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Short communication

COMPARISON OF CAUDAL EPIDURAL ANAESTHESIA WITH LIDOCAINE-DISTILLED WATER AND LIDOCAINE-MAGNESIUM SULFATE COMBINATION IN SHEEP

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Summary

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Epidural anaesthesia is commonly utilized in veterinary medicine to allow diagnostic, obstetrical, and surgical interventions in the perineal region of domestic animals. Lidocaine is one of the most frequently used epidural anaesthetics. The following study was carried out to compare the time of onset and the duration of analgesia produced by the administration of lidocaine-$MgSO_4$ combination with that produced by lidocaine-distilled water in the epidural space of sheep. Seven healthy adult (2 ± 0.5 years of age) sheeps (49±3 kg body weight) were used in this study. Significant difference ($P<0.001$) was noted for onset of analgesia between lidocaine-distilled water (2.07±0.73 min) and lidocaine-$MgSO_4$ (4.57±1.27 min). The latter combination produced analgesia of significantly longer duration (174.0±12.19 min) than that of lidocaine-distilled water (53.42±4.7 min). There were no significant differences in standing time between groups. Also, there were no significant differences at the different post administration periods (min 10, 30, 45 and 60) compared to baseline values of heart rate, respiratory rate and body temperature for both groups of sheep. The utilization of the studied lidocaine-$MgSO_4$ combination would allow obstetrical and surgical procedures of a long duration relatively soon after the epidural injection, without re-administration of the anaesthetic agent.

Key words: epidural anaesthesia, lidocaine, $MgSO_4$, sheep

Epidural anaesthesia is commonly utilized in veterinary medicine for diagnostic, obstetrical, and surgical interventions in the perineal region of large animals (Elmore, 1980; Skarda, 1996). The most frequently used epidural anaesthetic is lidocaine; mepivacaine, bupivacaine, and procaine are also used (Day & Skarda, 1991). With the exception of bupivacaine, these agents provide analgesia of relatively short duration and may necessitate re-administration of the agent to allow completion of the procedure. In addition, local anaesthetic agents indiscriminately block motor, sensory, sympathetic fibres (Day & Skarda, 1991) causing ataxia, hindlimb 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 opioids, alpha-2 agonists (Luttinger *et al.*, 1985; Eisenach *et al.,* 1996). Epidural use of ketamine has been reported in horses, cattle, and dogs but it had short duration of analgesia without recumbency or ataxia (Haskins *et al.*, 1985; Islas *et al.,* 1985; Naguib & Adu Gyamfi, 1988; Gomez de Segura *et al.,* 1993; Kamiloglu *et al.*, 2003). Recently, magnesium sulfate, which blocks N-methyl-D-aspartate (NMDA) receptors, same as ketamine, was used for intrathecal anaesthesia 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 (Liu *et al.,* 2001; Schulz-Stübner *et al.,* 2001). Magnesium has also shown 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-Stübner *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 sheep, to assay onset and duration times and monitor the time course of heart rate, respiratory rate and body temperature.

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 of both combinations (pH=5.7 for lidocaine-$MgSO_4$ and pH=6.7 for lidocaine-distilled water) were determined by a 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 healthy adult (age 2 ± 0.5 years) sheep, weighing 48±3 kg, were used. No surgery was performed to sheep. Feed was withheld 24 h and water − 8 h prior to the experiment. For the epidural anaesthesia, the animals were in right lateral recumbency 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 & Clarke, 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 level; the needle was removed with the catheter in place. A mixture of 2% lidocaine at 1 mL/7 kg + 1 mL distilled water was slowly injected into the epidural space. Two weeks later the procedure was repeated with 2% lidocaine at 1 mL/7 kg + 1 mL 10% $MgSO_4$.

Heart rate (HR), respiratory rate (RR), and rectal body temperature (BT) were recorded before (baseline, min 0) and at 10, 30, 45, and 60 min 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 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 analysis of variance (ANOVA) for heart rate, respiratory rate and body temperature data and paired t-test for the times of onset, duration and standing at a level of significance $p<0.05$

Epidural analgesia was produced in all sheep following administration of lidocaine-distilled water and lidocaine-$MgSO_4$. Time to onset of analgesia was significantly prolonged following lidocaine-$MgSO_4$ (4.57±1.27 min) in comparison to lidocaine-distilled water (2.07± 0.73 min). Lidocaine-$MgSO_4$ produced significantly ($P<0.001$) longer duration of analgesia (174.0±12.19 min) than that produced by lidocaine-distilled water (53.42±4.7 min), but there was no significant difference in standing times between groups (Table 1). Cutaneous analgesia ranged from coccygeal vertebrae to approximately L1 in 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 both groups. The values of BT, HR and RR were not significantly different vs baseline values throughout the study in the control and experimental groups (Table 2).

$MgSO_4$ has been used in the epidural analgesia in rats (Karasawa *et al.,* 1998; Asokumar *et al.,* 2002). $MgSO_4$ is a non-

Table 1. Anesthetic indices of epidurally administered lidocaine–distilled water (control group) and lidocaine-$MgSO_4$ (experimental group) in sheep (mean ± SD; n=7)

Indices	Lidocaine-distilled water (control group)	Lidocaine-$MgSO_4$ (experimental group)
Onset of analgesia, min	2.07 ± 0.73	4.57 ±1.27 *
Duration of analgesia, min	53.42 ± 4.70	174.0 ±12.19 *
Time to stand, min	181.0 ± 9.73	176.8 ± 7.80

* statistically significant difference between control and experimental groups ($p<0.001$).

Table 2. Heart rate (beats/min), respiratory rate (breath/min) and rectal temperature (°C) after epidurally administered lidocaine–distilled water (control group) and lidocaine-$MgSO_4$ (experimental group) in sheep (mean ± SD; n=7)

Indices	Groups	Time after epidural administration, min				
		0	10	30	45	60
Heart rate	control	89±7	90±7	88±7	87±6	93±8
	experimental	85±3	76±3	69±2	71±3	68±4
Respiratory rate	control	25.2±1.4	21.0±1.5	17.0±1.6	17.0±1.2	18.0±1.0
	experimental	25.4±1.1	23.2±2.0	20.2±2.0	18.8±1.1	18.8±1.0
Rectal temperature	control	39.0±0.03	38.78±0.08	38.68±0.07	38.7±0.09	38.72±0.10
	experimental	39.1±0.10	38.90±0.20	38.50±1.60	38.4±0.20	38.20±0.20

competitive NMDA receptor antagonist that acts similarly to ketamine (Kara *et al.,* 2001). 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 the literature. As far as we know, this is the first study on the effect of lidocaine-$MgSO_4$ combination for epidural anaesthesia of sheep. Pain stimulation can cause release of aspartate and glutamate neurotransmitters that bind to N-methyl amino acids receptors and cause calcium and sodium ions inflow and potassium outflow that result in pain stimulation sensation in the CNS (Asokumar *et al.,* 2002). Magnesium sulfate blocks calcium influx and non competitively antagonize NMDA excitatory receptors that cause prevention of central sensitization caused by peripheral nociceptive stimulation (Ascher *et al.,* 1987; Liu *et al.*, 2001; Schulz-Stübner *et al.*, 2001; Asokumar *et al.*, 2002; Kara *et al.*, 2002). Mizutani *et al.* (1995) had reported prolongation of pain recognition after IV administration of $MgSO_4$ in humans. Prolonged duration of intrathecal analgesia following administration of 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) had used fentanyl-$MgSO_4$ and lidocaine-$MgSO_4$ respectively in the spinal anaesthesia of men and observed a significant increase in the duration of analgesia in both studies. These results support the prolonged duration of analgesia observed in our study after epidural injection of lidocaine-$MgSO_4$ in comparison to control group.

Prolonged onset of analgesia time was observed after epidural injection of lidocaine-$MgSO_4$ mixture in comparison to lidocaine-distilled water. It could be suggested that lowering the pH to 5.7 by adding $MgSO_4$ to lidocaine (0.22 mg/kg, pK_a =7.7), could alter the levels of ionized and non-ionized forms of lidocaine, lower the non-ionized (cell membrane permeable) form, and thus could prolong the beginning of analgesia (Catterall, 1995).

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

Body temperatures, heart rates and respiratory rates were not significantly different from baseline values in the control and experimental groups throughout the study. Marzouk *et al.* (2003) have neither observed any cardiovascular side effects after intrathecal injection of fentanyl-$MgSO_4$ in men.

In conclusion, the combination of 2% lidocaine with 10% $MgSO_4$ administered epidurally to sheep resulted in prolonged duration of perineal analgesia and cutaneous analgesia extending from coccyx to L1. This mixture appears to be the best choice for single-dose epidural administration in sheep that are to be submitted to long duration procedures without cardiovascular and respiratory side effects. Further research is necessary to determine the various doses of $MgSO_4$ for epidural administration and to assess histopathologically its effects on neuron fibres in the epidural space.

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