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COMPARISON OF TRAMADOL AND ROBENACOXIB POSTOPERATIVE ANALGESIC EFFICACY IN DOGS

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Abstract

Analgesia is the main concern regarding pacient's postoperative rehabilitation. The main aim of this study was to compare the analgesic effect of Robenacoxib and Tramadol when administrated after surgery. Forty client-owned dogs undergoing genital surgery at the Clinic of Obstetrics and Gynecology (Faculty of Veterinary Medicine of Bucharest) were taken into study. Anaesthetic and supportive care protocols were standardized. Tramadol (2 mg/kg) was administrated postoperatively every 6-8 hours, while Robenacoxib (1 mg/kg) was administrated once a day. Pain scores were estimated according to Glasgow scale of pain for animals. Patients in Tramadol group (n=20) were more quiet (15/20), they ate sooner after surgery (10/20), fewer of them cried and whimpered (10/20). Dogs in Robenacoxib group (n=20) did not lick around the incision line (17/20) and the wound healed faster (15/20). Tramadol alone provides longer-lasting analgesia compared to Robenacoxib, but does not have the same anti inflammatory effect. Robenacoxib has a better effect in wound healing. The combined administration of Tramadol and Robenacoxib should be the subject of a further study.

Key words: *analgesia, Tramadol, Robenacoxib, dog.*

INTRODUCTION

Pain is "an unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Merskey and Watson 1979). Surgical intervention are associated with perioperatory pain and inflammatory response. Surgery suppresses the immune system and this suppression is directly proportionate to the invasiveness of the surgery (Pollock et al. 1991). Pain and the resulting response have marked physiologic effects (lactic acidosis, gastrointestinal ileus, increased protein catabolism, decreased food intake, delayed wound healing) resulting in increased morbidity and mortality (Stafford 2006; Chapman and Gavrin 1999; Hansen et al. 1997) . Therefore, effective analgesia is an essential part of postoperative management. Postoperative pain is expected for at least the first 24 to 72 hours (Hellyer 2002).

Opioids and nonsteroidal antiinflammatory drugs are the usual treatment options for postoperative pain (Lee 2011).

Tramadol is a synthetic opioid of moderate potency. It has a dual mechanism of action: it binds to the μ1 opioid receptor and inhibits the monoaminergic pathway, which is responsible for noradrenaline and serotonin reuptake (KuKanich and Papich 2004) . In the dog it can be administered orally (Giorgi et al. 2009), intravenously (McMillan et al. 2008) , subcutaneously (KuKanich and Papich 2004) , intramuscularly (de Sousa et al. 2008) and epiduraly (Guedes et al. 2005).

Robenacoxib is a new nonsteroidal anti-inflammatory drug approved for the treatment of pain and inflammation in the dog (King et al. 2010; King et al. 2009; Jung et al. 2009) . Robenacoxib has a high degree of selectivity for inhibition of the cyclooxigenase 2 (COX-2) isoform and a short blood half-life combined with longer residence times at sites of inflammation (King et al. 2010; King et al. 2009) . In healthy beagle dogs, robenacoxib has a high safety index, causing no detectable toxicity when administered at daily dosages as high as 40 mg/ kg for 1 month or 10 mg/ kg daily for 6 months without gastrointestinal side effects (King et al. 2011) .

The aim of the study was to evaluate postoperative analgesia of tramadol and robenacoxib administered orally in dogs.

MATERIALS AND METHODS

Forty client-owned dogs (n=40) undergoing genital surgery at the Clinic of Obstetrics and Gynecology (Faculty of Veterinary Medicine of Bucharest) were taken into study. Age of the dogs ranged from 2 years to 7 years with a mean of 4.5 years. The body weight of the dogs ranged from 12 kg to 42 kg (mean=27 kg).
All animals were evaluated (physical examination, complete blood cell count, biochemistry profile) and were classified according to the American Society of Anesthesiologists scale (ASA 1 to 5). Only the ASA 1 to ASA 3 dogs were included in the study.
Dogs were fasted 12 hours and water was withdrawn 4 hours before the surgery. The animals underwent the same anesthetic protocol (table 1).

Table 1. Anaesthetic protocol

Substance	Dose
Medetomidine (Domitor®, Pfizer Animal Health, Romania)	10 µg/kg IM Wait 10 minutes
Butorphanol (Butomidor®, Richter Pharma, Austria)	0,2 mg/kg IM Wait 10 minutes
Propofol (Lipuro®, B Braun Medical, Romania)	6 mg/kg IV bolus
Endotracheal intubation	
Isoflurane (Anesteran®, Rompharm Co., Romania)	1.5 – 2%

Lactated Ringer's solution (B Braun Medical, Romania) was infused IV (10 ml/kg/h) throughout the surgical procedure.
After extubation the dogs were randomly divided in two groups. The first group (n=20) was treated with tramadol (Tramadol®, Ozone Laboratories Group, Romania) 2 mg/kg PO every 8 hours starting 2 hours after the extubation for 3 days. Robenacoxib (Onsior®, Novartis Animal Health, Switzerland) 2 mg/kg was administered once a day, PO to the second group (n=20) starting 2 hours after the extubation for 3 days.
Physiologic indicators of acute pain in animals include increased heart rate, increased heart pressure, peripheral vasoconstriction, cardiac disrhythmias, sweating, hyperventilation and reduced peristaltism (Pearson 2007).
Pain was assessed according to the Glasgow Composite Measure Pain Scale (GCMPS) for dogs, a practical and recognized way of evaluating postoperative pain (Murrell et al. 2008; Reid et al. 2007) . The GCMPS comprises six behavioural categories with associated descriptive expressions: vocalisation, attention to wound, mobility, response to touch, demeanour and posture/activity. Items are placed in increasing order of pain intensity and numbered accordingly. Pain scores were assigned before surgery (as a baseline) every 24 hours and maximum possible score was 24.
Data were recorded as mean±SD. The date were analyzed using an analysis of variance and unpaired t-test (IBM SPSS software, ver. 19 for Windows; IBM, New York, USA). A P value < 0.05 was considered statistically significant.

RESULTS AND DISCUSSIONS

Patients in tramadol group (n=20) were more quiet (15/20), they ate sooner after surgery (10/20), fewer of them cried and whimpered (10/20). Only one dog in tramadol group required additional analgesia in the first 24 hours after surgery. Adverse effects (nausea, salivation) appeared at 3 of the patients of the Tramadol group. 6 dogs of the tramadol group developed an acute inflammation around the incision site. The apparent calmer attitude of the dogs in this group is correlated with the sedative effects of tramadol. Similar observations were made following the administration of tramadol by epidural (Guedes et al. 2005), intravenous (McMillan et al. 2008; Giorgi et al. 2010) , intramuscular (de Sousa et al. 2008; Giorgi et al. 2010) or subcutaneous route (Buhari et al. 2012) . Also the analgesic effect is similar regardless of the route of administration, the oral route is easier to manage by the owners.
Dogs in robenacoxib group (n=20) did not lick around the incision line (17/20) and the wound healed faster (15/20). This is probably due to the anti-inflammatory properties of robenacoxib. There were no side effects (nausea, vomiting) in the robenacoxib group.

Our results confirm the analgesic proprieties of robenacoxib as already proven by previous studies for oral and subcutaneous routes of administration (Gruet et al. 2011; Edamura et al. 2012)

The median pain score did not significantly differ between the tramadol and robenacoxib treatments at any time point (figure 1).

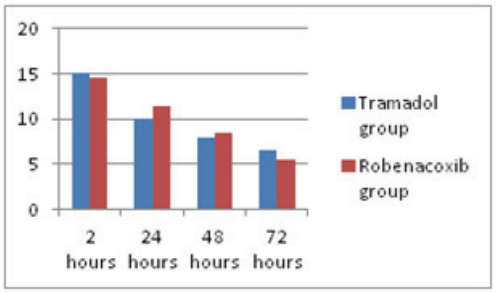

Figure 1. Evolution of pain scores in 72 hours

We can not exclude the influence of anesthetic substances on pain scores, especially during the first 2-4 hours after surgery.

Tramadol alone provides longer-lasting analgesia compared to Robenacoxib, but does not have the same anti inflammatory effect. Robenacoxib has a better effect in wound healing. The tolerability of both treatments was good as assessed from adverse effects and clinical signs. Although our study is the first to compare the postoperative analgesic efficacy of Tramadol and Robenacoxib, the combined administration of these two should be the subject of a further study.

CONCLUSIONS

Pain control method should depend on the type of procedure, severity of pain associated to the surgery, economic reasons and individual factors. Postoperative pain management is improved by including drugs that can be administered orally. Both tramadol and robenacoxib can be used for postsurgical pain management in the dog.

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