



Original Article

**Tramadol Vs. Meloxicam in Controlling Postoperative Pain in Dental Extractions in Cats**

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**Abstract**

**Objective-** To evaluate analgesic effect of meloxicam and tramadol following dental extraction in cats.

**Design-** Experimental study

**Animals-** 20 DSH cats diagnosed with 3rd or 4th stage of periodontal disease at their third mandibular premolar were entered the study in order to perform surgical dental extraction.

**Procedure-** A blood sample was taken prior to surgery to assess the level of cortisol and CPK. General anesthesia was performed using ketamine and diazepam (IV, 8.5 mg/kg+0.2 mg/kg) and inhalation of isoflurane following intubation. Third mandibular premolar was extracted in all of the patients using surgical procedure. The cats were randomized into two groups of A receiving meloxicam (IV, 0.2 mg/kg) and B, receiving tramadol (IV, 3 mg/kg) at the time of induction of anesthesia. The analgesics were continued after the surgery for 24 hours. The score of pain were recorded using UMPS and assessment of serum level of cortisol and CPK at 2, 4 and 24 hours after the surgery was performed.

**Results-** The highest score of pain was recorded at 4 hours after the surgery in both groups. Level of cortisol was significantly higher at 4 hours after the procedure in group B (P= 0.035). The increase in CPK was statistically significant at 2,4 and 24 hours after the surgery in group B when compared to group A (P<0.05).

**Conclusion and Clinical Relevance-** It was concluded that although tramadol and meloxicam were both effective in reducing pain at early hours after the surgery, meloxicam was more effective to control pain after the first few hours.

**Key words:** Dental pain, tramadol, meloxicam, cat

**Received:** 5 April 2016; **Accepted:** 13 September 2017; **Online:** 8 October 2017

**Introduction**

Pain management is considered to be very important during anesthesia by reducing the degree and onset of pain, providing patient's comfort and finally facilitates recovery of the patient. However, in oral surgeries, analgesia provides early return of the patient to oral feeding.<sup>1,2,3</sup> Currently opioids and NSAIDs are mostly

Used to manage the pain following dental surgeries.<sup>1,4</sup> Tramadol is a central acting synthesized opioid and demonstrates agonist action on mu receptors. Because it is considered as a non-scheduled drug in many countries, it is available in most of the situation when analgesia is required. The drug is used to manage moderate to moderately severe pain.<sup>5</sup>

Tramadol has been shown to be effective in reduction of dental pain when used alone or in combination with NSAID.<sup>6,7,8</sup> Meloxicam is a COX-2 selective NSAID. Evidence suggests that COX- 2 is the dominant COX isoform in the spinal cord and is associated the recognition of pain by central nervous system during inflammation. It is believed that they have fewer side effects and are less harmful to gastrointestinal

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mucosa.<sup>9</sup> The drug is usually used to control moderate pain.<sup>5</sup> It has been shown that meloxicam is effective in postoperative pain following endodontic treatments.<sup>10</sup> Production of pain in dental surgeries is mostly due to the inflammation of the dental or associated oral tissues. Therefore, pain occurs due to inflammation and swelling of the manipulated tissues following dental surgeries that requires administration of analgesics. Thus, we hypothesized that use of NSAIDs should be superior to use of opioids in controlling pain following dental surgeries. Therefore, the objective of this study was to compare analgesic effect of meloxicam and tramadol following dental extractions in cats. Also we decided to find out if there was superiority in use of either drug in dental procedures.

## Material and methods

### Animals

20 cats from both sexes, weighting  $3.1 \pm 0.35$  kg that were diagnosed with 3rd or 4th stage of periodontal disease in their third mandibular premolar were entered the study. Third mandibular premolar teeth were extracted using surgical technique. The cats were selected among different patients referred to the clinic for the routine dental exam. Following oral examination and dental probing, the presence of the advanced periodontal disease by presence of furcation exposure of the regarding tooth was confirmed. The animals were entered the study after the written consent was received from the owners.

### Procedure

A control blood sample was taken prior to surgery to assess the level of cortisol hormone and CPK enzyme. General anesthesia was performed using ketamine and diazepam (IV, 8.5 mg/kg+0.2 mg/kg) and inhalation of isoflurane in Oxygen following intubation.

The cats were randomly assigned into two groups of A receiving meloxicam (IV, 0.2 mg/kg) and B, receiving tramadol (IV, 3 mg/kg) at the time of induction of anesthesia. The analgesics were continued for 24 hours postoperatively every 8 hours.

Third mandibular premolar tooth was extracted in all of the patients by a same surgeon and using a similar procedure. In order to create an envelope mucogingival flap on buccal aspect of the tooth a No. 15 scalpel blade was used to make an incision around the gingiva. Then a periosteal elevator was

used to remove the attached gingiva from the bone and to elevate a flap. If the furcation of the roots was not evident, a high-speed turbine and the associate diamond bur were used to expose the furcation by removing alveolar bone. Next dental luxator was introduced into the periodontal space in order to luxate the tooth. Finally extraction forceps was used to extract the loosened tooth. Because the teeth were affected by stage 3 periodontal disease, therefore, tooth sectioning was not needed. The mucogingival flap was sutured to the lingual side of the extracted tooth using 4-0 polydioxanone following alveoplasty of the socket. Both subjective and objective indicators of pain were used in this study including score of pain, serum level of cortisol and creatine phosphokinase enzyme (CPK). The score of pain was recorded using University of Melbourne Pain Scale (UMPS) developed by Firth and Haldane 1999<sup>11</sup> by a single trained observer in cats in both groups at 2, 4 and 24 hours following the surgery. Blood samples were taken in the EDTA tubes at 2, 4 and 24 hours after the surgery. The samples were analyzed by an Immunoanalyser (Cobas® e 411 S/N 071227, Roche Diagnostics, Mannheim, Germany). To evaluate serum levels of CPK, blood was taken in 1.5 mL microvettes and tested on an Idexx Vet Lab Station. Similar time intervals were used for the assessment of CPK enzyme levels.

## Statistical analysis

Single point measurements, at any particular times, were analyzed using repeated measure ANOVA. Kruskal-Wallis test was implemented as a post hoc test using SAS. Changes in parameters over time were analyzed using GLM procedure in SAS, including repeated measures in the model. Data were presented as Mean $\pm$ SEM. A value of  $P < 0.05$  was considered significant.

## Results

All of the animals suffered from pain. There was no significant difference in score of pain between the groups ( $P > 0.05$ ). The highest score of pain was recorded at 4 hours after the surgery in both groups (Fig 1).

The increase in level of cortisol was occurred in all of the cats in both groups of this study. Although Mean $\pm$ SD of the level of cortisol was higher in group B at 2, 4 and 24 hours after the surgery, the increase was significant only at 4 hours after the procedure in group B ( $P = 0.035$ ). Also serum level of cortisol returned around its baseline values in group A 24 hours postoperatively (Fig 2). Serum level of creatine phosphokinase enzyme was increased at all measured hours after surgery in both groups.

However, the increase was statistically significant in group B at 2 ( $P= 0.082$ ), 4 ( $P= 0.021$ ) and 24 ( $P=0.010$ ) hours after the surgery when compared to the group A. The highest Mean± SD serum level of the enzyme was recorded at 4 hours after the surgery in the group B. Also 24 hours after the surgery, serum level of creatine phosphokinase enzyme was remained significantly higher in both groups compared to the preoperative values (Fig 3).

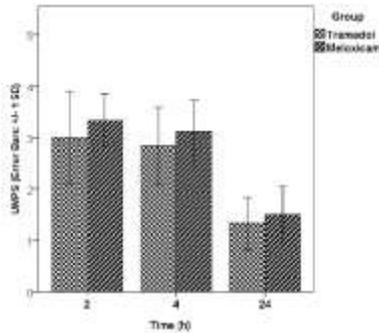


Figure 1. Comparative results of recorded UMP5 scores at different time intervals following dental extraction.

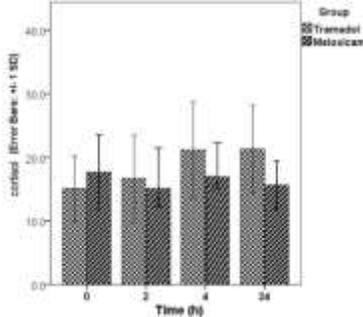


Figure 2. Comparative results of recorded serum level of cortisol (mmol/L) at different time intervals after dental extraction. ( Significant increase was observed at 4 hours after the procedure  $P>0.05$ )

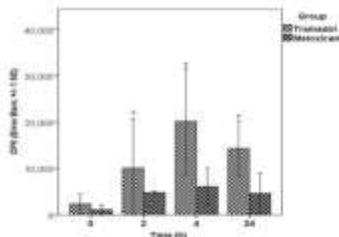


Figure 3. Comparative results of serum level of creatine phosphokinase enzyme (IU/L) at different time intervals after dental extraction (\*: Significant increase observed at 2,4 and 24 hours after the surgery  $P<0.05$ )

## Discussion

Pain management following dental pain prevents patient's discomfort and provides rapid recovery and early return of the patient to oral feeding. Care should be taken to select an effective analgesic regimen according to the degree of pain that the patient is supposed to suffer. Musculoskeletal and dental pain is produced because of the inflammation of the tissues due to the manipulation during the procedure. Therefore, in this study we aimed to determine if there was superiority in the use of NSAID rather than opioids in controlling the pain following dental extraction in cats. Classically NSAID and opioids are used to manage the post-operative dental and oral pain.<sup>1,4</sup> The important difference between these types of drugs is in their mechanism of action. Opioids elicit their analgesic effect by agonizing their receptors, while NSAID produce their analgesic properties by inhibiting the synthesis of prostaglandin through inhibition of the Cyclooxygenase enzymes.<sup>12,13</sup> We observed increase in all of the indicators of pain after dental surgery that we have used in this study. The highest pain was recorded at 4 hours after postoperatively. The highest pain score was reported to be at 5 hours after the premolar dental surgery.<sup>14</sup> We did not administer any additional rescue dose for analgesia after 24 hours following the procedure in all of the patients, since most of them were clinically appeared to be pain free. We did not observe significant different in degree of pain using the University of Melbourne Pain Scale at 2,4 and 24 hours after the procedure between the groups in this study. Serum cortisol concentration is recognized as one of the most objective criteria for pain assessment in animals and found to have direct relation with post-operative pain in dogs.<sup>15,16</sup> Also another marker of muscle injury is creatine phosphokinase enzyme (CPK) that has been used in the assessment of pain in veterinary medicine.<sup>17</sup> It has been shown that the serum level of the enzyme increases after the surgery and it has a positive correlation with degree of pain.<sup>18,19</sup> The increase in serum level of cortisol explains that all of the patients in this study suffer pain, however, significant increase in the values of cortisol hormone observed at 4 hour after the surgery in the group B ( $P=0.035$ ). Also the serum levels of creatine phosphokinase enzyme were significantly higher in 2, 4 and 24 hours after the surgery in the group B as well. Again the highest change recorded at 4 hours after the surgery in the group B. No similar study in the field of dentistry is available regarding the increase in CPK following dental surgeries. However, dynamic correlation was found in increase of CPK, cortisol and pain following ovariohysterectomy in cats.<sup>20</sup> Also it is shown that the increase in invasiveness of the surgery leads to increase in serum level of CPK post operatively in cruciate rupture surgeries in dogs as well as lumbar spine and disc surgeries in human.<sup>10,18-20</sup>

Maticic et al. in 2010 by comparing 2 different techniques in cranial cruciate rupture correction in dogs, indicated that the more invasive surgical technique could increase CPK either twice the less invasive one.<sup>10</sup>

Regarding the results of the present study, meloxicam was more effective in controlling pain after early hours following the dental surgery. NSAIDs are effective in management of periodontal, postoperative dental and endodontic pain.<sup>4</sup> Nekoofar et al in 2003, used meloxicam and reported that they were successful to control postoperative pain in patients undergone endodontic treatments using preoperative injection of meloxicam.<sup>21</sup> Also Paracetamol which like meloxicam is believed to be a Cox-2 selective NSAID was reported to be effective in controlling post-extraction pain of the 3<sup>rd</sup> molar teeth in human patients and also its analgesic effects are comparable to those of Ibuprofen.<sup>22,23</sup>

The results of the present study were in agreement with the results of the previous studies that compared the analgesic effects of opioids to NSAIDs in dental surgeries. Isirdia et al in 2012 during a pilot study compared the effectiveness of perioperative tramadol and meloxicam after 3<sup>rd</sup> mandibular molar extraction in human patients. The results showed that meloxicam was more effective to lower the intensity of pain than tramadol.<sup>24</sup> Also preoperative ketorolac showed to be more effective than tramadol in controlling pain after third molar surgery. It has been indicated that the single dose of tramadol is not effective in providing analgesia following dental extractions and multiple doses are needed.<sup>2,14</sup> Adverse effects of the NSAIDs should be considered during their use, especially when multiple doses are needed. Acute renal failure and even death have been reported after repeated doses of meloxicam in cats. However, it does not have adverse effect on glomerular filtration in short term usage.<sup>25,26</sup> NSAIDs inhibit prostaglandin production, this means that they are most effective when used prior to production of prostaglandin due to inflammation and the subsequent pain. Therefore, in order for meloxicam to have maximum effect in managing postoperative pain after dental surgeries, it should be used prior to surgery. In conclusion both meloxicam and tramadol were effective to control post-operative pain during the first few hours after dental extraction in cats. However, meloxicam seemed to be more effective in managing pain after the first few hours and during a day after dental extraction. Preemptive analgesia is recommended when considering NSAIDs for managing pain of dental surgeries.

## Acknowledgments

The authors appreciate the staff of the clinic for their help and care of animals.

## Conflicts of interest

None

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مقایسه اثرات بی دردی دو داروی ملوکسیکام و ترامادول در کنترل درد  
پس از عمل جراحی دندان در گربه ها

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**هدف:** -مقایسه اثرات بی دردی ایجاد شده ناشی از تجویز دو داروی ملوکسیکام و ترامادول در کنترل درد پس از کشیدن دندان سوم پریمولار مندیبل در گربه ها.

**طرح:-مطالعه تجربی**

**حیوانات-** ۲۰ قلاده گربه بالغ مبتلا به بیماری های پریدونتال درجه ۳ در دندانهای پریمولار مندیبل که به بیمارستان دامپزشکی ارجاع داده شدند.

**روش کار-** یک نمونه خون کنترل جهت اندازه گیری میزان کورتیزول و آنزیم کراتین فسفوکیناز اخذ شد. پس از القای بیهوشی با استفاده از دو دارو کتامین و دیازپام به صورت تصادفی یکی از دو داروی ضد درد ملوکسیکام ۰.۲ mg/kg (گروه A) و یا ترامادول (گروه B) ۳ mg/kg در گربه تحت جراحی به صورت وریدی تجویز شد و دندان پریمولار سوم مندیبل به روش جراحی کشیده شد. در زمانهای ۲ و ۴ و ۲۴ ساعت پس از جراحی نمونه خونی جهت اندازه گیری کورتیزول و آنزیم کراتین فسفوکیناز به آزمایشگاه فرستاده شد و نیز اندازه گیری میزان درد به روش UMPS در ساعت های ۲ و ۴ و ۲۴ پس از جراحی انجام شد.

**نتایج-** امتیاز درد اندازه گیری شده به روش UMPS در هر دو گروه نسبت به پیش از جراحی افزایش معنی دار نشان داد. اما پس از جراحی دندان امتیاز درد بین دو گروه در کلیه ساعات اندازه گیری شده تفاوت معنی داری مشاهده نشد ( $P>0.05$ ). میزان هورمون کورتیزول و آنزیم کراتین فسفوکیناز در دو گروه در تمامی ساعات اندازه گیری شده نسبت به قبل از جراحی افزایش یافته است که بیان کننده این است که هر دو گروه در جاتی از دردرا تجربه کرده اند. افزایش میزان هورمون کورتیزول در گروه اول در ساعت ۴ به صورت معنی دار می باشد. میزان آنزیم کراتین فسفوکیناز در ساعات ۲، ۴، ۲۴ در گروه ۱ به صورت معنی داری افزایش را نشان می دهد.

**نتیجه گیری و کاربرد بالینی-** در ساعات اولیه پس از جراحی کشیدن دندان سوم پریمولار اثرات ضد دردی دو دارو مشابه هم می باشد اما در زمانهای ۴ و ۲۴ ساعت پس از جراحی داروی ملوکسیکام در کنترل درد موثر می باشد. بنابراین تجویز داروی ملوکسیکام در دردهای پس از کشیدن دندان در گربه ها توصیه می شود.

**کلمات کلیدی-** درد دندان، ضدالتهاب غیراستروئیدی، مخدر، ترامادول، ملوکسیکام، گربه