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Comparison of epidural anesthesia with lidocaine-distilled water and lidocaine-magnesium sulfate mixture in goat

Amin Bigham Sadegh[1]*, Zahra Shafiei[2], and Seifollah Dehghani Nazhvani[3]

[1]*Department of Surgery and Radiology, Faculty of Veterinary Medicine, Shahreh-kord University, Shahreh-kord, Iran*

[2]*Resident of Veterinary Surgery, Department of Surgery and Radiology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran*

[3]*Department of Surgery, School of Veterinary Medicine, Shiraz University, Shiraz, Iran*

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ABSTRACT

Ruminants are generally not considered good subjects for general anaesthesia mainly because of the hazards of regurgitation and inhalation of ruminal contents or saliva into the lungs if the airway is left unprotected. Thus, regional anaesthesia produced by perineural or epidural injections of anaesthetic agents are most frequently employed in these species. The following study was carried out to compare directly the time of onset and duration of analgesia produced by a lidocaine-$MgSO_4$ combination with that produced by lidocaine-distilled water administration in the epidural space of goats. Seven healthy adult (2 ± 0.5 years of age) native goats (49 ± 3 kg) were selected for this study. Caudal epidural anesthesia was produced in all goats by 2% lidocaine (1 mL/7 kg) with 1 mL distilled water and two weeks later repeated by 2% lidocaine (1 mL/7 kg) with 1 mL of 10% $MgSO_4$. Time of onset, duration, standing and cranial spread of analgesia were recorded. Heart rate, respiratory rate and body temperature were recorded at 0 minutes prior to epidural administrations of each treatments as base line values and at 10, 30, 45 and 60 minutes after the epidural administration of each treatments. Statistical analysis included the paired Student's *t*-test and ANOVA (SPSS, soft ware of windows). $P<0.05$ was considered as a significant level. A significant difference ($P<0.05$) was noted for the onset of analgesia between lidocaine-distilled water (2.38 ± 0.38 min) and lidocaine-$MgSO_4$ (3.71 ± 0.38 min). Lidocaine-$MgSO_4$ produced analgesia of significantly longer duration (171.85 ± 8.07 min) than that of lidocaine-distilled water (61.42 ± 6.39 min). There were no significant differences in standing time between the two groups. There were no significant differences in HR, RR, and body temperature in comparison with the base line values in the lidocaine-distilled water and lidocaine-$MgSO_4$ groups. Using this combination, long duration obstetrical and surgical procedures could commence relatively soon after epidural injection and could be completed without re-administration of the anesthetic agent.

Key words: magnesium sulfate, N-Methyl-D-Aspartate, lidocaine, goat, epidural anesthesia

*Corresponding author:

Amin Bigham Sadegh, Department of Surgery and Radiology, Faculty of Veterinary Medicine, Shahreh-kord University, Shahreh-kord, Iran, P.O. Box: 115, Fax: +98 38 1442 4427; E-mail: dr.bigham@gmail.com

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Introduction

Ruminants are generally not considered good subjects for general anaesthesia mainly because of the hazards of regurgitation and inhalation of ruminal contents or saliva into the lungs if the airway is left unprotected (HALL and CLARK, 1991; TRIM, 1981). Thus, regional anaesthesia produced by perineural or epidural injections of anaesthetic agents is most frequently employed in these species. Epidural anesthesia is commonly utilized in veterinary medicine to allow diagnostic, obstetrical, and surgical intervention, in the perineal region of large animals (ELMORE, 1980; SKARDA, 1996). The most frequently used epidural anesthetic is lidocaine; mepivacaine, bupivacaine, and procaine are also used (DAY and SKARDA, 1991). With the exception of bupivacaine, this group of agents provides analgesia 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 ataxia, hind limb weakness, and recumbency. Epidural and intrathecal administration of agents with greater duration of action may be more appropriate for procedures requiring long duration analgesia. These agents include opioides, alpha-2 agonist (LUTINGER et al., 1985; EISENACH et al., 1996). Epidural use of ketamine has been reported in horses, cattle and dogs but it had short analgesia duration without recumbency or ataxia (GOMEZ DE SEQURA et al., 1998; HASKINS et al., 1985; ISLAS et al., 1985; NAGUIB and ADU-GYAMFI, 1988; KAMILOGLU et al., 2003). Recently, magnesium sulfate, which blocks N-Methyl-D-Aspartate (NMDA) receptors, same as ketamine, has been used in intrathecal anesthesia in rats (KARASAWA et al., 1998; ISHISAKI et al., 1999; LIU et al., 2001). As magnesium blocks the NMDA receptors and its ion channels, it can prevent central sensitization caused by peripheral nociceptive stimulation (SCHULZ-STUBNER et al., 2001; LIU et al., 2001). Magnesium also has antinociceptive effects in animal and human models of pain (KARA et al., 2002). These effects are primarily based on the inhibition of calcium influx into the cell and antagonism of NMDA receptors (SCHULZ-STUBNER et al., 2001; KARA et al., 2002). The purpose of this study was to investigate the effects of epidural injection of lidocaine-$MgSO_4$ mixture in goat, to assay onset and duration time and monitor the heart rate, respiratory rate and body temperature.

Materials and methods

One mL of 10% $MgSO_4$ (Nasr Fariman, Iran) was added to 1 mL/7 kg 2% lidocaine without epinephrine (Lidocaine Hydrochloride, Pastor, Iran) and one mL distilled water was added to 2% lidocaine (1 mL/7kg) without epinephrine. pH values were determined for lidocaine-$MgSO_4$ (pH = 5.7) and lidocaine - distilled water (pH = 6.7) by digital pH meter, (NEL, Model 821 Turkey with Ingold Electrod U457, French.) and did not show any sedimentation between lidocaine and $MgSO_4$ during mixing. Seven clinically healthy

goats, with mass of 48 ± 3 kg, were used. No surgery was performed on the goats. Feed was withheld for 24 h and water-8 h prior to the experiment. For the epidural anaesthesia the animals were in the right lateral recumbence position on a table with hind limbs extended forward. Following subcutaneous infiltration with 3 mL 2% lidocaine, a 16-gauge 8 cm-long Tuohy needle (Braun Melsungen AG) was inserted into the epidural space at the interspace between the last lumbal 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 and CLARK, 1991). A catheter with 3 lateral eyes, 0.6×1.05×100 mm, was threaded forward through the needle for 5 cm beyond the needle bevel; the needle was removed with the catheter in place. A mixture of 2% lidocaine (1 mL/7 kg) with 1 mL distilled water and two weeks later repeated by 2% lidocaine (1 mL/7 kg) with 1 mL of 10% $MgSO_4$ were injected slowly into the epidural space. Heart rate (HR), respiratory rate (RR), and rectal temperature were recorded before (baseline, 0) and at 10, 30, 45, and 60 mins after epidural administration of the solution. Analgesia was assessed by response to superficial and deep muscular pinpricks over the whole body and was defined as lack of movement or no attempt to kick or turn the head toward the site of the pinprick. Recovery from anaesthesia was in a quiet environment (room) and was determined as the moment that the animals were able to stand spontaneously and to maintain that position. The results were expressed as mean ± SD and submitted to a statistical variance analysis (ANOVA) for heart rate, respiratory rate and body temperature data and t test for time of onset, duration and standing data. $P<0.05$ was considered as a significant level.

Results

Epidural analgesia was produced in all goats following administration of lidocaine - distilled water and lidocaine-$MgSO_4$. Time to onset of analgesia was significantly prolonged following lidocaine-$MgSO_4$ (3.714 ± 0.38 min) in comparison to lidocaine- distilled water (2.38 ± 0.38 min). Lidocaine-$MgSO_4$ produced significantly ($P<0.05$) longer duration of analgesia (171.85 ± 8.07 min) than that produced by lidocaine-distilled water (61.42 ± 6.39 min), there was no significant difference in the standing time between the two groups (Table 1). Cutaneous analgesia ranged from coccyx vertebral to approximately L1 in the control and experimental groups. The cutaneous analgesia included the perineal region and was similar in spread on both sides of the spine to the level of L1 (in the control and experimental groups). Body temperatures, heart rates and respiratory rates were not significantly different in comparison with base line values throughout the study in the control and experimental groups (Table 2).

Table 1. Anesthetic indices (mean ± SD) epidurally administered lidocaine-distilled water and lidocaine-magnesium sulfate in 7 goat (min).

Indices	lidocaine - distilled water (min)	lidocaine - $MgSO_4$ (min)
Onset of analgesia	2.38 ± 0.38	3.714 ± 0.38[a]
Duration of analgesia	61.42 ± 6.39	171.85 ± 8.07[b]
Time to Stand	185.14 ± 7.31	183.42 ± 6.8

[a] and [b] means significance differences between onset and duration of analgesia in the control and experimental groups ($P<0.001$)

Table 2. Heart rates (beats/min), respiratory rate (breath/min) and rectal temperature (°C) of 7 goat under epidural anesthetic with lidocaine-distilled water and lidocaine-magnesium sulfate

Indices		Time interval (min)				
		0	10	30	45	60
Heart rate	control	89.85 ± 3.9	87.14 ± 4.70	91.8 ± 4.8	86.2 ± 5.6	86.42 ± 5.0
	experiment	87.4 ± 3.1	87.4 ± 3.7	89.0 ± 2.5	88.4 ± 3.1	89.1 ± 2.9
Respiratory rate	control	25 ± 2	21 ± 2	17 ± 2	16 ± 1.6	17 ± 1.6
	experiment	25 ± 2	23 ± 2	19 ± 2	18 ± 1	19 ± 1
Rectal temperature	control	39.2 ± 0.4	38.6 ± 0.4	39.5 ± 0.5	39.2 ± 0.4	39.3 ± 0.4
	experiment	39.1 ± 0.1	40.3 ± 0.4	38.1 ± 0.5	38.9 ± 0.5	40.3 ± 0.4

Discussion

$MgSO_4$ has been used in epidural analgesia such as ketamine in rats (KARASAWA et al., 1998; ASOKUMAR et al., 2002). $MgSO_4$ is a non competitive NMDA receptor antagonist that acts like ketamine (KARA et al., 2002). Injection of ketamine for perineal analgesia in dogs (HASKINS et al., 1985), horses (GOMEZ DE SEGURA et al., 1993) and cattle (KAMILOGLU et al., 2003) has been reported in literature. Probably this is the first study on the effect of lidocaine-$MgSO_4$ combination in epidural anesthesia of goats. Pain stimulation can cause release of aspartate and glutamate neurotransmitters that bind to N-Methyl amino acid receptors and cause calcium, sodium ion inflow and potassium out flow that results in pain stimulation sensation in the CNS (ASOKUMAR et al., 2002). Magnesium sulfate blocks calcium influx and non competitively antagonizes NMDA excitatory receptors that cause prevention of central sensitization caused by peripheral nociceptiove stimulation (ASCHER and NOWAK, 1987; SCHULZ-STUBNER et al., 2001; LIU et al., 2001; ASOKUMAR et al., 2002; KARA et al., 2002). MIZUTANI et al. (1995) reported prolongation of pain recognition after IV administration of $MgSO_4$ in humans. Prolonged duration of intrathecal analgesia following administration of a fentanyl - magnesium

combination has been reported in rats (KARASAWA et al., 1998; ASOKUMAR et al., 2002). Recently MARZOUK et al. (2003) and HAAJI-MOHAMMADI et al. (2004) used fentanyl-$MgSO_4$ and lidocain-$MgSO_4$ in spinal anaesthesia in human beings respectively, which significant increased the duration of analgesia observed during the two studies. These results support the prolonged duration of analgesia observed in our study after epidural injection of lidocaine-$MgSO_4$ in comparison to the control group.

Prolonged onset of analgesia time was observed after epidural injection of lidocaine-$MgSO_4$ mixture in comparison to lidocaine-distilled water. It can be suggested that lowering the pH to 5.7 by adding $MgSO_4$ (1 mL of %10) to lidocaine (0.22 mg/kg, pK_a = 7.7), could alter levels of ionized and nonionized forms of lidocaine and had a decreased non ionized form (cell membrane permeable form) so, the beginning of analgesia was prolonged (CATTERAL et al., 1995).

Dose related recumbency is expected following epidural administration of lidocaine because local anesthetics block both sensory and motor fibers (DAY and SKARDA, 1991). Recumbency was observed after epidural administration of lidocaine-distilled water and lidocaine-$MgSO_4$ administration in this study.

Body temperatures, heart rates and respiratory rates were not significantly different in comparison with base line values in the control and experimental groups throughout the study. Of course MARZOUK et al. (2003) did not observe any cardiovascular side effects after intratechal injection of fentanyl-$MgSO_4$ in humans.

In summary, the combination of 2% lidocaine with 10% $MgSO_4$ administered epidurally to goats resulted in prolonged duration of perineal analgesia and cutaneous analgesia extending from the coccyx to L1. Overall, this new mixture would appear to be the best choice for single-dose epidural administration in goats undergoing long duration procedures without cardiovascular and respiratory side effects.

Further research is necessary to determine the different dosages of $MgSO_4$ in epidural administration and its histopathological effects on neuron fibers in the epidural space.

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SAŽETAK

Preživači općenito nisu pogodni za opću anesteziju većinom zbog opasnosti od regurgitacije i inhalacije buražna sadržaja ili sline u pluća, ako su im zračni prohodi nezaštićeni. Zbog toga se u njih najčešće primjenjuje perineuralna ili epiduralna anestezija. Ovo istraživanje je provedeno radi izravne usporedbe nastupa i trajanja analgezije postignute primjenom lidokaina i magnezijeva sulfata te lidokaina i destilirane vode u epiduralni prostor u koza. Sedam zdravih odraslih koza (u dobi od 2 ± 0,5 godina) tjelesne mase od 49 ± 3 kg odabrano je za ovo istraživanje. U svih je provedena kaudalna epiduralna anestezija 2%-tnim lidokainom (1 mL/7 kg) i jednim mililitrom destilirane vode. Dva tjedna poslije, epiduralna anestezija bila je ponovljena 2%-tnim lidokainom (1 mL/7 kg) i jednim mililitrom 10%-tnog magnezijeva sulfata. Promatrano je vrijeme nastupa anestezije, njezino trajanje, postojanost i kranijalno širenje. Frekvencija bila i disanja te tjelesna temperatura izmjereni su prije davanja anestezije kao bazalne vrijednosti, a zatim 10, 30, 45 i 60 minuta nakon epiduralne injekcije. Rezultati su bili statistički obrađeni Student *t*-testom i ANOVA testom. $P<0,05$ smatran je značajnom razinom. Značajna razlika ($P<0,05$) bila je zabilježena u vremenu nastupa analgezije postignute lidokainom i destiliranom vodom (2,38 ± 0,38 min) te lidokainom i magnezijevim sulfatom (3,71 ± 0,38 min). Analgezija postignuta lidokainom i magnezijevim sulfatom trajala je znatno duže (171,85 ± 8,07 min) od one postignute lidokain-destiliranom vodom (61,42 ± 6,39 min). Nije ustanovljena statistički značajna razlika za frekvenciju bila, disanja i tjelesnu temperaturu u odnosu na bazalne vrijednosti u obih skupina. Primjenom kombinacije lidokain-magnezijev sulfat dugotrajni porodnički i kirurški zahvati mogu započeti relativno brzo nakon epiduralne injekcije te se mogu završiti bez ponovljene primjene anestetika.

Ključne riječi: magnezijev sulfat, lidokain, koza, epiduralna anestesija

Book review

Srebočan, V., E. Srebočan: Veterinary Toxicology, 2nd revealed and complemented edition, Medicinska naklada, 2009. ISBN 978-953-176-404-9.

University textbook "Veterinary toxicology, 2nd revival and complemented edition" is an important contribution to veterinary toxicology professional and scientific literature. In this edition there are 515 pages with 92 illustrations. The content of the book is modernized and complemented with knowledge's related to bitoxines from the poisonous plants and venoms animals and some poisons which were not described in the first edition. As toxicology is multidisciplinary science in veterinary medicine which is a part of clinical-, reproductive-, immunotoxicology, hygienic toxicology, phorensic toxicology and ecotoxicology so is the approach of this book. For every poisonous chemical following chapters are described: 1. physical-chemical characteristic; 2. use (exp. pesticides); 3. sources of poisoning; 4. toxicity; 5. metabolism (kinetic and mechanism of toxicological damage); 6. clinical symptoms; 7. gross and microscopic lesions; 8. diagnosis; 9. treatment; 10. residues; 11. sublethal effects (immunotoxicity, reproductive toxicity and carcinogenicity) and 12. ecotoxicology. Chemical substances described in this textbook are those to which animals are most exposed: chemicals which are used for plant protection (pesticides), chemical which can enter the food chain (pesticides, metals, industrial contaminants, micotoxines), chemicals which are used as a food (nonprotein nitrogen compounds), poisonous plants and venoms of poisonous animals. This university textbook are primarily dedicated to the students of veterinary medicine and field veterinarians but can be useful to the related professions: agricultural, food technology and biology.

Andreja Prevendar Crnić