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THE EFFECT OF MAGNESIUM SULPHATE ON LIDOCAINE EPIDURAL ANALGESIA IN GOATS

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ABSTRACT

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Five adult baladi goats were used to evaluate the effect of different doses of magnesium sulphate ($MgSo_4$) that were injected epidurally in combination with lidocaine Hcl 2% on the duration and area of analgesia as well as side effects. Animals were treated as follow: treatment I was injected with lidocaine Hcl 2% (1 ml/7 kg). Treatments II, III and IV were injected with lidocaine Hcl 2% (1 ml/7 kg) in combination with 25, 50 and 100 mg $MgSo_4$ 10%, respectively. Results revealed that onset of analgesia was delayed in treatments II, III and IV (3, 3.5 and 3.5 minute, respectively). Treatment IV produced the longest duration of analgesia (99.80 ± 2.35 min). There was a significant increase in the animal recumbency in treatment I as compared to other treatments. The extent of analgesic area was almost the same in all treatments that extended from perineum to T13. Ataxic effect recorded in different patterns in treated animals. Treatment I had the longest duration of recumbency followed by mild ataxia in treatment II. In other treatments, ataxia was not developed. In conclusion, the combination of 2% lidocaine with 100 mg $MgSo_4$10% injected epidurally in goats resulted in prolonged duration of analgesia extending from the perineum to the flank region without ataxia, cardiovascular or respiratory side effects.

***Key words**: Epidural, Goats, Magnesium sulfate, Lidocaine Hcl.*

INTRODUCTION

Ruminants are generally not considered good subjects for general anaesthesia mainly because of the hazards of regurgitation and inspiration pneumonia. Thus, regional analgesia especially epidural one is most frequently used in these species. Epidural analgesia is routinely used in ruminants for obstetric manipulations, caudal surgical procedures, and as an adjunct treatment for control of rectal tenesmus (Muir *et al.,* 2000 and Hall *et al.,* 2001).

Epidural analgesia is usually produced by local analgesic which usually lidocaine Hcl 2% solution (Hall *et al.,* 2001). Local analgesic agents indiscriminately block motor, sensory and sympathetic fibers that cause ataxia, hind limb weakness, and recumbency (Day and Skarda, 1991). Epidural administration of agents with greater duration of action is proper for procedures requiring long duration of analgesia. These agents include a fentanyl – magnesium combination in rats; lidocain-MgSo4 in sheep and goat and magnesium sulphate added to ketamine in sheep (Karasawa *et al.,* 1998; Bigham and Shafiei, 2008; Bigham *et al.,* 2009 and DeRossi *et al.,* 2012).

The main objective of current research is to evaluate the effect of the different doses of $MgSo_4$ injected epidurally combined with lidocaine Hcl 2 % in goats. As well as to determine the best dose produced longest duration of analgesia with minimal side effects.

MATERIALS and METHODS

Five adult baladi goats were used on four successive treatments with two weeks intervals. Goat's body weight was 28.4 ± 2.12 kg, and aged 16–30 months. Experiments were conducted at the Educational farm of Faculty of Veterinary Medicine, Suez Canal University. In all animals, feed was withheld for 12 h and water 2 h prior to the experiment. The lumbosacral intervertebral space was identified and aseptically prepared. Epidural puncture was performed, according to Hall *et al.* (2001). Animals were subjected to the following treatments. Treatment I was injected with lidocaine Hcl 2% (1 ml/7 kg) (Debocaine: 20mg/ml; El-nasr Pharm. Chemicals Co. for Al-Debeiky Pharma A.R.E.) and 1 ml preservative free sterile water while treatments II, III and IV were injected by using lidocaine Hcl 2% (1 ml/7 kg) combined with 25, 50 and 100 mg $MgSo_4$ 10% (Egypt Otsuka Pharm. Co) respectively. The total volume of the injected $MgSo_4$ was completed to be 1 ml by preservative free sterile water so as to be equal in all treatments.

Heart rate (HR), respiratory rate (RR), rumen motility (RM), and rectal temperature (RT) were recorded

before administration (baseline) and 5, 30, 60 and 120 minutes after injection. Onset and duration of the analgesic effect were also recorded.

Analgesia, and ataxia were assessed before drug administration (baseline) and at 5, 30, 60, and every 30 minutes until a sensation was returned. Analgesia was assessed by response to superficial and deep muscular pinpricks over the whole body. All animals received a standard painful stimulus with 23-gauge, 2.5-cm needle. In this way, the presence and the anatomic extend of the analgesia was determined. The skin response was recorded on a scale 0 to 3. Scale 0 indicated that response was detected after superficial skin prick (no analgesia). Scale 1 indicated that no response was detected after superficial skin prick. Scale 2 indicated that no response was detected after deep skin prick. Scale 3 indicated that no response was detected after deep muscle prick (maximal analgesia).

Motor effects and degree of ataxia were assessed by use of a scoring system of 1 to 4. (1) no ataxia, (2) mild ataxia , swaying slightly and animal in keeping a standing position, (3) Moderate ataxia – animal fall down with movement of the hind limbs, and (4) severe ataxia , animal recumbent but without movement of hind limbs.

Data were statistically analyzed by one way ANOVA using SPSS Version, 16 according to Snedecor *et al.* (1989). For Means separation, Duncan's (1995) multiple range test. Probability ≤ 0.01 was considered Highly Significant.

RESULTS

Lumbosacral epidural analgesia was produced in all treatments. Onset time of analgesia was significantly delayed in treatments II, III and IV in comparison with treatment I (1.60 ± 0.19 min). Treatment IV produced the longest duration of analgesia (99.80 ± 2.35 min). There was a significant difference in the standing time between treatment I and other treatments (Table 1).

The mean heart rates, respiratory rates, rumenal motility and rectal body temperatures for all treatments were recorded in Table 2. These data were not significantly different in comparison with base line values throughout the study in all treatments.

The extent of analgesia was almost the same in all treatments. The main analgesic areas were perineum, the hind limbs, and spread on both sides of the flank to the dermatomic region T13. The analgesic score was recorded in Table 3 which revealed that the mean maximal analgesic score in response to needle prick at the analgesic region was noticed at 5 min in all treatments and ended after 30 minutes in treatments I, II and III while it extended in treatment IV till 60 min.

The ataxic effect was more pronounced with the lidocaine treatment. Mild ataxia was appeared in treatment II at 5 minute and lasted for 25 minute On other hand, no apparent difference in the observed incidence of ataxia in treatments III and IV was observed (Table 4).

Table 1: Onset, duration of analgesia and time of stand after epidural administration in all treatments (mean ± SD).

Treatments	Onset (min)	Duration (min)	Time of stand (min)
I	$1.60^{b} \pm 0.19$	$59.00^{c} \pm 2.53$	$140.60^{a} \pm 2.50$
II	$3.00^{a} \pm 0.27$	$61.60^{bc} \pm 0.68$	$0.00^{b} \pm 0.00$
III	$3.50^{a} \pm 0.45$	$68.00^{b} \pm 2.83$	$0.00^{b} \pm 0.00$
IV	$3.50^{a} \pm 0.22$	$99.80^{a} \pm 2.35$	$0.00^{b} \pm 0.00$

Means carrying different superscript are highly significant (P≤ 0.01).

Table 2: Heart rate (beats/min), respiratory rate (breath/min), ruminal motility (per two min) and rectal body temperature (°C) after epidural administration in all treatments (mean ± SD).

Treatments		Time (min)					
		0	5	30	60	120	Total
HR	I	89.60±1.67	89.60±1.14	88.60±2.19	89.80±1.79	89.20±1.09	89.50^{A}±1.91
	II	90.20±1.48	90.20±1.48	89.60±1.82	89.80±0.84	90.20±1.48	90.10^{A}±1.29
	III	90.20±1.48	89.80±1.09	90.60±1.67	90.00±1.58	90.00±1.41	90.10^{A}±1.35
	IV	89.80±1.48	90.00±0.70	90.60±0.89	91.00±1.58	89.80±1.48	90.30^{A}±1.24
	Total	89.95^{B}±1.43	89.90^{B} ±1.07	89.85^{B}±1.78	90.15^{B}±1.46	89.80^{B}±1.32	
RR	I	21.60±2.07	21.40±2.61	21.40±1.67	21.40±2.41	21.20±1.09	21.60^{A}±1.97
	II	20.60±1.82	20.60±1.67	21.00±2.24	20.40±1.14	21.00±1.58	20.70^{A}±1.56
	III	20.80±0.84	21.20±1.30	21.00±1.00	20.80±1.30	21.20±0.84	20.93^{A}±1.08
	IV	21.80±1.31	21.40±1.14	21.20±1.30	21.40±1.82	20.80±1.64	21.37^{A}±1.33
	Total	21.20^{B}±1.54	21.15^{B}±1.66	21.15^{B}±1.49	21.00^{B}±1.65	21.05^{B}±1.23	
RM	I	2.40±0.55	2.20±0.45	2.40±0.55	2.40±0.55	2.40±0.55	2.37^{A}±0.49
	II	2.40±0.55	2.60±0.55	2.40±0.55	2.40±0.55	2.40±0.55	2.47^{A}±0.51
	III	2.40±0.55	2.40±0.55	2.40±0.55	2.20±0.45	2.40±0.55	2.40^{A}±0.49
	IV	2.60±0.55	2.40±0.55	2.60±0.55	2.40±0.55	2.40±0.55	2.46^{A}±0.51
	Total	2.45^{B}±0.51	2.40^{B}±0.50	2.50^{B}±0.51	2.35^{B}±0.48	2.40^{B}±0.50	
RT	I	39.66±0.38	39.70±0.28	39.68±0.37	39.68±0.37	39.74±0.18	39.73^{A}±0.29
	II	39.50±0.41	39.60±0.51	39.60±0.21	39.38±0.42	39.56±0.40	39.53^{AB}±0.38
	III	39.52±0.46	39.40±0.51	39.64±0.31	39.40±0.39	39.14±0.17	39.44^{B}±0.37
	IV	39.60±0.51	39.46±0.47	39.58±0.35	39.50±0.47	39.60±0.41	39.54^{AB}±0.41
	Total	39.57^{B}±0.41	39.54^{B}±0.44	39.62^{B}±0.29	39.49^{B}±0.39	39.51^{B}±0.37	

Means carrying different superscript are highly significant (P≤ 0.01)

Table 3: Analgesic score at different times in all treatments (mean ± SD).

Time (min)	Treatments				
	I	II	III	IV	Total
Baseline	0.00^{f} ±0.00	0.00f±0.00	0.00^{f}±0.00	0.00^{f}±0.00	0.00^{D}±0.00
5 min	3.00^{a}±0.00	3.00^{a}±0.00	2.80^{a}±0.447	3.00^{a}±0.00	2.95^{A}±0.22
30 min	3.00^{a}±0.00	3.00^{a}±0.00	3.00^{a}±0.00	3.00^{a}±0.00	3.00^{A}±0.00
60 min	0.80^{d}±0.83	1.00^{d}±0.00	1.40^{c}±0.89	3.00^{a}±0.00	1.55^{B}±1.05
90 min	0.00^{f}±0.00	0.00^{f}±0.00	0.00^{f}±0.00	2.4^{b}±0.54	0.60^{C}±1.09
120 min	0.00^{f}±0.00	0.00^{f}±0.00	0.00^{f}±0.00	0.00^{f}±0.00	0.00^{D}±0.00
Total	0.97^{B}±1.36	1.00^{B}±1.320	1.03^{B}±1.33	1.68^{A}±1.41	

Means carrying different superscript are highly significant (P≤ 0.01)

Table 4: Degree of ataxia at different times in all treatments (mean ± SD).

Time (min)	Treatments				
	I	II	III	IV	Total
Baseline	1.00 ^{d} ± 0.00	1. 00 ^{d}± 0.00	1.00 ^{d} ± 0.00	1.00^{d} ± 0.00	1.00 ^{C} ± 0.00
5 min	3.00 ^{a}± 0.00	1.60 ^{c}± 0.55	1.00 ^{d}± 0.00	1.00 ^{d}± 0.00	1.65 ^{A}± 0.87
30 min	3.00 ^{a}±.0.00	1.60 ^{c}± 0.55	1.00^{d} ± 0.00	1.00^{d} ± 0.00	1.65 ^{A}± 0.87
60 min	2.80 a± 0.45	1.00 ^{d}± 0.00	1.00 ^{d}± 0.00	1.00 ^{d}± 0.00	1.45 ^{B}± 0.83
90 min	2.400 b± 0.55	1.00 ^{d}± 0.00	1.00^{d} ± 0.00	1.00^{d} ± 0.00	1.35 ^{B}± 0.67
120 min	1.40^{c} ± 0.55	1.00 ^{d}± 0.00	1.00 ^{d}± 0.00	1.00 ^{d}± 0.00	1.10 ^{C}± 0.31
150 min	1.00 ^{d}± 0.00	1.00 ^{d}± 0.00	1.00^{d} ± 0.00	1.00^{d} ± 0.00	1.00 ^{C}± 0.00
Total	2.08^{A} ± 0.92	1.17 ^{B}± 0.38	1.00 ^{d}± 0.00	1.00 ^{d}± 0.00	

Means carrying different superscript are highly significant (P≤ 0.01)

DISCUSSION

Magnesium sulphate is a physiological noncompetitive N-Methyl-D-Aspartate (NMDA) receptor antagonist that blocks ion channels in a voltage-dependent fashion. Studies with different routes of magnesium sulphate administration (eg, subarachnoid or epidural) showed improved anesthetic and analgesic quality (Bilir *et al.,* 2007). Activation of NMDA receptors leads to calcium and sodium influx into the cell with an efflux of potassium and initiation of central sensitization and wind-up (Liu *et al.,* 2001; Buvanendram *et al.,* 2002). Magnesium blocks calcium influx and noncompetitively antagonizes NMDA receptor channels (Fawcet *et al.,* 1999). These effects have prompted the investigation of magnesium sulfate as an adjuvant for postoperative analgesia (Bilir *et al.,* 2007).

Prolonged onset of analgesia time was observed after epidural injection of lidocaine-$MgSO_4$ mixture in comparison to lidocaine alone. Similar result was obtained by Bigham and Shafiei (2008) and Bigham *et al.* (2009) who suggested that lowering the pH to 5.7 by adding $MgSO_4$ to lidocaine, 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.

As well as, in this study, the longest duration of epidural analgesia was achieved following administration of a lidocain-$MgSO_4$ combination in treatment IV (99.80 ± 2.35 min). This result is supported by Bigham and Shafiei (2008); Bigham *et al.* (2009) and Dehghani and Bigham (2009). On the other hand, epidural injection of magnesium sulfate alone induced a short duration of analgesia with more delayed onset of sensory blockade in sheep (DeRossi *et al.,* 2012).

It was observed in the current study that the combination of $MgSO_4$ with lidocaine Hcl seems to present an advantage over the administration of these drugs separately. Drugs can intensify the analgesic effect. This result supported by DeRossi *et al.* (2005) who found that addition of magnesium sulphate to lidocaine in caudal epidural administration increases the duration of the analgesic period in goats.

Heart rates, respiratory rates, rumen motility and rectal body temperatures, were not significantly different in comparison with base line values in all treatments throughout the time of the study. Similar results were obtained by Bigham and Shafiei (2008); Bigham *et al.* (2009) and DeRossi *et al.* (2012) who did not observe any cardiovascular side effects after spinal injection of $MgSO_4$ with different combination of analgesia or anesthesia in animals. These findings encourage the epidural use of $MgSO_4$ in goats.

Ataxic effect was observed in this study with the lidocaine treatment which could be attributed to the fact that local anesthetics block both sensory and motor fibers. Similar result was obtained by Day and Skarda (1991). On the other hand, no apparent difference in the observed incidence of ataxia in treatments III and IV while mild ataxia was appeared in treatment II at 5 minute and lasted for 25 minute. Previous study showed that intrathecally administered $MgSO_4$ has a good safety profile in animals (Chaminov *et al.,* 1997). Lejuste (1985) described an inadvertent intrathecal injection of 1000 mg magnesium sulfate that produced a transient motor block followed by a complete resolution within 90 min and no neurologic deficit at long-term follow-up. The findings of the present study disagree with Bigham and Shafiei (2008) and Bigham *et al.* (2009) who observed recumbency after epidural administration of lidocaine-distilled water and lidocaine-$MgSO_4$ (100 mg/ Kg).

In conclusion, results revealed that combination of 2% lidocaine with 100mg $MgSO_4$ 10% injected epidurally in goats resulted in prolonged duration of analgesia extended from the perineum to the flank region. Overall, there was a synergistic effect of these combination without side effects on ataxia, cardiovascular or respiratory.

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تأثير حقن كبريتات المغنيسيوم على التسكين حول الأم الجافية باستخدام الليدوكيين في الماعز

محمد حسين الدهراوى ، إبراهيم السيد هلال

تم استخدام خمسة ماعز بلدي بالغة لتقييم جرعات مختلفة من كبريتات المغنيسيوم حقنت حول الأم الجافية مع الليدوكيين هيدروكلورايد ٢% . حيث تم علاج الحيوانات على النحو التالي: العلاج الأول بواسطة الليدوكيين هيدروكلورايد ٢% بجرعة ١مل/٧كجم أما العلاج الثاني والثالث والرابع باستخدام الليدوكيين هيدروكلورايد ٢% بجرعة ١مل/٧كجم مع ٢٥ و٥٠ و ١٠٠ مجم من ١٠% كبريتات المغنيسيوم على التوالي . كشفت النتائج تأخر ظهور أثر المسكن في العلاجات الثاني والثالث والرابع الى ٣و ٣.٥ و ٣.٥ دقيقة على التوالي .هذا وقد سجلت المعالجة الرابعة أطول مدة تسكين وفقد الإحساس (٩٩.٨٠ دقيقة) كما كان هناك فرق كبير في وقت الوقوف بين العلاج الأول وغيرها من العلاجات. وكان مدى امتداد منطقة التسكين متماثل في كل العلاجات من منطقة العجان إلى الضلع الصدرى الثالث عشر وكان الترنح أكثر وضوحا مع العلاج الأول وفي المقابل لم يلاحظ أي اختلاف واضح في الترنح في العلاج الثالث والرابع. وخلصت الدراسة الى أن الجمع بين الليدوكيين هيدروكلورايد ٢% مع ١٠٠ مجم كبريتات المغنيسيوم ١٠% في الماعز أسفرت عن تسكين المنطقة من العجان إلى الضلع الصدرى الثالث عشر مدة طويلة دون ترنح أو ظهور أثار جانبية على الجهازين الدوري والتنفسي.