Insertion of catheters via the caudal route (between the first and second coccygeal vertebrae) to provide epidural analgesia of the thoracic or dorsolumbar regions is a feasible and safe method for use in premature and full-term human neonates and young infants. This technique poses less risk of injury to the spinal cord or dura than the risk associated with epidural or subarachnoid dorsolumbar injections in cattle. Another advantage is attaining local postoperative analgesia with small amounts of dilute anesthetics with or without lipophilic opioids at a spinal cord level, thereby inducing blockage of sensory and motor nerves at the surgical site.2 For certain surgeries via the dorsal portion of the paralumbar fossa (flank) in cattle, it is desirable that animals remain in a standing position. Various methods for local anesthesia have been used to provide anesthesia during laparotomy via a flank incision in standing cattle; these methods include infiltration (line block in association with an inverted L-block), paravertebral injection (distal and proximal), segmental subarachnoid injection, and high caudal epidural anesthesia.3 All these techniques can lead to incomplete anesthesia in the surgical area or can require a larger volume of anesthetic solution than is needed for the caudal approach. A higher volume of anesthetic in the epidural space can induce hypotension and prolonged recumbency. It may be difficult for an inexperienced veterinarian to administer segmental dorsolumbar epidural anesthesia between L1 and L2 or between T13 and L1 in cattle.4 However, this technique can provide advantages over other methods. Use of the caudal approach between the first and second coccygeal vertebrae and advancement of a catheter to the lumbar region is easy and offers no resistance to the cranial advancement of the catheter.

Evaluation of segmental dorsolumbar epidural analgesia with ketamine hydrochloride administered by use of nonstyletted multiple-port catheters via the caudal approach in cattle

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Objective—To evaluate use of nonstyletted multiple-port catheters for epidural administration of ketamine hydrochloride via the caudal approach to induce analgesia of the paralumbar fossa (flank) in cattle.

Animals—6 healthy bulls.

Procedures—1 week before experiments began, a multiple-port catheter was inserted by use of a Tuohy needle in all cattle via the caudal approach (between the first and second coccygeal vertebrae); the tip was threaded approximately 48 cm cranial into the dorsolumbar region. Each bull was administered ketamine (0.3, 0.5, or 0.7 mg/kg) at time 0. Heart rate, blood pressures, respiratory rate, rectal temperature, analgesia, sedation, and ataxia were determined before treatment (baseline [time 0]), at 5, 10, 15, 30, 45, 60, 75, and 90 minutes; and every 30 minutes thereafter until end of analgesia.

Results—All multiple-port catheters were threaded with negligible resistance into the dorsolumbar region in all bulls. All doses of ketamine were effective for inducing analgesia of the flank region of bulls in a standing position. Total analgesia time was dose dependent (35, 50, and 80 minutes for 0.3, 0.5, and 0.7 mg/kg, respectively). All doses of ketamine induced mild or moderate ataxia. Heart rate changes were within acceptable limits.

Conclusions and Clinical Relevance—Segmental dorsolumbar epidural analgesia with ketamine administered via multiple-port catheters by use of the caudal approach in cattle was feasible, and the cattle remained standing with minimal adverse effects. Further studies are necessary to determine whether this technique provides optimal conditions to allow surgery in standing cattle. (Am J Vet Res 2010;71:17–23)
within the epidural space in cattle. In humans, the cranial advancement of epidural catheters to the thoracic region via the caudal route is feasible and safe in young children. However, in older children and adults, difficulty can arise because of kinking of the catheter. The ability to successfully advance an epidural catheter in cattle from the caudal to the lumbar region depends on the ease of passage of the cauda equina. Verification of the location of the catheter tip is recommended when this approach is used. Determining the correct position of the catheter tip includes radiographic confirmation, electrical epidural stimulation in real time, or evaluation of an epidurogram.

Traditionally, local anesthetics have been used to provide epidural anesthesia in cattle, but other drugs, such as \(\alpha_2\)-receptor agonist drugs or ketamine, may offer some advantages. For example, ketamine apparently induces less hind limb weakness and does not have a dose-dependent duration of action. Epidural administration of ketamine is capable of inducing peri-neal analgesia in cattle by acting on NMDA receptors in the spinal cord. Ketamine acts as a noncompetitive NMDA antagonist on the spinal cord and likely blocks synthaptically evoked NMDA receptor-mediated currents. The NMDA receptors are widely distributed throughout the neuraxis and are intimately associated with physiologic processes related to acute and chronic pain states. There is evidence to suggest that ketamine binds in a stereospecific manner to opioid receptors in the brain and spinal cord. The objectives of the study reported here were to establish whether epidural administration of ketamine via the caudal route by use of a nonstyletted multiple-port catheter would induce analgesia in the flank region in conscious standing cattle and to determine the duration and systemic effects of that anesthesia and any interference with the motor system.

### Materials and Methods

#### Animals
Six healthy Nelore bulls were used in the study. Bulls were between 24 and 30 months of age (mean, 26 months) and weighed between 335 and 373 kg (mean, 355 kg). The study protocol was approved by the Federal University of Mato Grosso do Sul State Animal Care and Use Committee.

During the experimental period, bulls were housed outside in a corral with access to mixed-grass hay and water. Ambient temperature was approximately 25°C during the study. Twenty-four hours before each experiment, each bull was moved into a stanchion stall and a routine clinical examination was performed to ensure that the bulls were healthy and not lame.

#### Epidural insertion of catheters
A permanent epidural catheter was used to reduce the risks associated with repeated injections. For placement of the catheter, each bull was restrained in a chute. The skin over the first intercoccgeal space (between the first and second coccgeal vertebrae) was identified by moving the tail ventrally and dorsally. The area then was aseptically prepared with povidone-iodine and infiltrated with 2% lidocaine hydrochloride. A small incision (approx 1.5 cm in length) was made in the skin and subcutaneous tissues at this site. A 16-gauge, 12-cm Tuohy needle was inserted between the first and second coccgeal vertebrae, and a 16-gauge, 3.25-inch nonstyletted multiple-port catheter (90 cm in length) was inserted via the Tuohy needle. Correct placement of the Tuohy needle was confirmed by use of saline (0.9% NaCl) solution via the hanging-drop method and by a lack of resistance during insertion of the multiple-port catheter. The multiple-port catheter was threaded cranially with negligible resistance for a distance of approximately 48 cm as determined by externally measuring the distance from the space between the first and second coccgeal vertebrae to the space between L2 and L3. Proper placement of the catheter was confirmed by injecting 3 mL of 1% lidocaine solution to induce bilateral analgesia. The catheter was affixed with cyanoacrylate glue and wrapped in gauze. The catheter remained in place for the remainder of the study (4 to 6 weeks). At the end of the experiments, the catheters were removed and examined for gross evidence of infection (ie, inflammatory exudate or fibrin) and proper placement (ie, the catheter was straight, and no signs of catheter loops within the epidural space were observed). During the week after placement of the epidural catheter, the bulls were trained to stand quietly in restraining stocks.

#### Experimental procedures
Each bull was moved into a restraining chute before the beginning of each experiment. Each bull received 3 treatments in random order; there was an interval of at least 1 week between successive treatments. Three doses of epidurally administered ketamine hydrochloride (0.3, 0.5, and 0.7 mg/kg, respectively) were selected on the basis of other studies in cattle. The doses were administered at a rate of 0.5 mL/s through the previously placed catheter. Completion of injection was designated as time 0. Mean volume administered was 2.1, 3.3, and 6.0 mL for the 0.3, 0.5, and 0.7 mg/kg doses, respectively. After administration of ketamine, catheters were flushed with 0.5 mL of saline solution.

Heart rate, DAP, MAP, SAP, respiratory rate, rectal temperature, skin temperature, analgesia, sedation, and ataxia were determined before administration (baseline [time 0]); 5, 10, 15, 30, 45, 60, 75, and 90 minutes after administration; and every 30 minutes thereafter until the end of analgesia. Time to onset, duration, and anatomic distribution of analgesia were recorded. All bulls were subjected to a standard noxious stimulus consisting of insertion of a 23-gauge, 1-inch needle into the skin and deep muscles of the dorsal and ventral flank region, caudal ribs, and ileum area on both sides of the body. Pressure from a hemostat clamp (closed to the first ratchet) was also applied in the same regions (Figure 1).

Skin temperature was used as a complementary test for failure or success of the dorsolumbar epidural blocks. Skin temperature was measured with a noncontact infrared thermometer at specific points in the skin innervated by thoracic, lumbar, or sciatic nerves. The hair was clipped from the 4 points (caudal ribs, dorsal flank, ventral flank, and ilium regions; Figure 2). Skin temperature was measured for 60 minutes after ketamine injection; care was taken to measure the temperature distant (20 to 30 cm) to subcutaneous veins.
All experiments were conducted in the morning, with a target temperature of approximately 25°C to minimize differences in ambient temperature among treatments. Change in skin temperature was measured as an index of the efficacy of sympathetic nerve blockade. Analgesia was assessed for all treatments at the aforementioned intervals after injection via insertion of a needle in the skin or deep muscles or application of pressure from a hemostat clamp in the flank and adjacent dermatomal regions. Analgesia was scored by use of the following scale: 1, normal response (strong reaction to a painful stimulus with repeated kicking); 2, mild analgesia (no response to insertion of needle in the skin; animal movement with no kicking but swishing of the tail and signs of restlessness); 3, analgesia (no response to insertion of needle in skin or deep muscle; no swishing of the tail but signs of restlessness and turning toward the site of the painful stimulus); and 4, complete analgesia (animal remained calm and indifferent to application of a painful stimulus). Panniculus response and muscle twitches alone were not considered a painful response to these stimuli. All bulls had a lack of analgesia (a strong positive response to a noxious stimulus) before ketamine administration.

Depth of sedation was rated as follows: 1, no sedative effect; 2, reduced alertness and drooping of the upper eyelids; and 3, drooping of the head against the shoulder and mild drowsiness. Bulls were evaluated during the experiments for ataxia by releasing them from the stanchion and assessing their ability to walk. Ataxia was graded as follows: 1, no change in limb position from baseline; 2, mild ataxia with slight stumbling but easily able to continue walking; 3, moderate ataxia with marked stumbling while walking; and 4, severe ataxia and falling.

Indirect arterial blood pressure was measured via a cardiac monitor by use of a noninvasive oscillometric device with the cuff (12 to 19 cm) placed over the coccygeal artery. Heart rate was measured as the number of beats per minute, and respiratory rate was the number of chest movements per minute. Rectal temperature was measured with a digital thermometer.

**Statistical analysis**—All data were analyzed by use of a general linear model with a commercial software package. Data were grouped and summarized as mean ± SD. Data for SAP, DAP, MAP, heart rate, respiratory rate, skin temperature, and rectal temperature were grouped and analyzed by use of a 2-way repeated-measures ANOVA, with treatment and time as independent variables. When a significant difference or interaction was obtained, the Dunnett test or planned comparison was applied as appropriate. For analgesia, sedation, and ataxia variables, the nonparametric Friedman test was used, followed by multiple comparisons for ranked data via the Dunnett test, with time 0 as the baseline. In each analysis, differences were considered significant at values of \( P < 0.05 \).

**Results**

During the study period, successful caudal placement of a dorsolumbar catheter was confirmed in all bulls. A test dose of 3.0 mL of 1% lidocaine solution was sufficient to determine the correct position in the dorsolumbar region. Insertion of the Tuohy needle in the space between the first and second coccygeal vertebrae was achieved on the first attempt in all bulls. All multiple-port catheters were threaded approximately 48 cm with negligible resistance via the Tuohy needle site. Difficulty in advancing the epidural catheter was encountered in 3 bulls after the catheter had been advanced 12 to 14 cm; in each of these 3 cases, the catheter was withdrawn and reinserted successfully to the target region.

Successful anesthesia of the lumbar region was confirmed via loss of sensation as measured by sensory testing with insertion of a needle into the skin and deep muscles and with application of pressure from a hemostat clamp in the same regions. An increase in skin temperature in the anesthetized regions was detected for the 0.3 and 0.5 mg/kg treatments but not for the 0.7 mg/kg treatment. Time until a detectable increase in skin temperature (≥ 1°C) after segmental dorsolumbar epidural analgesia was 10 to 15 minutes for the 0.3 and 0.5 mg/kg treatments. Temperature change for the
0.7 mg/kg treatment was minor and not significantly different among areas (Figure 3).

The main areas of analgesia for the 3 treatments were the dorsal and ventral aspects of the flanks on both sides. Complete analgesia (grade 4) was obtained for the 3 ketamine treatments at a mean ± SD of 8 ± 4 minutes after administration. Mean duration of analgesia differed significantly for the 0.3, 0.5, and 0.7 mg/kg treatments (35 ± 8 minutes, 50 ± 12 minutes, and 80 ± 18 minutes, respectively; Figure 4). The anesthetized areas obtained with the 3 ketamine doses extended from dermatonic regions T12 to T13 up to L6 to S1. The 0.5 and 0.7 mg/kg treatments caused mild sedation (grade 2) at 15 to 45 minutes; however, the 0.3 mg/kg treatment did not cause any degree of sedation. All doses of ketamine caused ataxia, which was greater in the 0.7 mg/kg treatment (duration of approx 70 minutes). For the 0.7 mg/kg treatment, the bulls had moderate ataxia (grade 3), compared with mild ataxia (grade 2; duration of approx 25 minutes) for the 0.3 and 0.5 mg/kg treatments (Figure 5). None of the ketamine doses caused severe ataxia or falling (grade 4).

Heart rate decreased significantly with epidural administration of 0.5 and 0.7 mg/kg, compared with the baseline values. Heart rate decreased significantly from 75 to 90 minutes after the 0.5 mg/kg treatment and 30 to 60 minutes after the 0.7 mg/kg treatment. Respiratory rate, DAP, SAP, and MAP did not change significantly from baseline values following administration of any of the 3 ketamine treatments. A significant decrease in rectal temperature was detected for the 0.3 and 0.5 mg/kg treatments beginning at 30 minutes and 45 minutes after administration, respectively; this decrease remained unchanged for up to 150 minutes for both doses (Table 1).
Figure 5—Median ataxic score after dorsolumbar epidural administration of the 3 doses of ketamine via the caudal approach in 6 bulls. Ataxia was scored as follows: 1, no change in limb position from baseline (time 0); 2, mild ataxia with slight stumbling but easily able to continue walking; 3, moderate ataxia with marked stumbling while walking; and 4, severe ataxia and falling. See Figure 3 for remainder of key.

Table 1—Mean ± SD values for cardiovascular variables, respiratory rate, and rectal temperature in 6 bulls receiving ketamine hydrochloride at each of 3 doses (0.3, 0.5, and 0.7 mg/kg) by use of dorsolumbar epidural administration via a caudal approach.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ketamine (mg/kg)</th>
<th>Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>0.7</td>
<td>11</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>0.5</td>
<td>114</td>
</tr>
<tr>
<td>DAP (mm Hg)</td>
<td>0.5</td>
<td>37</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>0.5</td>
<td>100</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>0.5</td>
<td>28</td>
</tr>
<tr>
<td>Rectal temperature</td>
<td>0.3</td>
<td>4.0</td>
</tr>
</tbody>
</table>

Time of ketamine administration was designated as time 0.

*Within a row, value differs significantly (P < 0.5) from the baseline value (time 0).

Discussion

Analysis of the results reported here revealed that ketamine administered epidurally by use of a nonsty-letted multiple-port catheter inserted via the caudal approach induced analgesia in the dorsal and ventral flank regions in conscious standing cattle. Use of a catheter for epidural administration to induce analgesia in standing cattle has several advantages, which include elimination of the use of sedatives and muscle relaxants, such as α-receptor agonist drugs, both of which may contribute to postoperative respiratory depression. We did not detect evidence of trauma in the small number of animals evaluated. In human infants, an epidural catheter may readily be passed from the caudal to the thoracic region to provide regional anesthesia for upper abdominal surgery. The lumbar curve develops in children during the first years after birth; after it develops, the ease of threading epidural catheters to the thoracic region decreases sharply. In our study, the catheters were easily threaded to the desired dermatomal region. In 3 bulls, we were able to insert the epidural catheter 12 to 14 cm but then had difficulty advancing the catheter farther. This problem likely involved the caudal equina because after overcoming this obstacle, the epidural catheter advanced with ease. If such resistance is not easily overcome, no attempt should be made to advance a catheter farther because the catheter may curl up or double back in the epidural space.

In cattle, the major advantage of this technique is that accessing the caudal epidural space is technically easier and less hazardous than accessing the lumbar or thoracic epidural space. Epidural anesthesia via the dorsolumbar space (L1-2) or a segmental subarachnoid epidural via T13-L1 carries the potential risk of trauma to the spinal cord from sudden movements of an animal or because the epidural space in this area of
cattle is narrow. A caudal epidural for analgesia of the dorsal aspect of the flank in cattle or calves, an epidural in the lumbosacral space (L6-S1), or a subarachnoid epidural in calves requires larger and potentially toxic volumes of drugs to block the sciatic nerve of animals positioned in sternal or lateral recumbency. On the basis of these facts, these techniques should be performed by only adequately trained veterinarians. These techniques likely have not attained the same degree of popularity as caudal epidural analgesia in cattle for this reason.

The 3 doses of ketamine used in this study induced dose-dependent analgesic effects in the flank region in cattle. All the doses of ketamine induced rapid onset but with different durations of analgesia. The highest dose of ketamine (0.7 mg/kg) induced a more prolonged analgesia but with moderate ataxia. These effects were probably attributable, in part, to systemic uptake of ketamine. In several studies, investigators have determined that epidural or subarachnoid administration of lidocaine at high doses and high concentrations induces temporary or irreversible lesions of the nervous tissues and hypotension that can be a serious complication in hypovolemic animals. Systemically, ketamine induces an increase in arterial blood pressure and stimulates sympathetic nerve activity. This stimulation of the sympathetic nervous system likely did not increase skin temperature at the highest dose of ketamine in the study reported here. Epidural administration of anesthetics induces local vasodilatation and increases local blood flow by sympathetic nerve block, with a consequent increase in skin temperature in the blockade regions. In addition, ketamine is considered a highly lipophilic drug that is absorbed quickly by fat and other tissues of the epidural space. Distillation of drugs in the epidural space is in a cranial direction; therefore, a small volume of ketamine is appropriate.

Doses of ketamine of 1.0 mg/kg in cattle cause analgesic effects that last for approximately 70 minutes, whereas a similar dose in humans causes postoperative analgesia that lasts for approximately 24 hours. This duration of analgesia in cattle is difficult to evaluate because of the subjective nature of the analysis. However, this result would be of interest for decreasing stress at the time of surgery. Superficial (ie, skin) and deep muscle stimulation with a needle and pressure from a hemostat clamp are widely accepted tests for confirming analgesia after epidural injections in cattle. In our study, these tests provided a semiquantitative measure of analgesia. We considered the tests to be appropriate, albeit incomplete, methods of assessing the analgesic action of ketamine. A more accurate test could include a voltage-based noxious stimulus, surgery, or a skin incision and would complement the results obtained in the present study.

In the study reported here, epidural administration of ketamine at 0.3 mg/kg yielded 35 minutes of analgesic effect, whereas doubling the dose to 0.7 mg/kg yielded 80 minutes of analgesia in the regions tested. Ketamine is a noncompetitive antagonist of NMDA receptors and interacts with opioids, monoaminergic and muscarinic receptors, and voltage-sensitive calcium channels in the spinal cord. Caudal epidural administration of ketamine at a dose of 0.5 mg/kg in cattle yields approximately 30 minutes of perineal analgesia. This difference is likely attributable to the site of deposition of the 3 doses of ketamine in our study. The dorsolumbar epidural space is narrower than the caudal epidural space. In addition, the multiple-port catheters used in the present study expel drugs into the epidural space from 3 lateral ports, which increases the anesthetized area. Factors that may influence the duration of action and the size of the area involved in epidurally administered drugs are position of the needle bevel or catheter tip, capacity of the epidural space, neural uptake, vascular or lymphatic absorption, and elimination of the drugs. Factors that are not under direct control of the anesthetist, such as advanced age of an animal, distention of epidural veins in female animals as a result of full-term pregnancy, and increased quantities of fat in obese animals could also influence epidural spread and duration of analgesia.

Dorsolumbar epidural injection of the low, intermediate, or high dose of ketamine in this study induced variable degrees of ataxia in terms of intensity and duration. These doses of ketamine induced a short period of ataxia, compared with the duration of the analgesic effect. Epidural injection of ketamine does not enable the drug to reach motor nerve fibers, but when the drug is administered in combination with adrenaline, the treatment causes blockade of motor nerves. In the study reported here, dorsolumbar epidural administration of ketamine induced mild or moderate ataxia, which suggested a possible action as a local anesthetic. Intermediate and high doses induced mild sedation of shorter duration (30 minutes). This effect may have been attributable to the low systemic absorption of ketamine from the epidural space, as has been reported in horses and goats. The systemic effects of ketamine administered via epidural injection have been described in horses, goats, and cattle. In these studies, the effects on the cardiovascular system and respiratory rate were minimal. In the study reported here, a short-term decrease in heart rate was associated with the intermediate and high ketamine doses; however, none of the treatments induced changes in arterial blood pressures. Epidural administration of ketamine in humans has resulted in conflicting reports with regard to adverse effects. A decrease in rectal temperature after administration of anesthetics has been reported in goats. In the present study, the low and intermediate doses of ketamine induced a long-lasting decrease in rectal temperature. A decrease in rectal temperature is common after epidural administration of anesthetics and is thought to result from redistribution of heat from central to peripheral regions of the body as well as radiation heat loss from the skin surface to the environment secondary to sympathetically induced vasodilatation.

Dorsolumbar epidural administration of ketamine through multiple-port catheters via the caudal approach in conscious standing cattle yielded analgesia in the flank regions with a dose-dependent duration of action. All doses of ketamine used in this study resulted in mild or moderate ataxia of a shorter duration than the period of analgesia. Changes in heart rate were within acceptable limits in these healthy bulls. Additional studies are
needed to determine whether this technique provides optimal conditions for surgery via the flank region in standing cattle.


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i. EMAI-RX-300, Transmait, Hospitalares Medical Equipments, São Paulo, Brazil.

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