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The effect and spread of a lidocaine or a lidocaine/bupivacaine mixture administered into the infraorbital canal in dogs

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ABBREVIATIONS

C	Canine tooth
ET_{Iso}	End-tidal concentration of isoflurane
M2	Second molar tooth
PM4	Fourth premolar tooth
REMP	Reflex evoked muscle potential

Abstract

Objective To determine onset, duration and spread of lidocaine (L) or lidocaine/ bupivacaine (LB) administered into the infraorbital canal in dogs.

Animals Six healthy adult intact female hound dogs weighing 21.3 ± 1.4 kg.

Procedures Dogs were anesthetized with intravenous propofol, maintained with isoflurane in oxygen and ventilated in lateral recumbency. Stimulating needles were inserted into the gingiva lateral to both maxillary C, one P4 and one M2. Following noxious stimulation at each site the digastricus reflex was recorded as a REMP. Values from three baseline measurements, made at 10 minute intervals, were averaged. Lidocaine (1 mL of 2%) or lidocaine and bupivacaine (0.5%) (0.5 mL of each solution) were then deposited at about 2/3 the length of the infraorbital canal. Recordings were made at 5, 10, 15, 30, 45 and 60 minutes, then every 20 minutes for up to 7 hours. The REMP area for the unblocked canine tooth was used to normalize results for all three sites on the blocked side at each time and expressed as a percent of baseline.

Results With both treatments 5/6 C were blocked by 5 minutes and one by 10 minutes and only 3/6 P4 and one M2 were blocked. The average duration of the block for C was 120 ± 54 and 277 ± 43 (p=0.016), for P4, 168 ± 107 and 253 ± 83 and for M2, 15 and 45 minutes, for L and LB, respectively.

Conclusions and Clinical Relevance The deposition of 1 mL of L or LB, at about 2/3rds the length of the infraorbital canal, successfully blocked C but failed to consistently block P4 or M2. This specific technique should not be used during tooth extraction caudal to C.

Keywords bupivacaine, dog, infraorbital, lidocaine.

Introduction

Local anesthetic blocks decrease nociceptive input into the central nervous system during invasive procedures and thereby decrease the facilitation of nociceptive pathways that can worsen the experience of pain in the postoperative period.[1] Regional nerve blocks are used extensively in veterinary medicine both in the awake and anesthetized animal.[2-5] In the awake or chemically restrained animal this is essential to provide humane conditions for the procedure. In the anesthetized animal a regional nerve block can minimize sensory input and decrease the requirements for general anesthetic agents. Since most general anesthetics, particularly the inhalants, cause significant dose-dependent cardiopulmonary depression, a technique that allows the animal to be kept at a lighter plane of anesthesia is likely to decrease these negative effects.

An infraorbital nerve block was described in dogs as early as 1928[6] and further descriptions have been incorporated in most major veterinary anesthesia text books, but there is very little information on the effectiveness of the block.[7] The infraorbital nerve that courses through the infraorbital canal supplies sensory neurons to the superior premolar teeth from the middle superior alveolar branches and to the incisor and canine teeth on the ipsilateral side from the rostral superior alveolar branches. However, the caudal premolar and molar teeth are supplied by the caudal superior alveolar branches that originate from the maxillary nerve before it enters the infraorbital canal.[8] The gingiva on the aboral side of the maxillary teeth is supplied by the same nerves. Hence a local anesthetic introduced into the infraorbital canal would not be expected to block the caudal premolar and molar teeth unless it spreads caudally along the nerve to block the caudal superior alveolar branch. Such caudal spread into and beyond the end of the canal was demonstrated when radiographic contrast media were deposited into the infraorbital canal.[7]

A variety of methods have been used to test the presence of an effective dental nerve block in dogs. Electrical stimulation has been used in other investigations where the anode was attached to each tooth, coated with electrode gel to provide good contact with the surface of the tooth, and the cathode inserted into the gingival mucosa.[7,9] This technique may have stimulated both the pulpal and gingival nociceptors. The REMP is a method to quantify the response to a noxious stimulus applied to the teeth and gingiva. It is objective and provides a reliable definition of a block because it can show the presence of a full block as well as gradations of recovery. A cold thermal stimulus, achieved by application of a cotton ball sprayed with refrigerant, was used to assess a mental nerve block.[10] The response of heart rate and blood pressure,[9,10] movement[10] and change in the minimum alveolar concentration (MAC) of an inhalation anesthetic agent have all been used as outcome measures.[9]

Lidocaine and bupivacaine are commonly used in veterinary practice as local anesthetics with shorter and longer durations of action, respectively. Mixtures of lidocaine and bupivacaine have been used to speed the onset of action compared with bupivacaine alone[11] while increasing the duration of action compared with lidocaine alone.[12] In some circumstances the mixture may even be more effective than lidocaine alone.[13]

The objective of this study was to determine the onset, duration and spread of an infraorbital block using reflex evoked muscle action potentials following an injection of lidocaine or a mixture of lidocaine and bupivacaine in anesthetized dogs.

Materials and Methods

This study was approved by the Institutional Animal Care and Use Committee. Six adult intact female mesaticephalic hound dogs weighing 21.3 ± 1.4 kg were used. Each dog was deemed to be healthy based on normal physical examination and complete blood count and biochemistry profile within reference ranges for the institution's laboratory. The stage of the estrus cycle was not assessed during the experiments. Food was withheld 12 hours before the study, although water was available ad libitum until the dogs were transported to the laboratory. The original design of the study was to compare lidocaine with bupivacaine and the treatments were assigned in random order[a] with the first side (left or right) also assigned randomly. Unfortunately, due to inconsistencies, the results from the bupivacaine part of the study were not useable and in the blocks that were recorded the duration of effect exceeded 10 hours, so it was decided to do a further separate study with the mixture of lidocaine and bupivacaine with the expectation that the duration of the block would be less than with bupivacaine alone. This meant that the order of treatments was not randomized. At least 2 weeks were allowed between each study using the same dogs and the side of injection was again randomized.

A venous catheter was placed percutaneously into a cephalic vein (20 gauge, 4.8 cm[b]). Anesthesia was induced with propofol[c] intravenously (IV), using a slow infusion (approximately 1 mg/kg/minute), until endotracheal intubation could be achieved. The animals were then maintained on isoflurane[c] in oxygen delivered using a partial rebreathing circle system. The dogs were randomly assigned to left or right lateral recumbency on a warm water heating pad and body temperature was maintained using a warm air circulating blanket. An esophageal thermometer[d] was introduced and advanced so that the tip was over the heart and body temperature monitored throughout to maintain it between 36.8 and 38.3ºC. The end-tidal partial pressure of carbon dioxide (P_{ETCO_2}) and expired concentration of isoflurane (ET_{Iso}) were monitored using a Raman gas spectrometer[e]. Intermittent positive pressure ventilation[f] was used to maintain a P_{ETCO_2} of 31 ± 3 mmHg. The isoflurane was adjusted to maintain a plane of anesthesia with a lack of movement in response to the gingival stimulation. This resulted in an ET_{Iso} of 1.9 ± 0.1 %. Pulse rate and systolic arterial blood pressure were monitored using a Doppler[g] on the metacarpal region and a blood pressure cuff, measured to have a width of 40% of the circumference of the antebrachium. Lactated Ringer's solution was administered IV at 5 mL/kg/h.

Two shielded stimulating unipolar needle electrodes[h] per site were inserted approximately 5 mm apart into the gingiva on the aboral side of the C, P4 and M2 maxillary teeth of the side to be injected (with the dog in lateral recumbency) and over the canine tooth of the contralateral side. The needles were inserted as close to the dental gingival border as possible. The contralateral C served as a control in order to normalize the values determined from the injected side, as expressed in the calculation below. Two shielded needles were also inserted into the caudal belly of the digastricus muscle with a ground electrode inserted subcutaneously over the dorsal cervical region. The REMP[14] was recorded from the digastricus muscle using a Nihon Koden Viking IVD evoked potential system[i]. An electrical stimulus was applied to each pair of gingival electrodes and the current was increased and then decreased until there was a maximal amplitude of the first REMP wave with minimal stimulus artifact. The current intensity varied between 30 and 80 mA and we used a 0.5 ms pulse width at a frequency of 1 Hz for 20 seconds. Three baseline values for each site were then recorded at 10-minute intervals with each cycle taking 2-3 minutes to complete. An injection was then made into the infraorbital canal using 1 mL of 2% lidocaine or 0.5 mL of 2% lidocaine, mixed with 0.5 mL 0.5% bupivacaine. The 27-gauge 3.2 cm needle[j] was advanced into the canal from the mucosal surface and into the infraorbital foramen until the tip of the needle was about 2/3 the length of the canal, as judged by the distance from the insertion point to a sagittal line drawn from the medial canthus of the eye (estimated caudal end of the canal). The syringe was then attached and aspirated to ensure that the tip of the needle was not in a blood vessel, and then the solution was injected. The needle was withdrawn and no pressure was applied over the site. Further REMP recordings were made at 5, 10, 15, 30, 45 and 60 minutes and then every 20 minutes for 7 hours or until the area under the recordings from the control and treated canine teeth were similar (the areas were calculated by the machine in real time). At the end of each study carprofen (2 mg/kg) was administered IV before the dogs were recovered from anesthesia.

For analysis, the normalized area under the first wave was used as the main measurement. Latency (time from stimulus to start of the wave), duration (time from beginning to return to same voltage) and amplitude (height of the wave) were also examined (Fig. 1). A calculation was made to normalize all the values according to the control recordings. The three baseline values for the contralateral canine tooth were averaged (C) and the ratio of each subsequent timed value (TC) established (C/TC) (normalized control). The value recorded on the injected side (timed treatment, TT) was expressed as a percentage of its baseline value (treated control, TRC) and this was multiplied by the normalized control value for that time.

$$Normalized\ value\ (\%) = \frac{C}{TC} \times \frac{TT}{TRC} \times 100$$

Any value <15% was taken as evidence of significant desensitization (successful block). The duration was measured as the time to the first point at <15% and the time to the first point >15%. The duration of the block for the canine tooth was compared between the two treatments using a one tailed Wilcoxon signed rank test. The other teeth were not tested statistically because of the small numbers of successful blocks. Latencies, durations and amplitudes of the waves during recovery were also not tested statistically because of the variable numbers of data points. Statistical significance was accepted if $p<0.05$.

Results

Infraorbital injection of L blocked the gingiva over C in 5/6 dogs by 5 minutes and in the remaining dog by 10 minutes. The P4 were blocked at 5 minutes in two dogs and in one other at 10 minutes but not in the remaining three animals. The M2 was blocked at 5 minutes in one dog. The duration of the block for C was 120 ± 54 minutes (range: 80-220 minutes), duration for three P4 was 168 ± 107 minutes (range: 45-240 minutes), and for one M2 was 15 minutes.

After injection of LB, the gingiva over C was blocked in 5/6 dogs by 5 minutes and in the remaining one by 10 minutes. The P4 was blocked at 5 minutes in one dog and by 10 minutes in two other dogs. The M2 was blocked at 5 minutes in one dog. Duration of the nerve block for C was 277 ± 43 minutes (range: 220-340 minutes), and this time was significantly different from L ($p = 0.016$). The duration of block of three P4 in LB was 253 ± 83 minutes (range: 160-320 minutes). The single M2 block lasted 45 minutes.

The average normalized values for the normalized REMP area values indicate that the C block had recovered to almost 100% by 300 minutes with L (Fig. 2) but only to about 25% by 340 minutes with LB (Fig. 3). The three P4 blocks were back to 100% by 200 minutes with L and still at about 60% by 340 minutes with LB. It also shows that there was an effect on M2 but only one dog had a value of <15% with each treatment. The latency and duration of the waves could not be measured if the amplitude was 0, so the average latencies are only reported from times when there were no more 0 values and there were at least five dogs with recorded values at that time (i.e. once values were no longer being recorded from two dogs the other values were not counted). After L there were no calculable latencies based on the above criteria for C (Not available, NA) but P4 and M2 were 97 ± 8 and 91 ± 6%, respectively. After LB the normalized percent latencies for these periods were 110 ± 10, 112 ± 3 and 100 ± 3 % for C, P4 and M2, respectively. After L the normalized percent durations of the waves were NA, 101 ±16 and 103 ± 13 and after LB 82 ± 10, 89 ± 6 and 104 ± 6% for C, P4 and M2, respectively. After L the normalized percent amplitudes were NA, 115 ± 51, and 103 ± 27 % and after LB, 29 ± 7, 59 ± 12 and 119 ± 20% for C, P4 and M2, respectively. The dogs were observed for 24 hours post procedure and none of the dogs showed associated signs of postoperative pain (depression, not eating, rubbing the face, excessive lip licking).

Discussion

Both treatments resulted in nerve block of the canine teeth, in most cases, within 5 minutes. Deposition of lidocaine, which has a relatively rapid onset of action, in close proximity to the nerve would be expected to result in a rapid block. Likewise, it was expected that the longer duration of action of bupivacaine would confer a longer duration of nerve block from LB than L alone. In a clinical situation the shorter duration of nerve block obtained with lidocaine may be useful where dental extractions are not expected to take much time and postoperative analgesia is to be managed with other drugs, whereas the lidocaine-bupivacaine combination can provide analgesia lasting over 3.5 hours that is adequate for many rostral maxillary extractions and may extend into the postoperative period.

The technique used for assessing the onset and duration of nerve block in this study was stimulation of the gingiva while simultaneously recording the REMP. The recordings obtained were from a repeated stimulus (20 repetitions) that were averaged by the computer so the results are not comparable to those of Whalen where a multiphasic wave was recorded from single stimuli.[14] It also became apparent that the reflex was bilateral and therefore the stimulus could be applied on the same or opposite side to the injection in the infraorbital canal. This allowed the changes over time on the unblocked side to be used to normalize the values obtained from the injected side. Only the gingiva over the canine tooth was used for the control because of the difficulty in keeping the needles in place on the recumbent side for P4 and M2. Overlapping right to left innervation is possible but this has not been described in the dog. The choice of <15% of the normalized control value as an indication of block, was based on examination of the data. It was evident that below this value there were small increases and decreases over time but above this value the normalized values tended to increase sequentially representing a regression of the block. The innervation of the aboral gingiva is the same as for the adjacent teeth although there may be some differences in the types of neurons supplying the tooth pulp and the gingiva. In a study in rats comparing pulpal and gingival neurons there were fewer small pulpal neurons and that they are much less likely to bind isolectin B4 (IB4) than the gingival neurons.[15] These differences are unlikely to alter the response to acute stimulation.

In the present study stimulation of the gingiva over the opposite canine tooth was included as a control value. In pilot studies it was noticed that the amplitude of the REMP did not stay constant but tended to decrease over time. It was not clear whether this was related to the effect of the local anesthetic, the isoflurane or a fatigue of the reflex, although increasing anesthetic depth blunted the reflex. The latencies of the REMP did not appear to change with time and the durations of the waves were close to the baseline values throughout, so the major contributor to the change in area was the change in amplitude.

The block described in this study deposited the local anesthetic at approximately two-thirds the length of the infraorbital canal with some expectation that the drug would move caudally from the site of injection. However, this caudal spread appeared to be inconsistent and did not significantly affect the caudal superior alveolar nerve. From other studies it would appear that the depth of injection is important. Depositing lidocaine approximately 0.5 cm into the infraorbital canal did little to blunt the response to rhinoscopy.[4] Mepivacaine, deposited about 0.5 cm into the infraorbital canal, was tested by evaluating changes in isoflurane MAC in response to an electrical stimulus applied to a maxillary canine tooth.[9] While a 23% reduction in MAC was measured, heart rates and blood pressures increased suggesting that, at least in some dogs, the block was not completely effective. Instillation of chloroprocaine using catheters inserted into the infraorbital canal was used and the REMP applied to examine the efficacy of the block.[7] With this method, it was possible to block responses from the maxillary C, P4 and first molar teeth. However, M2 was not tested. Although the dogs in that study were of similar size to the ones in this study and the volume of injectate was also 1 mL, the depth of insertion of the catheter was not fully described. A more recent study in cadavers used a catheter that was advanced to the level of the lateral canthus of the eye, placing the end of the catheter beyond the caudal end of the canal.[16] The authors examined nerve staining following injection of 0.5 mL of methylene blue and decided that at least 6 mm of the maxillary nerve had to be stained for a positive effect. In that study of 37 cadavers, 65% had more than 6 mm staining, 27% had some staining and 8% had none. The data from the present study and the data from these other studies indicate that it is important to deposit the local anesthetic at least at the caudal end of the infraorbital canal, if not further. The use of a catheter, rather than a needle, as in two of the studies above[7,16] may allow the drug to be deposited near the nerve with minimal risk of trauma and less likelihood of injection into the medial pterygoid muscle. In all of the above studies it is possible that simply increasing the volume of drug injected may have enhanced caudal spread and increased the likelihood of blocking the more caudal teeth.

There are at least four other techniques described for blocking the maxillary nerve, and hence obtaining better desensitization of the caudal teeth. The one originally described in 1928[5,6] used a percutaneous approach from under the zygomatic arch directing the needle rostrally toward the caudal end of the infraorbital canal (pterygopalatine fossa). This approach was investigated in the above cadaver study with only 8/37 maxillary nerves having at least a 6-mm stain.[16] However, the people carrying out the injections were inexperienced with the technique, which could account for the high failure rate. Two other lateral approaches are described, one advancing the needle perpendicularly from the zygomatic arch and one directing the needle caudally past the coronoid process towards the origin of the maxillary nerve at the rostral alar foramen.[17] Lastly an intraoral approach is described with the needle being directed dorsally from behind M2 and medial to the zygomatic arch.[18] None of these last three approaches have been studied objectively.

Although a saline control would have eliminated the influence of chemical, temperature or volume effects, it was not included because a previous study in dogs had demonstrated no effect of saline on the REMP.[7] However, in that study the first recording was at 10 minutes, whereas in a study in humans the REMP was recorded at 1-minute intervals and a 50% decrease was noted at 2 minutes returning to the baseline value by 5 minutes.[19] The first recording in the present study was at 5 minutes, and so it is likely that an effect from a saline control would have passed. However, having the first measurement at 5 minutes also limits the study's ability to detect an earlier onset of anesthesia. A further limitation of this study is that the lidocaine study was completed before the lidocaine-bupivacaine treatment, thus there is a risk of a temporal effect on the data. The mean of the REMP areas for the two treatments were less than 10% different for the baseline control canine teeth suggesting that overall conditions before the injection were similar. One dog only was injected on opposite sides for the two treatments, despite randomization of the side of injection, consequently, results in the LB block in the other five dogs could have been influenced by tissue damage. However, it was noted that the increase in duration of block after LB treatment over L was similar in comparison with the other dogs.

In summary the deposition of lidocaine or a mixture of lidocaine and bupivacaine at about two-thirds the length of the infraorbital canal provided a complete block for the maxillary canine tooth. The block of P4 or M2 was not sufficiently reliable to be used for invasive dental procedures in a clinical setting. The duration of block was longer lasting with the addition of bupivacaine than with lidocaine alone. A volume of 1 mL was used in this study in dogs weighing ~20 kg (0.05 mL/kg) and the effect of volume of solution on the outcome of this block needs to be examined further.

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Figure Legends

Figure 1.Typical baseline reflex evoked muscle potential showing the variables measured. The Y axis on the left represents the start of the stimulus. The thick lines are the determinations, by the computer, of the beginning and end of the REMP.

Figure 2. Mean and SD of the normalized % of the area of the reflex evoked muscle potential (REMP) for the calculated area under the first wave of the reflex-evoked muscle potentials following gingival stimulation over the canine, fourth premolar and second molar teeth in 6 dogs (except where indicated). A zero % represents a complete block and 100% is where the response is equal to the unblocked side. Values greater than 100% are possible if either the area of the unblocked or blocked REMP increased over its baseline values. The data were obtained after infraorbital injection of 1 mL lidocaine (2%).

Figure 3. Mean and SD of the normalized % of the area of the reflex evoked muscle potential (REMP) for the calculated area under the first wave of the reflex-evoked muscle potentials following gingival stimulation over the canine, fourth premolar and second molar teeth in 6 dogs (except where indicated). A zero % represents a complete block and 100% is where the response is equal to the unblocked side. Values greater than 100% are possible if either the area of the unblocked or blocked REMP increased over their respective baseline values. The data were obtained after injection of 0.5 mL lidocaine (2%) plus 0.5 mL bupivacaine (0.5%).

370 **Footnotes**

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[a] www.randomizer.org accessed July 6th 2015.
[b] Insyte, Becton Dickinson, Sandy, Utah.
[c] Abbott Animal Health, Abbot Park, Ill.
[d] YSI, Dayton, Ohio.
[e] Ohmeda Rascal II, GE Healthcare, Helsinki, Finland
[f] Bird mark IV, Bird Corporation, Palm Springs, Calif.
[g] Parks Inc, Aloha, Ore.
[h] Grass 10 mm stimulating electrodes, Warwick, Rhode Is.
[i] Nihon Koden America, Calif.
[j] Monoject, Covidien, Mass.