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Original Research

Epidural Lidocaine, Nalbuphine, and Lidocaine–Nalbuphine Combination in Donkeys

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ABSTRACT

Nalbuphine is a lipophilic semisynthetic κ-agonist/μ-antagonist opioid that has been used for epidural anesthesia in humans and dogs but not in donkeys. The purpose of the present study was to report the effect of epidural nalbuphine either alone or in combination with lidocaine compared with lidocaine alone. Six adult clinically healthy Baladi Egyptian donkeys were used. All donkeys were allocated into one of the three groups with a 2-week washout period using a Latin Square design. Group 1 injected with lidocaine hydrochloride 2% at a dose of 0.22 mg/kg. Group 2 injected with nalbuphine hydrochloride 2% at a dose of 0.4 mg/kg, and Group 3 injected with a combination of lidocaine hydrochloride 2% at a dose of 0.11 mg/kg and nalbuphine hydrochloride at a dose of 0.2 mg/kg. Epidural nalbuphine alone resulted in analgesia of significant ($P < .05$) long duration (198.3 ± 12.6 minutes) but of significant ($P < .05$) slow onset (14.3 ± 1.8 minutes). The combination of lidocaine–nalbuphine resulted in rapid onset (6.7 ± 1.2 minutes) and prolonged duration (147 ± 5.6 minutes) of analgesia. Rapid and intense analgesia was produced with lidocaine–nalbuphine combination when compared with lidocaine or nalbuphine alone. Mild ataxia was reported only in lidocaine and lidocaine–nalbuphine groups. Mild sedation was achieved after administration of nalbuphine groups either alone or in combination with lidocaine. The obtained results suggest that lidocaine–nalbuphine combination could be used efficiently for performing surgical interventions required long duration and effective analgesia.

1. Introduction

Epidural anesthesia is a regional anesthetic technique commonly performed in equine practice to allow diagnostic, obstetrical, and surgical interventions. The technique provides analgesia to the perineal, sacral, lumbar, and caudal parts of the thoracic region. Caudal epidural anesthesia has been used to provide perioperative analgesia to the anus, rectum, perineum, vulva, urethra, and bladder [1]. The most common indications for epidural anesthesia in the donkey include rectal and vaginal prolapse and treatment of tail or perineal melanomas [2].

Lidocaine is the most frequently local anesthetic drug used for epidural anesthesia although mepivacaine, bupivacaine, and procaine may be used [3]. With the exception of bupivacaine, these agents provide anesthesia of short duration that requires readministration of the agent for completion of the surgical procedures [3,4]. Local anesthetic agents indiscriminately block sensory, sympathetic, and motor fibers. Blocking of motor fibers causes ataxia, hind limb weakness, and occasionally recumbency, whereas blocking of sympathetic fibers causes vasodilation by inhibition of action potentials through sodium channels blockade [4,5].

Various drugs have been used for prolongation of action of local anesthetics for surgical procedures that required

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long duration of analgesia. These drugs may include opioids, alpha-2 adrenergic agonist, and ketamine that selectively block sensory fiber providing sufficient analgesia without effect on hind limb function [6–8]. Supraadditive antinociceptive action has been reported by combining local anesthetic and opioids when given epidurally [9,10]. Nalbuphine is a lipophilic semisynthetic opioid chemically related to both oxymorphone (pure opioid agonist) and naloxone (pure opioid antagonist). It has relatively potent μ-antagonist and κ-agonist activity. The μ-antagonist property of nalbuphine allowed production of fewer μ-mediated side effects such as respiratory depression, pruritus, and vomiting [11,12].

Nalbuphine has been used for epidural analgesia in humans [13–15] and dogs [12,16]. To the authors' knowledge, nalbuphine epidural analgesia in donkeys has not been reported yet. The purpose of the present study was to study the analgesic effect of epidural nalbuphine in donkeys either alone or in combination with lidocaine compared with lidocaine alone.

2. Materials and Methods

2.1. Animals

The present study was carried out on six adult clinically healthy Baladi Egyptian donkeys (three males and three females) aged between 2 and 6 years old (mean 3.8 ± 1.3 years) and weighing 150–220 kg (mean 189 ± 23 kg). Before enrollment in the study, all donkeys underwent complete physical and hematological examinations to exclude the evidence of systemic disease. All study procedures were done in accordance to the Institutional Animal Care and Use Committee of Faculty of Veterinary Medicine, Cairo University.

2.2. Study Design

Each donkey was allocated into one of the three groups with a 2-week washout period using a Latin Square design.

Group 1 injected with lidocaine hydrochloride 2% (Xylocaine AstraZeneca LP, Wilmington) at a dose of 0.22 mg/kg.

Group 2 injected with nalbuphine hydrochloride 2% (Nalbuphine Amoun pharmaceutical Co, Egypt) at a dose of 0.4 mg/kg.

Group 3 injected with a combination of lidocaine hydrochloride 2% at a dose of 0.11 mg/kg and nalbuphine hydrochloride at a dose of 0.2 mg/kg.

In all groups, the total volume of the injected solution was equalized to 5 mL by adding distilled water. Before each injection, food but not water was withheld for 12 hours. The area above the first intercoccygeal space was aseptically prepared. An 18-G spinal needle was inserted into the epidural space between the first and second coccygeal vertebrae with the bevel pointed forward. Then, injection was done during standing, and proper placement of the needle was ensured by loss of resistance and by ease of injection. Injected drugs were administered slowly into the epidural space more than approximately 30 seconds by the same investigator (F.A.T.).

2.3. Animal Evaluation

Analgesia, sedation, and motor effects were assessed by the same observer (E.A.H) who was blind to the given injection. The onset, duration, and anatomic distribution of analgesia were recorded for all groups. Analgesia was defined as lack of response to pin prick and pressure from hemostat clamp applied from the perineal region and moved cranially toward the thoracic region till response was observed. The analgesia was assessed each minute after the injection of drug(s) till the onset of analgesia was recorded and scored. The time from the onset of analgesia to the time of reappearance of response to painful stimulation was recorded as the duration of analgesia.

Evaluations of analgesic, motor, and sedative effects were done at 15-minute interval till a response to painful stimulation reoccurred. The degree of analgesia was recorded according to the antinociceptive score where 1, normal response to both skin prick and hemostat clamp; 2, mild analgesia (depressed reaction to skin prick or hemostat clamp); 3, moderate analgesia (no response to superficial skin pricks and hemostat clamp); and 4, complete analgesia (no response to deep muscle pricks). Motor effects from epidural injection of the drug(s) were evaluated through testing the presence of ataxia by allowing the donkey to walk for 10 steps and observing the gait [17] at the same interval, and the motor effect was scored as score 1, no change in limb position from baseline; 2, mild ataxia (slight stumbling but able to continue walking); 3, moderate ataxia (marked stumbling, walking but very ataxic); and 4, severe ataxia (falling). Flaccidity of tail, loss of anal reflex, and relaxation of female vulva were also reported during evaluation of motor response. Sedative effect was assessed based on the position of the head and neck, eye lid, and muzzle. Sedation was scored as score 1, no sedative effect; 2, slight drop of head with drooping of the upper eyelid; and 3, drooping of the muzzle.

Vital parameters including heart rate, respiratory rate, and rectal temperature were recorded at baseline (time 0) and at 15-minute interval after injection till the end of the study.

2.4. Statistical Analysis

Data were expressed as mean ± standard deviation. Kolmogorov–Smirnov test was used to assure the normality of distribution of the obtained data. A one-way analysis of variance followed by Duncan test (post hoc test) was used to compare means for the heart rate, respiratory rate, and rectal temperature. The analgesia, sedation, and motor scores were analyzed using Mann–Whitney *U*-test. Data were analyzed using SPSS software 21 (IMP SPSS Inc, Chicago, IL). Differences were considered statistically significant if the P value $<.05$.

3. Results

Epidural injection of lidocaine, nalbuphine, and lidocaine–nalbuphine combination was simple, convenient, and well tolerated by all donkeys. No precipitation was observed when lidocaine and nalbuphine were mixed into one solution.