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Original Research

Comparison of Analgesic Effects of Caudal Epidural 0.25% Bupivacaine with Bupivacaine Plus Morphine or Bupivacaine Plus Ketamine for Analgesia in Conscious Horses

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ABSTRACT

The aim of this study was to compare the effects of caudal epidural bupivacaine alone (BP), bupivacaine plus morphine (BPMP), and bupivacaine plus ketamine (BPKE) for perineal analgesia in horses. Each of the six saddle horses received a caudal epidural catheter and underwent 3 treatments: BP, 0.25% (0.04 mg/kg) bupivacaine hydrochloride without epinephrine; BPMP, 0.02 mg/kg of bupivacaine combined with 0.1 mg/kg of morphine-preservative free; and BPKE, 0.02 mg/kg of bupivacaine combined with 0.5 mg/kg of ketamine. The order of treatments was randomized. The cardiovascular system, respiratory rate, quality of analgesia, sedation, and motor blockade were assessed before drug administration (baseline), at 5, 10, 15, and 30 minutes, and every 30 minutes thereafter until loss of analgesia. The median time to onset of analgesia was 5 minutes after BP treatment, faster than after BPKE or BPMP treatments, which were 10 minutes and 15 minutes, respectively ($P < .05$). The BPMP treatment produced analgesia (315 minutes) for a longer duration than BP treatment (210 minutes) or BPKE treatment (240 minutes), in the regions of the tail, perineum, and upper hind limb in horses. All treatments presented mild sedation or motor blockade. There were minimal effects on the cardiovascular system and respiratory rate. BPMP may be preferable to a high dose of BP or BPKE. Caudal epidural BPMP can be an appropriate choice for regional perineal analgesia in horses.

1. Introduction

Epidural blockade with bupivacaine is one of the most common analgesic techniques for providing regional anesthesia in humans during surgery and analgesia during the postoperative period [1]. Postoperative analgesia in horses undergoing perineal surgery is often ignored because the animals rarely show signs of pain. However, these animals may exhibit poor appetite and depression that are detrimental to the well-being of the animal and its postoperative recovery.

Bupivacaine is an amidoamine local anesthetic of high potency, which has a long duration due to its high liposolubility [2]. Currently, clinical study results are controversial regarding the intensity and duration of sensory blockade caused by changing the volume and concentration of local anesthetic solutions. Although increasing the concentration of local anesthetics has been believed to improve the quality of an epidural blockade, clinical studies have shown inconsistent results [3,4]. Indeed, high drug concentrations reduce neuronal blood flow, causing ischemia [5]. Local anesthetic concentration is more important than dose of the development of neurotoxicity [6].

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A low concentration of bupivacaine (0.25%) decreases the duration of anesthesia but increases its efficiency and safety in epidural injections [7].

Various drugs may act as adjuvants when combined with local anesthetics to prolong the duration and efficiency of caudal epidural analgesia in horses. These drugs include opioid analgesics [8-11], ketamine [12,13], and α_2-adrenergic agonists [14]. Morphine, like other opioids, is absorbed into the cerebrospinal fluid and is believed to act on receptors in the substantia gelatinosa of the dorsal horn of the spinal cord [15]. Significantly better postoperative analgesic has been demonstrated with the combination of bupivacaine and morphine [7,16,17] as compared with either bupivacaine or morphine used alone in humans. Ketamine is an anesthetic drug capable of inducing perineal analgesia via *N*-methyl-D-aspartate (NMDA) receptors in the spinal cord. NMDA receptors are widely distributed throughout all levels of the neuraxis and are intimately associated with physiological processes relating to acute and chronic pain states [18]. There is evidence to suggest that ketamine binds stereospecifically to opioid receptors in the brain and spinal cord [19]. This study was designed to assess the analgesic efficacy, motor blockade, and systemic effects of caudal epidural administration of bupivacaine (BP) 0.25%, bupivacaine plus morphine (BPMP), or bupivacaine plus ketamine (BPKE) in horses.

2. Materials and Methods

The study and experimental design were approved by the Committee for Animal Experimentation of our institution. Six healthy saddle horses (four males and two females) weighing 330-470 kg (mean, 406 kg) and aged 8-16 years (mean, 12 years) were selected. All animals were maintained in stalls in the Faculty of Veterinary Medicine and Animal Science during the experimental period. Horses were provided water and hay ad libitum, and each animal underwent three treatments in a crossover study design: BP treatment was 0.25% (0.04 mg/kg) bupivacaine hydrochloride without epinephrine (Neocaína, Cristália Chemical and Pharmaceutical Products, Itapira, Brazil) (mean dose, 6.5 mL), BPMP treatment was 0.02 mg/kg of bupivacaine without epinephrine combined with 0.1 mg/kg of 1% morphine-preservative free (Dimorf, Cristália Chemical and Pharmaceutical Products) (mean dose, 7.3 mL), and BPKE treatment was 0.02 mg/kg of bupivacaine without epinephrine combined with 0.5 mg/kg of 5% ketamine (Ketamine, Cristália Chemical and Pharmaceutical Products) (mean dose, 7.3 mL).

Before the experiments began, all horses received a caudal epidural catheter placed at the Co_1-Co_2 coccygeal interspaces and advanced 8-12 cm cranially, with the tip of the catheter located approximately between S_2-S_3 (midsacrum level). The skin area over the first intercoccygeal (Co_1-Co_2) space was identified and aseptically prepared with povidone-iodine and infiltrated with 2% lidocaine (2 mL; Hipolabor Pharmaceutical Inc., Belo Horizonte, Brazil) at the entry point. The space was identified by moving the tail up and down while palpating the depression between the first and second coccygeal vertebra. A small incision (about 0.8 cm) was made in the skin and subcutaneous tissue of this region. A 16-G Tuohy needle (Perican, B Braun, São Gonzalo, Brazil) and a 16-G, unstyletted closed-tip catether with three lateral eyes (Portex Epidural Catheter; Smiths Medical ASD, Inc., Keene, NH) were used for caudal epidural catheterization and drug administration. Correct needle placement was confirmed by the hanging-drop method and noting no resistance during catheter insertion. A test dose of 1% lidocaine (4-5 mL) was used to confirm the location of the catheter. The catheter was cut to a total length of 30 cm and connected to a valve without filter (Fig. 1). The external part of the catheter was fixed with cyanoacrylate glue (Loctite; Super Bonder, Henke, Itapevi, Brazil) and wrapped in gauze. The catheter remained in place for the entire trial (4-6 weeks). At the end of the experiments, the catheters were withdrawn and checked for gross evidence of infection and proper insertion.

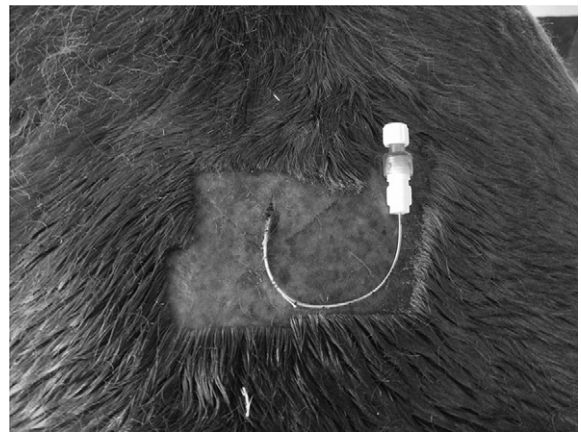

Fig. 1. A 16-G Tuohy needle and an unstyletted closed-tip 3 lateral eyes catheter were used for caudal epidural (Co_1-Co_2) catheterization and drug administration. The tip of a 90-cm, 16-G epidural catheter was inserted into the epidural Tuohy needle (8-12 cm). The catheter was cut to a total length of 30 cm and connected to a valve. The external part of the catheter was fixed with cyanoacrylate glue and wrapped in gauze.

During the week after catheter placement, the animals were trained to stand quietly in restraining stocks. Each horse randomly received three treatments with at least 1 week between treatments. The drugs were administered at a rate of 0.5 mL/s through the catheter. After drug administration, the catheters were filled with saline solution. To minimize the differences in ambient temperature between treatments, all experiments were conducted in the morning, with a target temperature of approximately 25°C.

Heart rate (HR), respiratory rate (RR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), rectal temperature (RT), analgesia, sedation, and motor blockade were determined before drug administration (baseline) and at 5, 10, 15, and 30 minutes, and every 30 minutes thereafter until a score <3 was achieved in a pain scoring system. Skin temperature (ST) was taken at these intervals up to 60 minutes and used as a complementary test for failure or success of the perineal epidural blockades. ST measurements were performed using a noncontact infrared thermometer (Minitemp; Raytek Corporation, Santa Cruz, CA) at marked points on the skin of the tail, perineum, or posterior upper hind