significant ($P<0.05$) decrease in score from 4 hr in group A (4.83±0.82) that further declined up to 24 hours post-operatively (Fig. 1). However, in group B, significant ($P<0.05$) decrease was observed from 8 hours (5.5±0.37) up to 24 hours post-operatively (Fig. 1). The MPS values of group A and group B differed significantly ($P<0.05$) at each time interval of the study period and the values were lower in group A as compared to group B at each time interval of post-operative period.

Maximum DIVAS values 2 hr post-operatively were 20.16±0.36 and 23.67±0.36 in group A and B respectively. In subsequent assessment periods there was significant decrease ($P<0.05$) in values from 4 hr in group A

(13.5±0.24) and group B (16.33±0.36) up to 24 hr post-operatively (Fig. 2).

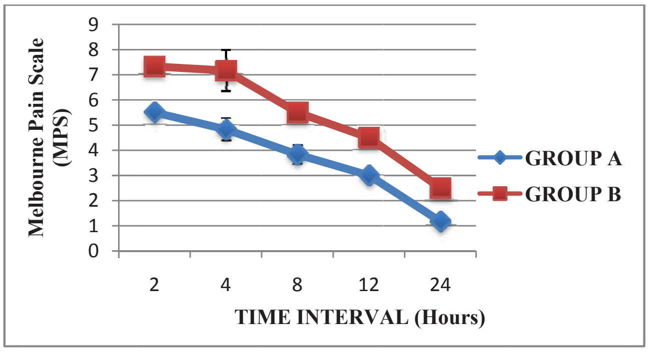

Fig. 1: Melbourne Pain Scale (MPS) values at different time intervals

However, the values in group A were lower than that in group B at each post-operative interval of recording. The DIVAS values of group A and group B differed significantly (P<0.05) at each time interval of the study period.

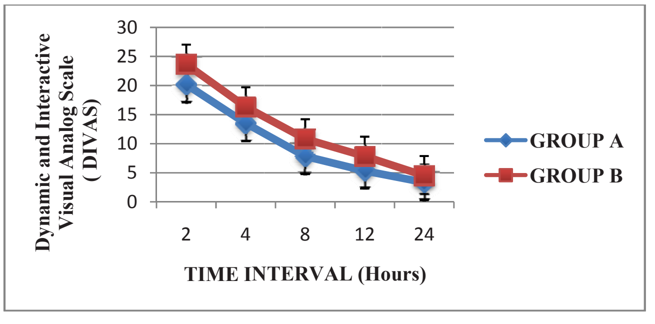

Fig. 2: Dynamic and Interactive Visual Analog Scale (DIVAS) values at different time intervals

Maximum GCPS values for both the groups were recorded 2 hr post-operatively. In subsequent assessment period there was significant decrease (P<0.05) in the GCPS value at each assessment period. Probably the most reliable and properly validated scale in veterinary medicine is the Glasgow Composite Measure Pain Scale (GCMPS) (Orskov, 2010). Values between the groups also differed significantly (P<0.05) till the end of study period (Fig. 3). Although in both the groups the values decrease continuously with each passing interval never the less, in group A the values obtained were lower than that in group B at each interval of the assessment period. The most commonly tested scale for assessing acute post-operative pain in dogs is the Glasgow Composite Measures Pain Scale (Holton *et al*., 2001). Frequent assessments are necessary as pain in not a static process and the benefits of interaction with analgesics must be evaluated (Robertson, 2003).

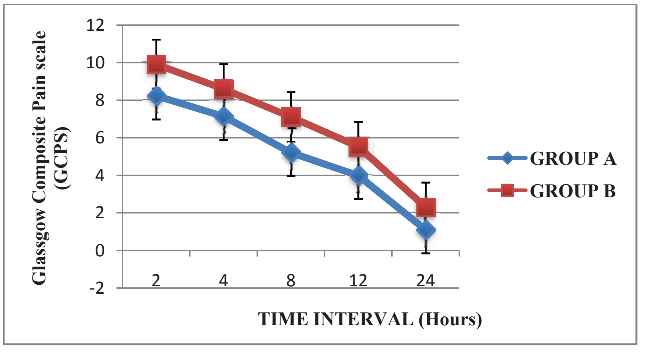

Fig. 3: Glassgow Composite Pain scale (GCPS) values at different time intervals

No rescue analgesic were needed in the present study as all MPS (<8); DIVAS (<30 mm) and GCPS (<10) values were below their respective threshold levels. Dalla-porta Acosta *et al*. (2005) and Shih *et al*. (2008) were also of the opinion that the rescue analgesics are not needed when the pain scores are less than the threshold value.

One animal of group A and two animals of group B showed intermittent vocalization on touch and rest of the animals did not show such response. In the present study the vocalization might have been caused due to pain, anxiety, fear or delirium because of anaesthesia as opined by Watson *et al.* (1996) and Conzemius *et al. (*1997). Similar findings have been reported by Fazli, 2005 and Dar *et al*., 2013. As it involves number of factors it is therefore unreliable to take it as a sole criterion for pain assessment as has also been reported by Hellyer (1999).

All the animals resumed their normal dietary intake except two animals in group B who did not resume feeding up to 12 hours post-operatively. It may be because of stress or pain and the results are in agreement with the finding of Liles and Flecknell (1993) and Flecknell *et al*. (1999) who found that an increase in neuro-endocrine response to pain and stress is associated with decrease in food and water intake. Appetite and thirst have been reported to be poor indicator of acute pain (Hellyer, 1999). Postural abnormalities like tucked up appearance and restlessness were not evident in any animal in the present study.

However, low score deviations like lateral recumbency, standing with head up and standing with head down noticed up to 12 hours post-operatively are indicative of pain in dogs. The observations are in agreement with the findings of Robertson (2003).

Only one animal in group B was found licking the surgical site post-operatively. Excessive licking, biting, scratching or shaking of pain area can lead to self-mutilation (Mehta, 2006).

All the animals of both the groups showed response to palpation of wound area. The group A animals showed this response to palpation up to 12 hours post-operatively, whereas animals of Group B showed response to palpation throughout the study period. Initially response to palpation was severe up to 6 hours and then the response reduced up to 24 hours post-operatively. Results showed that the wound palpation was one of the best observations for pain assessment. As the pain due to ovario-hysterectomy usually persists for 24 hours (Hardie *et al*., 1997), the response to palpation reduced with passage of time in the present study. Similar findings have been recorded by Watson *et al*. (1996) and Robertson (2003).

None of the animals were aggressive during the study period. Some of the animals of group B were overtly friendly, whereas animals of group A were submissive. Among various behaviours studied in the present study response to palpation was the most consistent behaviour among all the groups. However, not all signs were present at one time and no single sign could indicate the degree of pain.

The present study revealed that analgesic efficacy and potency of carprofen was more as compared to that of meloxicam. Carprofen was superior to meloxicam at each interval of post-operative period. Slingsby and Waterman-Pearson (2000) estimated post-ovariohysterectomy analgesia in the cat by use of carprofen, ketoprofen, meloxicam, or tolfenamic acid and found that all four drugs provided good post-operative analgesia, whereas Ricketts *et al*. (1998) evaluated carprofen and other NSAIDs including meloxicam and found that carprofen was more potent analgesic than others.

CONCLUSION

Study revealed that the pain scores decreased significantly following analgesia with carprofen and meloxicam. Carprofen was found to be better analgesic than meloxicam in terms of its effect in reducing the behavioural pain responses post-operatively.

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