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Comparison of Production of Pain and Oxidative Stress after Induction of Local Nerve Block or Use of NSAIDs following Painful Dental Procedures in Dogs

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ABSTRACT

The objective of the present study was to investigate the superiority of rostral maxillary nerve blocks using the combination of lidocaine and bupivacaine or pre-operative administration of meloxicam in controlling the pain following the surgery in dogs undergoing dental pulpotomy in the rostral maxilla. Twelve dogs with healthy teeth were included in this study. Under general anesthesia, each dog was randomly assigned to receive either rostral maxillary nerve block with the combination of lidocaine and bupivacaine (0.4 ml per site) (Group A) or intravenous meloxicam (0.2 mg/kg) (Group B) prior to pulpotomy. Pulpotomy was performed in the right or left upper corner incisor teeth of each dog using a single technique. The score of pain was recorded using UMPS at 3, 5, and 24 hours after surgery and assessment of serum level of cortisol and indicators of oxidative stress including Total Antioxidant Capacity (TAC) and value of malondialdehyde (MDA) in hemolysis of red blood cells prior to surgery and at 30 min, 3 and 24 hours post-operatively. The highest score of pain was recorded at 5 hours after a pulpotomy, which was significantly higher in group B in comparison to group A ($p = 0.026$). Mean ± SD level of cortisol was significantly higher in group B at 30 min, 1 and 3 hours after pulpotomy in dogs of group B compared to group A ($p < 0.05$). TAC values were significantly lower in group A compared to group B. ($p < 0.05$). However, Mean ± SEM values of MDA were significantly higher in group A at different time intervals in comparison to group B. ($p < 0.05$). It is concluded that rostral maxillary nerve block by using the combination of lidocaine and bupivacaine in painful dental procedures seems more effective than administration of meloxicam to control pain resulted from pulpotomy in dogs in early hours.

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Introduction

Dental procedures are among those that tend to cause pain and can be resolved through local nerve blocks within the pained area in Humans.[1] However, according to the American Veterinary Dental Society act the use of general anesthesia is still considered a necessity. Majority of different anesthetic products used in all forms of surgery still have the tendency to feel pain and lacks analgesia. Therefore, using an analgesic regimen in anesthetic protocols is recommended. Also due to inflammation of the oral tissues, using non-steroidal anti inflammatory drugs (NSAIDs) in post-operative management is effective but it is not always successful.

Nerve blocks during dental procedure adjunct to anesthesia facilitates providing regional analgesia and have some post-operative analgesia as well. Also, it decreases the demand that the patient needs to keep it under anesthesia, means decreasing the mac of the inhalant anesthetic to keep patients much lighter.[1,2] We like to keep our patients really in light level of anesthesia and wake up extremely quickly. It not only maximizes cardiac out-put and blood pressure, but also the patient is much safer and all physiologic parameters are kept in their maximum levels. Another advantage of nerve blocks in dental procedure is that by keeping the patient in lighter levels of anesthesia while pain free, hypothermia is prevented. Aguiar in 2015 showed that the use of rostral nerve block is effective in pain control following dental extractions in cats.[3] Other studies indicated the effectiveness of adjunct regional nerve block in decreasing post-operative pain after orthopedic procedures in dogs.[4,5] In addition, it has been shown that the use of NSAIDS like meloxicam ketorolac, in pain relief after dental surgeries is effective and even superior than that of tramadol.[6,7]

Therefore, we aimed to compare the analgesic effects of rostral maxillary nerve blocks using the combination of lidocaine and bupivacaine with pre-operative administration of meloxicam in dogs undergoing dental pulpotomy in the rostral maxilla to test the superiority of either of the technique to alleviate pain.

Materials and Methods

The present study was conducted after the approval was received from the University Research and Ethics Committee, Islamic Azad University of Garmsar, Iran.

After the general health checkup, the 12 mixed breed healthy male dogs weighing 18 ± 3 kg with healthy teeth were included in this study. The food was restricted for 8 hours in all subjects prior to surgery. A control blood sample was taken prior to surgery to assess the level of cortisol hormone, and indicators of oxidative stress including total antioxidant capacity (TAC) and value of malondialdehyde in hemolysis of red blood cells (MDA). In all dogs, general anesthesia was performed using acepromazine (0.01 mg/kg) as premedication and the combination of ketamine and diazepam (IV, 8.5 and 0.2 mg/kg, respectively) for induction of anesthesia. The anesthesia was maintained by inhalation of isoflurane in oxygen following intubation. The oral chlorhexidine solution 1.2% was used for aseptic preparation of the oral cavity.

Prior to the procedure, each dog was randomly assigned to either group A or B. In group A rostral maxillary and rostral mandibular nerve block using infiltration of combination of lidocaine 2% (1 mg/kg) and bupivacaine 0.5% (1 mg/kg) by 20 gauge needle were administered. In group B, meloxicam (0.2 mg/Kg) was injected subcutaneously at the time of induction of anesthesia. Then in both groups the vital pulp therapy procedure started by creating a cervical cavity with an inverted bur in the incisors of both upper and lower jaw. Explorer was used to confirm the pulpal exposure as soon as the pink color of pulp was exposed through the thin layer of dentin. Cavities were washed with normal saline. A total number of 24 incisor teeth were prepared in this way. After preparation of the cavity and control of bleeding, vital pulp therapy was performed using MTA. Also, zonalin cement was used to cover the created cavity.

Both subjective and objective indicators of pain were used in this study including score of pain and serum level of cortisol. Also changes in oxidative stress by measuring serum levels of TAC and MDA were recorded. The score of pain was measured using University of Melbourne Pain Scale (UMPS) by a single trained observer in dogs in both groups at 3, 5, and 24 hours following the procedure. Blood samples were taken in the EDTA tubes prior to pulpotomy and at 30 min, 1, 3 and 24 hours after the procedure. The samples were analyzed by an Immunoanalyser (Cobas® e 411 S/N 071227, Roche Diagnostics, Mannheim, Germany). Also the commercial kit was used to measure values of TAC (TAC test kit, Randox laboratories Ltd. G.B) and malondialdehyde (Thiobarbituric acid technique) in hemolysis of red blood cells.

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 ± SEM. A value of $p < 0.05$ was considered significant.

Results

All of the animals were recovered from anesthesia uneventfully. Obtained result are classified as follows:

Comparative Results of Recorded UMPS Score at Different Time Intervals following Pulpotomy.

All of the animals suffered from pain. There was no significant difference in score of pain prior to surgery between the groups ($p > 0.05$). The highest score of pain was recorded at 5 hours after pulpotomy that was significantly higher in group B in comparison to group A ($p = 0.026$). Also, the trend of the changes of UMPS during the study indicated that the score of pain was significantly decreased at 24 hours following the procedure in the both groups ($p < 0.05$) (Table 1).

Comparative Results of Recorded Serum Level of Cortisol (mmol/L) at Different Time Intervals after Pulpotomy.

The increase in level of cortisol was occurred in all of the dogs in both groups of this study at 30 min after the procedure, however, the increase was higher in group B (Table 2). Mean ± SD of the level of cortisol was significantly higher in group B at 30 min, 1 and 3 hours after pulpotomy in dogs of the group B compared to group A ($p < 0.05$), but no significant difference was found at serum level of cortisol at 24 hours after pulpotomy between the groups ($p > 0.05$). Also serum level of cortisol returned around its baseline values in both groups 24 hours postoperatively (Table 2).

Comparative Results of Measured Level of TAC (mmol/L) and MDA (nmol/ml) at Different Time Intervals after Pulpotomy.

Mean ± SEM TAC values at different time intervals showed significant difference between the two groups of the study. TAC values were significantly lower in group A compared to group B. ($p < 0.05$). However, mean ± SEM values of MDA were significantly higher in group A at different time intervals in comparison with group B ($p < 0.05$) (Table 3).

Table 1. Comparing Mean ± SEM scores of pain between the groups of the study at different times following pulpotomy.

Group	Prior to pulpotomy	3 hours after pulpotomy	5 hours after pulpotomy	24 hours after pulpotomy
A	0	0.44±1.9	1.7±0.28	0.5±0.22
B	0	1.7±0.31	2.1±0.81*	0.95±0.32

Data with * superscript differs significantly within columns ($p < 0.05$)

Table 2. Comparing Mean ± SEM serum level of cortisol (mmol/L) at different times after pulpotomy.

Group	Prior to pulpotomy	30 min after pulpotomy	60 min after pulpotomy	3 hours after pulpotomy	24 hours after pulpotomy
A	3.62±1.66	3.78±1.10	2.21±0.85	2.20±0.67	2.98±0.57
B	3.96±1.03	4.54±2.03*	4.68±1.06*	4.32±0.88*	3.06±0.24

Data with * superscript differs significantly within columns ($p < 0.05$)

Table 3. Mean of MDA and TAC in group A and B prior to surgery, and at 30 min, 1, 3 and 24 hours after pulpotomy.

Measured Variable	Group	T 0	T 30 min	T 60 min	T 3 h	T 24 h
MDA (nmol/ml)	A	78050.8*	74630.2*	^6253.6*	93780.4*	110180.6*
	B	41534	40549.6	56253	49036.8	53755.8
TAC (mmol/ml)	A	10.7	11.5	11.6	11.04	10.08
	B	12	15.1*	14.7*	14.2*	14.08*

Data with *superscripts showed significant difference within columns at the 0.05 significance level.

Discussion

Pain management following dental procedures 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.[8,9] Therefore, in this study we aimed to determine if there is superiority in the use of local nerve block rather than NSAIDS in controlling the pain following pulpotomy in dogs. Classically NSAIDs and opioids are used to manage the post-operative dental and oral pain. NSAIDs produce their analgesic properties by inhibiting the synthesis of prostaglandin through inhibition of the cyclooxygenase enzymes.[10] Also, local nerve blocks are being used widely during many procedures adjunct to general anesthesia like orthopedic, obstetric and dental surgeries.[4] All of the pain indicators used in this study showed increase after the dental surgery and the highest pain recorded at 5 hours post-operatively. The highest pain score was reported to be at 5 hours after the premolar dental surgery.[12] 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 pain free. We did not observe significant different in degree of pain using the University of Melbourne Pain Scale at 3 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.[13,14] The increase in serum level of cortisol explains that all of the patients in this study suffered pain, however, significant increase in the values of cortisol hormone was observed at 30 min, 1 and 3 hours after pulpotomy in the group B (p = 0035). An hour after pulpotomy mean cortisol levels started to decrease in group A and remained in almost the same levels until a day after. It has been shown that the analgesic effect of lidocaine starts about 1-2 minutes after the injection and it lasts about 1 to 1.5 hour. Since the effect for bupivacaine start 15-30 min following the injection and lasts for 6-8 hours. Therefore, first lidocaine and then bupivacaine elicit their analgesic effects.[15] Our results indicated that the both drugs worked properly to alleviate dental pain and stress occurred after pulpotomy.

NSIADs are effective in management of periodontal, postoperative dental and endodontic pain.[8] Nekoofar *et al.* in 2003, used meloxicam and reported that they were successful to control postoperative pain in patients undergone endodontic treatments.[16] Also, paracetamol like meloxicam is believed to be a COX-2 selective NSIAD and is reported to be effective in controlling post-extraction pain of the 3rd molar teeth in human patients and also its analgesic effects are comparable to those of ibuprofen.[17] Isiordia *et al.* in 2012 during a pilot study compared the effectiveness of perioperative tramadol and meloxicam after 3rd mandibular molar extraction in human patients. The results showed that meloxicam was more effective to lower the intensity of pain than tramadol.[6] However, in the present study, by considering the changes in score of pain and cortisol levels in two groups, we found that local nerve block could represent more analgesia than NSAIDs used prior to the dental procedure. Adverse effects of the NSAIDs should be taken into account 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.[11] 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.

Indicators of oxidative stress are considered in many anesthetic procedures. TAC is decreased when more oxidative stress is predicted during a procedure. Our results showed that the amounts of TAC were significantly higher in group B at different time intervals recorded after pulpotomy, while MDA amounts which is the final product of lipid per-oxidation were significantly in the dogs of group B during the study. These results supported that meloxicam could produce less oxidative stress in comparison with local nerve block.

In conclusion both meloxicam and tramadol are effective to control post-operative pain in dental pulpotomy in incisor teeth of dogs, however, local nerve blocks applied by the combination of lidocaine and bupivacaine seems to be more effective than pre-operative meloxicam in managing pain after the first few hours and during a day after the procedure. In contrast meloxicam produced less change in the

indicators of oxidative stress. Preemptive analgesia is recommended when considering NSAIDs for managing pain of dental surgeries.

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Conflict of Interest

Authors would like to declare that the manuscript has no conflict of interest.

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