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Original Research

Evaluation of Nociception, Sedation, and Cardiorespiratory Effects of a Constant Rate Infusion of Xylazine Alone or in Combination with Lidocaine in Horses

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ABSTRACT

This study aimed to evaluate the effects of a constant rate infusion (CRI) of xylazine or xylazine in combination with lidocaine on nociception, sedation, and physiologic values in horses. Six horses were given intravenous (IV) administration of a loading dose (LD) of 0.55 mg/kg of xylazine followed by a CRI of 1.1 mg/kg/hr. The horses were randomly assigned to receive three treatments, on different occasions, administered 10 minutes after initiation of the xylazine CRI, as follows: control, physiologic saline; lidocaine low CRI (LLCRI), lidocaine (LD: 1.3 mg/kg, CRI: 0.025 mg/kg/min); and lidocaine high CRI (LHCRI), lidocaine (LD: 1.3 mg/kg, CRI: 0.05 mg/kg/min). A blinded observer assessed objective and subjective data for 50 minutes during the CRIs. In all treatments, heart and respiratory rates decreased, end-tidal carbon dioxide concentration increased, and moderate to intense sedation was observed, but no significant treatment effect was detected in these variables. Ataxia was significantly higher in LHCRI than in the control treatment at 20 minutes of infusion. Compared with baseline values, nociceptive threshold increased to as much as 79% in the control, 190% in LLCRI, and 158% in LHCRI. Nociceptive threshold was significantly higher in LLCRI (at 10 and 50 minutes) and in LHCRI (at 30 minutes) than in the control treatment. The combination of CRIs of lidocaine with xylazine produced greater increases in nociceptive threshold compared with xylazine alone. The effects of xylazine on sedation and cardiorespiratory variables were not enhanced by the coadministration of lidocaine. The potential to increase ataxia may contraindicate the clinical use of LHCRI, in combination with xylazine, in standing horses.

1. Introduction

Several complications, such as hypotension, hypoxemia, myositis, and nerve paralysis, may arise in horses as a result of the effects of general anesthetics on the cardiovascular and respiratory system and also because of recumbency and positioning [1]. To avoid such complications, many surgical and diagnostic procedures can be performed in the standing horse under sedation and local anesthesia [2].

The α_2-adrenoceptor agonists comprise the class of drugs most frequently used to facilitate standing medical procedures in horses. This class of drugs is known to produce sedation, analgesia, and muscle relaxation [2]. However, monotherapy with α_2-adrenoceptor agonists may result in insufficient analgesia for some surgical procedures; in such circumstances, the α_2-adrenoceptor

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agonists are administered in combination with opioids or local anesthetics to improve analgesia. Systemic administration of opioids was shown to produce short-term antinociception in horses [3], but its use was associated with decreased gastrointestinal motility [4]. Although administration of opioids has also been shown to cause excitement and increased locomotor activity in horses [3], there is evidence that these effects can be prevented if these drugs are administered in combination with sedatives such as α_2-adrenoceptor agonists [5].

Lidocaine has been used as a constant rate infusion (CRI), with the aim to provide intraoperative analgesia during surgery [6-8] and to reduce the requirement of inhalational anesthetics for maintenance of anesthesia in horses [6,9]. Administration of lidocaine CRI has also been reported in conscious horses and was associated with thermal antinociception [10]. To the authors' knowledge, the use of lidocaine CRI in combination with α_2-adrenoceptor agonists has not been reported in conscious horses.

The study reported here aimed to evaluate the effects of CRIs of xylazine alone or in combination with lidocaine on nociception, sedation, and physiologic values in standing horses. We hypothesized that the combination of xylazine with lidocaine would result in greater antinociception than xylazine alone.

2. Materials and Methods

2.1. Animals

The study was approved by the Institutional Animal Care and Use Committee (protocol 103/2010). Five mixed breed mares and one stallion (Mangalarga Marchador), weighing 307 ± 49 kg (mean $\pm$ SD), were used in this study. Horses were judged to be in good health on the basis of results of physical examination, complete blood count (CBC), and serum biochemistry analyses. Horses with preexisting lameness were excluded from the study. Food, but not water, was withheld from horses for 12 hours before each experiment.

2.2. Instrumentation

During the study, the horses were restrained in stocks by a loose lead rope attached to their halter. Horses were instrumented with a 14-gauge jugular venous catheter for subsequent drug administration. The catheter was connected to a three-way stopcock and was secured in place with suture. The horses were allowed to acclimate for 30 minutes before each experiment was started. Thereafter, heart rate (HR), respiratory rate (f_R), end-tidal carbon dioxide concentration ($ETCO_2$), head height, and nociceptive threshold were determined for use as baseline values. HR was measured by auscultation with a stethoscope, whereas f_R and $ETCO_2$ were monitored by a side-stream capnograph (M2000, J.G. Moriya, São Paulo, Brazil) whose sampling tube was positioned inside the horse's nostrils. Head height was considered the distance from the ground to the lowest point of the lower lip and was determined using a tape measure attached to the stocks. Degree of sedation was assessed by using a subjective scale ranging from 0 to 3, with 0: no sedation; 1: mild sedation with head only slightly lowered; 2: moderate sedation with the head lowered below the manubrium but with the horse responsive to an audible stimulus (by clapping hands behind the animal); and 3: intense sedation with the head lowered below the manubrium and no response to an audible stimulus. Degree of ataxia was also evaluated by using a subjective scale with 0: no ataxia; 1: the horse was stable but slightly swaying; 2: the horse was swaying and leaning against the stock; and 3: the horse was leaning against the stock and swaying with its hind limbs crossed and its forelimbs buckling at the carpal joints.

To evaluate nociceptive threshold, an electrical stimulus (50 Hz and 0.3 ms) was applied to the horse by the use of two electrodes connected to a transcutaneous electrical nerve stimulation (TENS) device (Physiotonus Four, Bioset, Rio Claro, São Paulo, Brazil). Electrodes were placed on the clipped skin over the lateral palmar nerve of the right forelimb after previous local application of conductive gel. The positive electrode was placed on the abaxial surface of the right proximal sesamoid, and the negative electrode was placed 3 cm proximal to the positive electrode. Electrodes were kept in place by an adhesive wrap around the limb. During testing, the electrical current was gradually increased until a clear avoidance response (lifting of the leg) was apparent. At that moment, the stimulus was stopped, and the corresponding intensity of the stimulus provided by the TENS device was recorded. At least two measurements of nociceptive threshold were obtained at each time point. If a different value was obtained during the first and second measurements, a third measurement was obtained, and all values were averaged for the analysis.

Although the TENS unit allows the gradual increase of the electrical stimulus, the display of the device provides arbitrary units and not the output current. To determine the current intensity delivered in each level, the electrodes of the TENS unit were connected to a two-channel digital storage oscilloscope (DS5062MA, Rigol, Oakwood Village, OH). The level of stimulus was progressively increased, and the corresponding current intensity (in mA) registered by the oscilloscope was recorded. Four sets of measurements were performed, and percentage variations among the four measurements, obtained for each level of stimulus, were calculated. These procedures did not use animals and were performed after all the experiments with horses were concluded. Values of nociceptive threshold determined in the horses (in arbitrary units), before (baseline) and after administration of each of the three treatments, were converted to the corresponding current intensity (in mA) determined with the oscilloscope.

2.3. Study Design and Treatments

The study was designed as a randomized, placebo-controlled, and blinded crossover study. Horses received a loading dose (LD) of xylazine (0.55 mg/kg, IV; Sedazine, Fortdodge, Campinas, São Paulo, Brazil), administered over 1 minute, followed by a CRI of xylazine (1.1 mg/kg/hr) using a syringe pump (ST 670, Samtronic, São Paulo, Brazil). Ten minutes after the beginning of the xylazine CRI, each horse was randomly assigned to receive one of three treatments IV as an LD (administered over 5 minutes), followed by a CRI: control treatment, physiologic saline (LD: 0.125 mL/kg, CRI 1 mL/kg/hr); lidocaine low CRI (LLCRI), lidocaine (LD: 1.3