Journal of Equine Veterinary Science 48 (2017) 82–85

Contents lists available at ScienceDirect

Journal of Equine Veterinary Science

journal homepage: www.j-evs.com

Short Communication

Preemptive Analgesia, Including Morphine, Does Not Affect Recovery Quality and Times in Either Pain-Free Horses or Horses Undergoing Orchiectomy

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ARTICLE INFO

Article history:
Received 11 November 2015
Received in revised form 18 March 2016
Accepted 22 March 2016
Available online 6 April 2016

Keywords:
Anesthesia recovery period
Equine
Opioid
Preemptive analgesia

ABSTRACT

Recovery quality and times from general anesthesia in horses may be influenced by surgery, analgesia with morphine or combinations of both. Twenty-three adult healthy horses were enrolled in this prospective experimental trial in a clinical setting and were randomly allocated to one of the following groups: anesthesia only (GA; n = 6), preemptive analgesia and anesthesia (GAA; n = 5), anesthesia and castration (GC; n = 6), or preemptive analgesia, anesthesia, castration, and intraoperative local analgesia (GCA; n = 6). All horses were sedated with intramuscular (IM) xylazine (0.5 mg/kg). Anesthesia was induced with intravenous (IV) guaifenesin (100 mg/kg) and thiopental (5 mg/kg) and maintained with isoflurane in oxygen. Animals in groups with preemptive analgesia received IM morphine (0.2 mg/kg) and dipyrone (10 mg/kg) and IV flunixin meglumine (1.0 mg/kg) immediately before sedation. Recoveries from general anesthesia were rope-assisted. Recovery scores (from 8 [excellent recovery] to 70 [worst recovery]) and times were compared between groups, using a one-way analysis of variance followed by a Tukey's test ($P < .05$). Mean ± standard deviation (SD) and range recovery scores were 22 ± 14 (8–45), 9 ± 2 (8–12), 14 ± 5 (8–22), and 12 ± 1 (10–13) in groups GA, GAA, GC, and GCA, respectively. Mean ± SD times to stand in minutes were 21 ± 10, 18 ± 7, 33 ± 12, and 35 ± 21 in groups GA, GAA, GC and GCA, respectively. No statistically significant differences were found for any of the variables. Neither preoperative administration of analgesics, including morphine, nor castration interfered with the recovery qualities and times in horses undergoing general anesthesia. Preemptive morphine did not worsen anesthetic recovery quality in horses.

Ethical considerations: The authors certify that legal and ethical requirements have been met with regard to the humane treatment of animals described in the study and specifying the Faculty of Veterinary Medicine and Zootecnia (FMVZ), Univ Estadual Paulista (UNESP), Botucatu, São Paulo, Brazil Animal Care and Use Committee that has overseen this process (protocol number 186/2009).

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http://dx.doi.org/10.1016/j.jevs.2016.03.015

1. Introduction

Recovery is the most critical phase of general anesthesia in horses. One third of the most common causes of death occur during this period, accounting for 25.6% of long-bone fractures and 7% of myopathies [1]. A good intraoperative analgesic plan in horses undergoing surgical procedures is mandatory to avoid pain in the postanesthetic period [2,3]. Pain may lead to early attempts to stand, ataxia, and incoordination, with inappropriate muscular strength, influencing the recovery negatively [4].

When using opioids in the perianesthetic period, one should consider that the excitatory effects of these drugs may prevail over their analgesic effects especially in pain-free horses [5]. Moreover, their impact on recovery quality remains controversial. Good recoveries followed morphine intravenous (IV) boluses (0.1–0.2 mg/kg) [3,6] and constant rate infusions (0.1–0.2 mg/kg/h) [7,8]. Other studies reported bad recoveries with box-walking behavior [9,10], this being suggested to be due to the typical central nervous system (CNS) excitatory effects related to higher doses of opioids in horses.

The aim of this study was to evaluate whether recovery quality and times in horses are influenced by surgery, preemptive analgesia with morphine, or a combination of both. Our hypothesis was that horses anaesthetized only (no surgery) and those undergoing surgery and receiving preemptive analgesia would recover better than those that did not receive morphine and than those undergoing surgery with no preemptive analgesia.

2. Material and Methods

The study was approved by the Institutional Animal Scientific Use Ethical Committee (CEUA 186/2009). Written owner consent was obtained from the horses undergoing surgery. Horses that were only anaesthetized were property of the institution.

2.1. Animals and Instrumentation

Twenty-three adult horses were classified healthy after clinical and laboratory assessment and were assigned American Society of Anesthesiologists (ASA) class I. There were mainly two types of horses included in this study. Those client-owned horses undergoing surgery were randomly allocated to group GC, anesthesia and castration ($n = 6$) or to group GCA, preemptive analgesia with morphine (Dimorf, Cristália, Lindóia, São Paulo, Brazil), dipyrone (Finador, Ourofino, Cravinhos, São Paulo, Brazil) and flunixin meglumine (Desflan, Ourofino, Cravinhos, São Paulo, Brazil) before anesthesia and castration ($n = 6$). Those property of the institution included only to undergo general anesthesia were randomly allocated to group GA; anesthesia only ($n = 6$) or to group GAA, preemptive analgesia with morphine, flunixin meglumine, and dipyrone before anesthesia ($n = 5$). Randomization in each type of horse (undergoing surgery or not) was performed by means of a computer program (Excel, Microsoft). Group GA included four geldings and two mares aged 9 ± 3 years and weighing 332 ± 48 kg, GAA included three geldings and two mares aged 10 ± 5 years and weighing 369 ± 68 kg, GC included six male horses aged 4 ± 2 years and weighing 319 ± 48 kg, and GCA included six male horses aged 4 ± 2 years and weighing 302 ± 27 kg. Anesthesia and the surgical procedures were performed by the same anesthetist and surgeon.

All the horses were sedated with xylazine (0.5 mg/kg; Sedomin; Konig, Buenos Aires, Argentina) by intramuscular (IM) injection. An IV catheter (14G, B. Braun, Melsungen, Germany) was placed in a jugular vein, and anesthesia was induced 5 minutes after sedation by IV administration of guaifenesin (100 mg/kg; Eter Gliceril Guaicol, L.P.S. Agrofarma, Mogi Mirim, São Paulo, Brazil) and thiopental (5.0 mg/kg; Thiopentax, Cristália, Lindóia, São Paulo, Brazil), administered separately. After tracheal intubation, the horses were hoisted onto a surgical table covered with soft foam rubber pillows and positioned in dorsal recumbency. The endotracheal tube was connected to a large animal anesthetic circle system, with an out-of-circle vaporizer and a large animal ventilator (Mallard Medical Skypark Drive Redding, CA). Anesthesia was maintained with isoflurane (Isoforine, Cristália, Lindóia, São Paulo, Brazil) in oxygen (O_2), and intermittent positive pressure ventilation was applied. Tidal volume was set at 15 mL/kg with a peak inspiratory pressure of 20 to 30 cm H_2O to maintain normocapnia, which was considered as end-tidal carbon dioxide ($EtCO_2$) values between 4.66 and 6.00 kPa (35–45 mm Hg). The isoflurane vaporizer setting was adjusted by the anesthetist (who was unaware if the animal had received analgesia) to maintain an adequate plane of anesthetic depth, with palpebral reflex diminished but not abolished.

Monitoring included heart rate, peripheral arterial hemoglobin saturation by pulse oximetry, inspired and end-tidal partial pressures of inspired and end-tidal expiratory CO_2, O_2, and inspired and end-tidal isoflurane concentrations (Monitor Cardiocap 5, Datex Ohmeda, Helsinki, Finland). The facial artery was catheterized (20 G, Introcan Safety, B Braun, Melsungen, Germany) for measurement of systolic arterial pressure, diastolic arterial pressure, and mean arterial pressure (MAP). The pressure transducer (TruWaveTM, Edwards Lifesciences, Haina, San Cristobal, Dominican Republic), which was previously calibrated against a mercury column, was zeroed to atmospheric pressure and positioned at the level of the right atrium. When MAP decreased to < 60 mm Hg, dobutamine (Dobutamina, Biosintética Farmacêutica Ltd, São Paulo, Brazil) was administered intravenously as required with a maximal dose of 5 μg/kg/min.

Horses receiving preemptive analgesia, those in GAA and GCA groups were administered morphine (0.2 mg/kg) and dipyrone (10 mg/kg) IM and flunixin meglumine (1.1 mg/kg) IV immediately before the administration of xylazine. Horses in GCA were administered intraoperatively 2% lidocaine (Lidocaina, Cristália, Lindóia, São Paulo, Brazil) with adrenaline (10 mL) into each spermatic cord before surgery.

2.2. Recovery from Anesthesia

Horses were recovered in a padded recovery box with the lights on, without O_2, and assisted with head and tail ropes when the horses attempted to stand up. Horses remaining more than 30 minutes in lateral recumbency received an auditory stimulus. Quality of recovery from general anesthesia was evaluated as described by Donaldson et al [11], based on attitude, activity in recumbency, move to sternal and stand position, number of attempts to sternal and stand position, sternal phase, strength, coordination, and knuckling. The lowest possible score was 8 (excellent recovery), and the highest was 70 (worst possible recovery). At the end of the surgical procedure, weaning of controlled ventilation was performed by gradual reduction of the respiratory frequency. When two breaths were observed with a tidal volume about 10 mL/kg, the vaporizer was turned off, and the horses were disconnected from the anesthetic machine. The same anesthetist who performed the anesthetic procedures evaluated scores for all the recoveries and recorded recovery times. These included times to first head movement and to achieve sternal recumbency and standing position from disconnection of the anesthetic machine. The numbers of attempts to sternal and to stand were also noted. Horses in GC received the same analgesic protocol after standing, but no medication was administered for recovery.

2.3. Statistical Analysis

Data were tested for normality of distribution by the Kolmogorov–Smirnov test. Recovery scores and times were compared between groups, using a one-way analysis of variance and followed by a Tukey's test. For all analyses, the significance level was set as 5%.

3. Results

Recovery scores and times are summarized in Table 1. No statistically significant differences were found for any of the variables evaluated.

Times of general anesthesia and surgery for all animals were about 47 ± 4 minutes. All animals received dobutamine, except one in GC and other in GCA; no significant differences in the dobutamine administration were observed between groups. No adverse effects, such as excitation or increased locomotor activity were seen in the postoperative period in any of the horses.

The power analysis of recovery scores was 96%, calculated with five animals and the largest difference between two means and the means of all the standard deviations.

Table 1
Recovery scores, attempts to stand, and times to move the head, to sternal recumbency and to standing for 23 horses after administration of general isoflurane anesthesia.

Group	Scores	Number of attempts to stand	Time to head movement (min)	Time to sternal recumbency (min)	Time to standing (min)
GA	22 ± 14 (8–45)	3.3 ± 2.5	13 ± 5	14 ± 4	21 ± 10
GAA	9 ± 2 (8–12)	2.0 ± 1.0	10 ± 2	12 ± 4	18 ± 7
GC	14 ± 5 (8–22)	2.8 ± 1.5	20 ± 5	25 ± 5	33 ± 12
GCA	12 ± 1 (10–13)	2.0 ± 0.8	23 ± 19	22 ± 19	35 ± 21

Data are presented as mean ± standard deviation (range). The horses were randomly allocated to group anesthesia only (GA; n = 6), preemptive analgesia and anesthesia (GAA; n = 5), anesthesia and castration (GC; n = 6) or preemptive analgesia, and anesthesia, castration, and intraoperative local analgesia (GCA; n = 6).

4. Discussion

In our clinical model of pain, administration of preemptive analgesia, including morphine, flunixin, and dipyrone did not affect the quality and times of anesthetic recovery in horses undergoing castration.

To the authors' knowledge, there are no studies comparing the recovery scores and times in individuals undergoing surgery or pain-free horses, receiving morphine or not. Theoretically, in horses receiving morphine, CNS excitatory effects may predominate in pain-free individuals [5], and recoveries from general anesthesia may be shorter and worse than in those undergoing surgery under clinical circumstances. However, this is not what we saw in our results. Recovery scores in our group anaesthesia only (GA) were comparable to those reported by Donaldson et al [11] after isoflurane anaesthesia. The inclusion of the GAA group (horses anesthetized receiving preoperative analgesia) aimed to observe the possible effects of analgesics, if any, in recovery animals without painful stimuli. Although receiving other analgesics, we can say that the administration of morphine in pain-free horses did not worsen the recovery qualities.

This absence of differences between treatments GA and GAA may be justified mainly by two reasons. First, the low dose of morphine used, especially by the IM route. Under clinical circumstances, doses of opioids are normally administered via IV, with analgesic purposes in combination with alpha$_2$-agonists, producing a synergistic antinociceptive effect [12]. Administration via IM may reduce this synergistic effect. Second, the use of xylazine via IM may have prolonged its use until the recovery period, masking potential differences in recoveries between groups.

Horses castrated with preoperative analgesia (GCA) were likely to feel real pain and probably the analgesic effects of the morphine prevailed over its potential excitatory effects. These results are comparable with those reported by Mircica et al [6] in 84 clinically healthy horses, where after IV preoperative boluses of morphine (0.1 and 0.17 mg/kg), recovery qualities were better, but the differences between horses receiving morphine and those not receiving morphine were not statistically significant. Similar recovery scores were obtained in horses undergoing surgery without preoperative analgesia (GC).

Nevertheless, our work is not free of limitations. First, the small number of horses was not an apparent limitation as the power of the test was strong. Nonetheless, with our study design, it is difficult to draw conclusions with regard to the influence of only morphine in the recovery period. Second, the administration of other analgesics in the groups receiving preoperative analgesia and lidocaine and undergoing castration may have influenced our results. However, the use of nonsteroidal anti-inflammatory drugs and local anesthesia is a current protocol under clinical circumstances. Finally, the evaluation of the recovery qualities was not as reported in previous studies. Although the recovery scoring was based on the study by Donaldson et al [11], two facts may have influenced the final scores, including the use of a rope-assisted technique and the auditory stimulus received after 30 minutes of lateral recumbency.

Furthermore, it may be argued that a marked difference of age was present between groups, influencing recovery qualities. However, the range of age included all adult, healthy, and ASA I–classified horses. In a recent retrospective study, Dugdale et al [13] reported that recovery quality, although influenced by age, was highly associated with ASA status. Finally, the individual behavior of each horse should also be considered.

In conclusion, preemptive administration of morphine, dipyrone, and flunixin before induction of anesthesia did not apparently influence recovery qualities and times from general anesthesia in isoflurane-anesthetized horses, either after castration or in pain-free individuals.

Acknowledgment

The authors did not declare any conflict of interest.

This work was supported by the São Paulo Research Foundation (FAPESP) for financial support (processes 2010/00786-6 and 2010/08967-0).

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