Adequate pain management should prevent suffering and reduce morbidity after thoracotomy in dogs. Insufficient or poor analgesia after thoracic surgical procedures can lead to the accumulation of secretions, with subsequent atelectasis and pneumonia. Moreover, prolonged immobility related to pain may lead to complications such as deep vein thrombosis and pulmonary embolism. Several analgesic and anesthetic techniques are used to control pain after thoracotomy. Systemic opioids, usually in combination with anti-inflammatory drugs, are often used after thoracotomy. However, high doses of opioids may lead to respiratory depression with subsequent hypercarbia and hypoxemia, nausea, and bowel dysfunction. Anti-inflammatory drugs may be contraindicated in some cases or associated with complications such as platelet dysfunction. Some local anesthetic techniques such as intercostal nerve block and interpleural regional analgesia are simple to perform and used as preemptive analgesia (administered preoperatively) and as postoperative analgesia, respectively, in humans and dogs. Epidural anesthesia is an effective method of pain control but has potential risks, such as dural perforation, bleeding, infection, hypotension, and urinary retention. It may be difficult for an inexperienced veterinarian to administer segmental epidural anesthesia between lumbar or thoracic vertebrae. Insertion of catheters via the caudal route is a feasible and safe method to provide epidural analgesia of the thoracic region in children or dorso-lumbar region in bulls. Another advantage with this technique is attainment of local postoperative analgesia with small amounts of dilute anesthetics with or without lipophilic opioids administered at the spinal cord.
Insertion of a catheter between L7 and S1 and advancing it cranially to the thoracic region within the epidural space is a feasible procedure in dogs. For prolonged segmental epidural analgesia after thoracic surgery, use of long-acting local anesthetics, such as bupivacaine or ropivacaine, would be ideal. However, potentially high serum concentrations of bupivacaine from absorption from the epidural space (dose dependent) may induce adverse effects such as CNS toxicity and myocardial depression. Lido- 
caine is the local anesthetic most commonly used in epidural anesthesia in dogs, with duration of action of 1 to 2 hours. Blood concentrations are less likely to be detrimental and could be associated with additional systemic analgesia. Ketamine is a potent noncompetitive antagonist of N-methyl-D-aspartate receptors involved in the transmission and modulation of nociceptive information by the spinal cord. Ketamine as an adjuvant to bupivacaine for caudal epidural block in children induces analgesia that lasts approximately 22 hours with less supplemental analgesic requirement. Results of previous studies indicate that lidocaine administered epidurally or ketamine administered in the subarachnoid space in combination with other drugs increases the duration of the analgesic or anesthetic period. The objectives of the study reported here were to establish whether epidural administration of ketamine and lidocaine via the lumbosacral route by use of a nonstyletted multiple-port catheter would induce analgesia in the thoracic region in dogs and to determine the duration of systemic and motor effects of the combination.

Materials and Methods

The study protocol was approved by the Federal University of Mato Grosso do Sul State Animal Care and Use Committee. Six adult mixed-breed dogs (3 males and 3 females) with a mean ± SD weight of 18.4 ± 5.2 kg and age of 26 ± 3 months (range, 24 to 30 months) were used. All dogs were maintained in individual cages in the small animal anesthesia room of the Faculty of Veterinary Medicine and Animal Science facilities throughout the experimental period. Each dog received 2% lidocaine hydrochloride (3.8 mg/kg), 5% ketamine hydrochloride (3.0 mg/kg), and both in a randomized order with at least 1 week between treatments. The volume of the drugs was kept constant at 0.25 mL/kg body weight by the use of saline (0.9% NaCl) solution, when necessary.

One or more weeks before the beginning of the experiments, each dog was anesthetized with midazolam (0.3 mg/kg, IM), and ketamine hydrochloride was administered IV. The animal was monitored by means of ECG and pulse oximetry. Under aseptic conditions, an 18-gauge Tuohy needle was introduced into the lumbosacral space (L7-S1) with the dog in sternal recumbency. The hanging-drop technique was used to verify the presence of the needle in the epidural space, which was confirmed by a lack of resistance during insertion of a closed-tip, 3-orifice epidural catheter. The multiple-port catheter was threaded cranially with negligible resistance for a mean ± SD distance of 35 ± 3 cm from the insertion point. This distance was determined by external measurement of the distance from the L7-S1 space to the T4-5 or T5-6 space. The catheter was cut at a length of approximately 35 cm, the external part of the catheter was connected to a valve placed subcutaneously, and the incision was closed. After this procedure, routine antimicrobial treatment was administered for 3 days. Proper placement of the catheter was confirmed by injection of 3 mL of a 1% lidocaine solution through the valve to induce bilateral analgesia. Analgesia was confirmed by detection of forelimb weakness and reduced response to pinching of the thoracic and forelimb regions.

All dogs received each treatment on different occasions. The drugs were administered at a rate of 0.5 mL/s through the implanted catheter. After administration of drugs, catheters were flushed with 0.5 mL of saline solution to flush the dead space of the valve and catheter. Ambient temperature in the laboratory room was approximately 23°C during experiments.

Heart rate, SAP, DAP, MAP, respiratory rate, rectal temperature, analgesia, sedation, and motor block were determined before drug administration (baseline [time 0]) and at 5, 10, 15, 20, 30, 40, 50, 60, 90, 120, 150, and 180 minutes after administration. Time to onset, duration, and anatomic distribution of analgesia were recorded. All dogs were subjected to a noxious stimulus consisting of insertion of a 23-gauge, 1-inch needle into the skin and, if no reaction to this occurred, into deep muscles of the thoracic region, forelimb, and upper flank area on both sides of the body. Two additional regions, hind limbs and feet, were also tested bilaterally for analgesia to the noxious skin stimulus.

Analgesia was rated on the following scale: 1, normal response (strong reaction to a painful stimulus, sudden withdrawal, muscle contraction, or vocalization); 2, mild analgesia (no response to insertion of needle in the skin and no muscle contraction, but restlessness); 3, moderate analgesia (no response to insertion of needle in the skin or deep muscle, but turning toward the site of the painful stimulus); and 4, complete analgesia (calm and indifferent to application of a painful stimulus). All dogs had a lack of analgesia (strong reaction to a painful stimulus) before drug administration. Depth of sedation was rated by evaluation of central effects induced by the drugs by use of the following scale: 1, no sedative effect; 2, mild sedation (reduced alertness with no other signs); 3, moderate sedation (drowsiness and slight drop of the head); and 4, severe sedation (marked drowsiness). Motor blockade was assessed by evaluation of a dog's ability to stand on its forelimbs. A 3-point rating scale was used: 1, normal motor response (stands on the forelimbs and hind limbs); 2, moderate motor blockade (presence of weakness of the forelimbs and mild weakness of the hind limbs); and 3, complete motor blockade (paralysis of the forelimbs and weakness of the hind limbs).

Indirect arterial pressure was measured via a cardiac monitor by use of an oscilometric device with the cuff placed over the brachial artery. Heart rate was measured as the number of beats per minute, and respiratory rate was the number of thoracic movements per minute. Rectal temperature was measured with a digital thermometer.
All data were analyzed by use of a general linear model with a commercial package. Data were grouped and summarized as mean ± SD or median ± confidence interval. Data for SAP, DAP, MAP, heart rate, respiratory rate, and rectal temperature were grouped and analyzed by use of 2-way repeated-measures ANOVA with treatment and time as independent variables. When a significant (P < 0.05) difference or interaction was obtained, a Dunnett test was applied, as appropriate. For analgesia and ataxia variables, the nonparametric Friedman test was used, followed by multiple comparisons for ranked data performed by use of the Dunnett test, with time 0 as the baseline. In each analysis, values of P < 0.05 were considered significant.

Results

During the study period, successful lumbosacral placement of the tip of the thoracic catheter was confirmed radiographically, and the test dose of 3.0 mL of 1% lidocaine solution was used to determine the correct position in the thoracic region in all dogs. Response to pinprick pain stimulation applied to the studied regions satisfactorily indicated the efficacy and spread of analgesia in all dogs.

The main areas of analgesia for the 3 treatments were the thorax and forelimb bilaterally. The median time to onset to analgesia was ≤10 minutes in all treatments (lidocaine, 5 minutes; ketamine and lidocaine plus ketamine, 10 minutes), and only the lidocaine plus ketamine treatment induced mild analgesia in the hind limbs (grade 2). The median duration of analgesia was significantly shorter for ketamine (30 minutes) and lidocaine (40 minutes) than for lidocaine plus ketamine (90 minutes; Figures 1 and 2). Satisfactory analgesia was considered to have been obtained when dogs did not respond to needle pricks in the regions surveyed (scores 3 and 4). All treatments caused motor blockade, which was greater for lidocaine plus ketamine, where the peak effect began at 5 minutes and continued until 30 minutes, than for lidocaine (20 minutes) or ketamine (10 minutes). The motor blockade mainly affected the forelimbs, affecting the hind limbs only slightly (grade 2; Figure 3). Only the treatments with ketamine (ketamine or lidocaine plus ketamine) resulted in sedation, which was mild (score 2).

Cardiorespiratory measurements were summarized (Table 1). Heart rate and respiratory rate did not change significantly from baseline values following thoracic epidural administration of lidocaine, ketamine, or lidocaine plus ketamine treatments. There were no significant alterations in SAP, DAP, and MAP after administration of lidocaine or ketamine, compared with basal values. Significant decreases in SAP at 20 to 150 minutes and in MAP at 5 to 150 minutes were observed for lidocaine plus ketamine treatments. Rectal temperature remained stable after lidocaine, ketamine, or lidocaine plus ketamine treatments following thoracic epidural administration.

Discussion

Results of the present study supported the findings of previous experimental work in humans and other animals and confirmed the efficacy of ketamine at prolonging the duration of epidural blockade. To our knowledge, this is
the first experimental study to use ketamine as an adjuvant to lidocaine administered epidurally in the thoracic region in awake dogs. To increase the duration of anesthesia and gain better control of pain in the postoperative period after thoracotomy, long-acting local anesthetics such as bupivacaine are used. In the present study in dogs, a short duration of anesthesia (90 minutes) was obtained with ketamine combined with lidocaine. However, in children, the combination of bupivacaine with ketamine (0.5 mg/kg) provided postoperative analgesia at 10 hours, reaching approximately 22 hours after caudal epidural administration. This duration of analgesia in dogs is difficult to evaluate because of the subjective nature of the analysis. Nevertheless, this result would be of interest for decreasing stress and adverse effects attributable to pain after thoracic procedures. In the present study, response to bilateral needle pricks identified the cranial and caudal limits of effects of drugs in the epidural space and concomitant anesthesia of spinal segments. These tests provided a semi-quantitative measure of analgesia. We considered the tests to be appropriate, albeit incomplete, methods of assessing the anesthetic action of these drugs in dogs. A more accurate test could include a voltage-based noxious stimulus, surgery, or a skin incision. In the present study, thoracic epidural administration of ketamine induced motor blockade, suggesting a possible action of the drug as a local anesthetic. The ketamine and lidocaine combination induced a longer duration of motor blockade; however, this was shorter than the period of analgesia. The more prolonged effect might have been related to lidocaine because ketamine caused a moderate motor blockage of shorter duration.

Table 1—Mean ± SD values for cardiovascular variables and respiratory rate measured at various times in 6 dogs administered 2% lidocaine hydrochloride (3.8 mg/kg), 5% ketamine hydrochloride (3.0 mg/kg), or both by use of thoracic epidural administration via the lumbosacral approach. See Figure 1 for remainder of key.

Table 1

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Baseline values were obtained prior to drug administration.

*Value differs significantly (P < 0.05) from baseline.

AJVR, Vol 72, No. 12, December 2011

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Systemically, for the cardiovascular system, ketamine administration is associated with increased heart rate and systematic and pulmonary vascular resistance.\(^{20}\) Caudal epidural administration of ketamine does not induce cardiovascular changes in goats\(^{22}\) and dogs.\(^{23}\) However, in the present study, the ketamine and lidocaine combination caused decreases in SAP and MAP but no change in heart rate after thoracic epidural administration. Epidural anesthesia can result in sympathetic blockade. The thoracic viscera and forelimbs are innervated by the spinal cord, whereas the abdominal viscera and hind limbs receive sympathetic supply from the caudal portion of the spinal cord.\(^{23}\) During cranial or caudal segment epidural anesthesia, hypotension is induced mainly by increasing the capacity of vascular beds (a decrease in systemic vascular resistance caused by sympathetic blockade)\(^{23}\) as well as the subsequent decreasing preload. However, the heart is innervated via the cardiac nerve originating in the cranial spinal segments (T1 through T4).\(^{30}\)

This may explain, in part, why the decreases in SAP and MAP were significant in the lidocaine plus ketamine treatment group but not in lidocaine or ketamine treatment groups and why the heart rate was not altered in any of the 3 treatment groups. A noninvasive oscillometric method was used to measure arterial blood pressure. Direct arterial blood pressure monitoring is the most accurate method of assessing blood pressure; however, it is impractical in most conscious animals, and oscillometric measurement can provide an estimate of changes in blood pressure.

Ketamine seems to be a safe agent when used as an adjuvant to local anesthetics in the epidural space.\(^{19,22,25}\) Administration of ketamine with preservative intrathecally into bawoons is not associated with evidence of macroscopic or microscopic abnormalities.\(^{32}\) In the present study, thoracic epidural administration of ketamine with preservative did not result in clinical signs of neurotoxicosis in dogs after several weeks. Moreover, repeated intrathecal administration of preservative-free ketamine to rabbits in single-dose studies\(^{31}\) (1.5 mg/kg, q 24 h, for 14 days) does not cause neurotoxicosis.

The present study revealed that thoracic epidural analgesia is improved by use of a lidocaine and ketamine combination administered through a multiple-port catheter via the lumbar sacral approach induced a period of analgesia longer than that obtained with ketamine or lidocaine alone in conscious dogs. This combination also elicited a sympathetic blockade that included thoracic and lumbar segments and decreases in arterial blood pressure. Additional studies are needed to determine whether this technique satisfactorily relieves postoperative pain after a surgical thoracic procedure, whether it can be extended safely and effectively by repeated administration, and whether it causes respiratory depression in dogs.

References