Research in Veterinary Science 91 (2011) 434–438

Contents lists available at ScienceDirect

Research in Veterinary Science

journal homepage: www.elsevier.com/locate/rvsc

Comparison of lidocaine, tramadol, and lidocaine–tramadol for epidural analgesia in lambs

S. Habibian [a], A.S. Bigham [b,*], E. Aali [c]

[a] Department of Basic Science, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran
[b] Department of Veterinary Surgery and Radiology, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran
[c] Department of Pharmacology, Iran Medical University, Tehran, Iran

ARTICLE INFO

Article history:
Received 16 October 2009
Accepted 27 September 2010

Keywords:
Tramadol
Lidocaine
Lamb
Epidural analgesia

ABSTRACT

Epidural anesthesia is commonly utilized in veterinary medicine to allow diagnostic, obstetrical, and surgical intervention, in the perineal region of domestic animal. The following study was carried out to directly compare the time of onset and duration of anesthesia produced by a tramadol and lidocaine–tramadol combination with that produced by lidocaine administration in the epidural space of lamb. Seven healthy female lambs of undefined breed weighing 15–20 kg were selected for this study. Epidural anesthesia was produced in all lambs by 2% lidocaine and with 2 weeks intervals repeated by combination of lidocaine–tramadol and tramadol alone. Analgesia was defined as lack of a response to pin prick test and pressure from hemostat clamp (closed to the first ratchet) applied first in the perineal area and then moved cranially toward the thoracic region until a response (movement associated with pin prick test or hemostat pressure) was observed. Time to onset, duration and cranial spread of analgesia were recorded. Heart rate (HR), respiratory rate (RR), and rectal temperature were recorded before (baseline, 0) and at 15, 30, 45, 60, 75, 90, 105 and 120 min after epidural administration of the solution. The results were expressed as mean ± SD and were analyzed by a one-way analysis of variance and Duncan's test as a post hoc for heart rate, respiratory rate and body temperature and also, for time of onset and duration of analgesia. Graphpad Prism version 5 software program was used for all analyses. A value of $P < 0.05$ was considered significant. The tramadol produced a significant ($P < 0.05$) longer duration of analgesia than lidocaine alone and lidocaine–tramadol combination. Also, lidocaine–tramadol combination produced a significant ($P < 0.05$) longer duration of analgesia than lidocaine alone. Complete analgesia began more delayed in the tramadol treatment than lidocaine–tramadol and lidocaine alone. The combination of lidocaine–tramadol produced analgesia of longer duration than lidocaine and onset time was approximately same as lidocaine group.

1. Introduction

Ruminants generally are not considered good subjects for general anesthesia mainly because of hazards of regurgitation and inhalation of ruminal contents or saliva into the lung if the airway is left unprotected (Trim, 1981; Hall et al., 2001). Thus, regional anesthesia produced by the perineural or epidural injections of anaesthetic agents is often employed in these species. Epidural anesthesia is one of the regional anesthetic techniques indicated for surgical procedures caudal to the diaphragm. In comparison to line infiltration and paravertebral nerve blocks, epidural anesthesia is preferable as it uses low doses of anesthetic, is more versatile, and there are few limitations associated with its use (Cruz, 1992). The technique is popular in both small and large animals (Elmore, 1980; Skarda, 1991). The most frequently used epidural anaesthetic is lidocaine; although mepivacaine, bupivacaine, and procaine are used (Day and Skarda, 1991). With the exception of bupivacaine, these agents provide anesthesia of relatively short duration and may necessitate re-administration of the agent to allow completion of the procedure. In addition, local anesthetic agents indiscriminately block motor, sensory, sympathetic fibers (Day and Skarda, 1991) that cause vasodilation (due mainly to the inhibition of action potentials via sodium channel blocking in vasoconstrictor sympathetic nerves) (Newton et al., 2007), ataxia, hind limb weakness, and occasionally recumbency. Epidural and intrathecal administration of agents with greater duration of action may be more appropriate for procedures requiring long duration anesthesia. These agents include opioids and α-2 adrenergic agonists induce analgesia by highly selective actions on spinal receptors thereby providing significant anesthesia with decreased likelihood of rear limb dysfunction (Luttinger et al., 1985; Eisenach et al., 1996; Natalini and Robinson, 2000). Tramadol, a synthetic racemic mixture of the 4-phenyl-piperidine analogue of codeine,

* Corresponding author. Tel.: +98 9173120994; fax: +98 3814424427.
E-mail address: dr.bigham@gmail.com (A.S. Bigham).

0034-5288/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.rvsc.2010.09.023

has received widespread acceptance in human medicine since it was first introduced in 1977 in Germany (Osterloh et al., 1978; Schenck and Arend, 1978). Its efficacy is attributed to a dual mechanism of action, namely, the interaction with opioid μ receptors and the monoaminergic effect on spinal pain modulation through inhibition of the reuptake of norepinephrine and serotonin. Tramadol does not have δ or κ receptor affinity (Raffa et al., 1992) but its affinity for μ receptors is approximately 10 times less than codeine and 6000 times less than morphine. The (+) enantiomer of tramadol has a low affinity for μ receptors, inhibits the cellular reuptake of serotonin (5-hydroxytryptamine, 5-HT) and increases its extracellular release. The (−) enantiomer more effectively inhibits norepinephrine reuptake and increases its cellular release by autoreceptor activation (Raffa et al., 1992; Desmeules et al., 1996; Scott and Perry, 2000). More recent studies have shown that tramadol also has local anesthetic action either by producing analgesia after intradermal injection (Pang et al., 1998; Altunkaya et al., 2003), or by reducing pain associated with propofol administration (Pang et al., 1999; Wong and Cheong, 2001). The pharmacological profile of tramadol such as activation of opioid receptors, inhibition of the monoaminergic system and local anesthetic effects (Collart et al., 1993; Raffa et al., 1993; Altunkaya et al., 2003), makes it an attractive drug for epidural administration. Epidural injection at the lumbosacral site are particularly useful after operations involving the pelvic viscera and/or limbs, for example, tibial plateau levelling osteotomy (TPLO) in dogs. In humans, epidural tramadol has been used in both adults and children, suggest that epidural tramadol can be used to provide prolonged postoperative analgesia without serious side effects (Baraka, 1993; Delilkan and Vijayan, 1993; Prosser et al., 1997; Siddik-Sayyid, 1999; Yaddanapudi et al., 2000; Ozcengiz et al., 2001; Gunes et al., 2004; Demiraran et al., 2005; Prakash et al., 2006), however Wilder-Smith et al. (1998) suggest that preoperative adjuvant epidural tramadol does not improve postoperative analgesia in comparison with lidocaine and placebo trials. Epidural use of tramadol has been reported only in the horse for evaluation of the analgesic effects of epidurally administered morphine, alfentanil, butorphanol, tramadol, and U50488H (Natalini and Robinson, 2000) and in the dog for postoperative pain relief after stifle surgery (Guedes et al., 2005). The aim of this study is to compare the time of onset and duration of analgesia produced by a tramadol and lidocaine–tramadol combination with that produced by lidocaine administration in the epidural space of lamb and monitor the time course of heart rate, respiratory rate and body temperature.

2. Materials and methods

This work was approved by the Ethics Committee of our University. Seven female lambs (2 to 4 months of age) of undefined breed weighing 15–20 kg were selected for this study. All animals were healthy and were housed in stalls individually. Three treatments were applied to every animal with a minimum of a 2 week interval between them. No surgery was performed in the lambs. Food was withheld for 24 h and water 12 h prior to the experiment. For the epidural anesthesia the animals were in right lateral recumbency on a table with hind limbs extended forward and the lumbosacral area clipped and scrubbed with povidone iodine (10% Betadine®, 10% Betadine, Nasr Co., Fariman, Iran). Following subcutaneous infiltration with 1 mL 2% lidocaine, a 18-gauge 8 cm-long spinal needle (Spinocan®, Spinal needle, Braun Melsungen Co., Melsungen, Germany) was inserted into the epidural space at the interspace between the last lumbar and first sacral vertebrae. The epidural space was identified by loss of resistance to injection of 2 mL of air after piercing the ligamentum flavum (Hall et al., 2001). Each lamb received each of the three treatments of a 2 week interval between them in a Latin square design.

The treatment 1 was 2% lidocaine hydrochloride 1 mL/7 kg (2.86 mg/kg body weight, 2% injectable sterilized solution, Preservative-free Lidocaine Hydrochloride, Pasteure Institute, Tehran, Iran), treatment 2 was combination of lidocaine and tramadol, it was 1 mL/7 kg of the mixture, with 1 mg/kg of tramadol 5% (0.02 mL/kg or 0.14 mL/7 kg, 50 mg/ml injectable sterilized solution, Tramadol, Darou Pakhsh. Pharma. Chem. Co., Tehran, Iran) and completed to the desired volume with lidocaine (0.86 mL/7 kg or 2.46 mg/kg) the dosage rate of tramadol chosen was determined as 1/10 of the systemic dosage used in humans (Driessen and Reimann, 1992). Treatment 3 was tramadol, it was 1 mL/7 kg of tramadol mixed with sterile water, (1 mg/kg of tramadol 5% or 0.14 mL/7 kg of tramadol and 0.86 mL/7 kg of sterile water). All drugs were administered over approximately 30 s.

Time to the onset, duration, and anatomical distribution of the analgesia were recorded. Time from the injection to loss of the sensation was considered as time of the onset of the analgesia. Time between loss and reappearance of pain response was considered as duration time of analgesia. Analgesia was defined as lack of a response to pin prick test and pressure from hemostat clamp (closed to the first ratchet) applied first in the perineal area and then moved cranially toward the thoracic region until a response (movement associated with pin prick test or hemostat pressure) was observed. The observer assessing analgesia was blind to the treatments. Response was measured each minute until no reaction occurred and then at 5 min intervals until a response reoccurred.

The lambs were evaluated throughout the study for presence of ataxia by walking them at 5 min intervals until 60 min and at 15 min intervals thereafter until the ending the study. This evaluation was done at the same time intervals in both groups. The ataxia was graded as mild (slight stumbling, easily able to continue walking), moderate (marked stumbling, walking but very ataxic), or severe (falling) (Grubb et al., 2002).

Heart rate (HR), respiratory rate (RR), and rectal temperature were recorded before (baseline, 0) and at 15, 30, 45, 60, 75, 90, 105 and 120 min after epidural administration of the solution. In this study the results with various time intervals were compared with base line value and time interval data were not compared with each other. The results were expressed as mean ± SD and were analyzed by a one-way analysis of variance and Duncan's test as a post hoc for heart rate, respiratory rate and body temperature and also, for time of onset and duration of analgesia. Graphpad Prism version 5 software program was used for all analyses. A value of $P < 0.05$ was considered significant.

3. Results

The epidural injection was easy to perform and well tolerated by all experimental animals. The tramadol produced a significant ($P < 0.05$) longer duration of analgesia (318.6 ± 5.08 min) than lidocaine (54.43 ± 3.28 min) alone and lidocaine–tramadol combination (100.7 ± 4.80). Also, lidocaine–tramadol combination produced a significant ($P < 0.05$) longer duration of analgesia than lidocaine alone. There was no sedimentation observed between lidocaine and tramadol during the mixing. Analgesia was produced in the regions of the tail, perineum, hind limbs, and flank and caudodorsal rib areas in lambs. Analgesia began at 14.29 ± 1.24 min in the tramadol treatment, being more delayed than in the treatments with lidocaine–tramadol and lidocaine, 5.58 ± 0.40 and 4.14 ± 0.26 min, respectively (Table 1). The extent of analgesia obtained with the tramadol treatment was similar to that obtained with the tramadol–lidocaine and lidocaine treatments, extending