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Spinal Analgesia in Donkeys by Magnesium Sulphate

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Abstract

The objective of this study was to evaluate the analgesic effect of magnesium sulphate with special reference to its recommended doses for spinal analgesia in donkey and its effect on animals' vital parameters (pulse and respiratory rates, body temperature). Twenty four clinically healthy donkeys of both sexes were divided randomly into a subarachnoid group (group I=15 animals) and a control group (group II=9 animals). Animals in group I were subdivided into three equal subgroups, Ia, Ib and Ic and recieved magnesium sulphate intrathecally in doses of 1, 2 and 4 ml respectively. Those in group II were subdivided also into three equal subgroups IIa, IIb and IIc and recieved normal saline intrathecally in doses of 1, 2 and 4 ml respectively. All animals were put under clinical observation. Animal analgesia was monitored at various standard dermatomes by pinching a fold of skin by an artery forceps. Vital signs monitoring included pulse and respiratory rates, body temperature, hind limb as well as the desensitized areas. Lumbosacral IT injection of 1 ml, 2 ml and 4 ml magnesium sulphate resulted in analgesia that started after 1-2min. from the end of injection and lasted for 14.32+3.51, 46.60+10.69 and 78.20+9.83 min. respectively. Analgesia involved the flank area in the subgroup Ia (1 ml) and extended in both subgroups Ib (2 ml) and Ic (4 ml) to include the gluteal region, tail, perineum, udder or scrotum, lateral aspect of the thigh till the level of the stifle joint distally and extended cranially to the level of the first rib. Recumbancy occurred only in 3 animals in subgroup Ib and 2 animals in subgroup Ic. Physiological changes were within normal limits throughout the whole experimental time. Intrathecal $MgSO_4$ 10% has an analgesic effect in donkeys with minimal physiological changes but 2-4 ml are needed for extended analgesia, these data must be checked under surgical conditions.

Keywords: Intrathecal; Magnesium sulphate; Analgesia; Donkeys

Introduction

Magnesium (Mg^{2+}) is the second most abundant intracellular cation and an essential ingredient in the body's electrolyte and metabolic constitution. It serves as an essential co-factor in multitude enzymes reactions, especially those involved in energy metabolism, phosphate transfer, muscle contractility and neurochemical transmission [1]. Magnesium sulfate ($MgSO_4$) used for many years on an empirical basis for the control of convulsions in patients with pre-eclamptic toxemia [2,3].

It has been suggested that substances with calcium channel-blocking effect and NMDA (N-Methyl-D-Aspartate) receptor antagonist may prevent pain and facilitate treatment of established pain states [4,5]. Magnesium is a physiological calcium channel blocker agent [6] and NMDA receptor antagonist that suppress induced adverse behavioral reactions and autotomy caused by nerve injuries in animals [7-9]. To our knowledge there are no published papers on the use of magnesium sulfate for spinal anesthesia in donkeys.

The aim of the present study was to investigate the analgesic effect of intrathecal magnesium sulphate in donkeys with special reference to its analgesic doses and its effect on the animal's vital signs.

Materials and Methods

Animals

The experimental protocol was approved by the ethical committee of the Faculty of Veterinary Medicine, Assiut University, Egypt.

The present study was performed on 24 clinically healthy donkeys of both sexes, 90-120 kg body weight. The animals were housed in good ventilated stables at the Teaching Veterinary Hospital, Faculty of Veterinary Medicine, Assuit University with food and water ad libitum. The animals were divided randomly into two main groups, a subarachnoid group (group I=15 animals) and a control group (group II=9 animals).

Animals in the subarachnoid group (group I) were subdivided into three equal subgroups Ia, Ib and Ic (each of 5 animals) and received magnesium sulphate intrathecally (Magnesium sulfate, 10 ml sterile ampoule, 100 mg/ml ~0.41 mmol/ml, EIPICO) in doses of 1, 2 and 4 ml respectively. Animals in the control group (group II) were also subdivided into three equal subgroups IIa, IIb and IIc (each of 3 animals) and recieved normal saline intrathecally in doses of 1, 2 and 4 ml respectively (**Table 1**).

Injection technique

Injection technique was carried out while animals in standing position under physical restrain under complete aseptic precautions.

With the thumb and middle fingers, sacral tuberosities were palpated and with the index finger the depression leading to the lumbosacral intervertebral foramen was felt. The tip of the spinal needle with stylet (9 cm long, 18 gauge) was directed about 5 degrees cranially from perpendicular plane toward the spinal cord. The needle was slowly advanced with the bevel point directed cranially. The subarachnoid space was identified by free flow of cerebrospinal fluid (CSF) from the needle hub after removal of the stylet or aspirating it within a sterile syringe. Amount of CSF was aspirated equal to the amount of the drug injected intrathecaly in each case. As the IT injection was achieved, the spinal needle with its stylet was withdrawn. The skin was pressed by a piece of cotton soaked in tincture of iodine 3% to control bleeding and infection.

Animals thereafter were put under clinical observation. Analgesia (absence of any response such as kicking, biting or moving) was determined by pinching a fold of skin by artery forceps every minute to determine the onset time, and then checked every 5 minutes to follow the duration time. Status of the hind limbs, boundaries of desensitized areas, pulse and respiratory rate, body temperature were monitored preinjection and at 5, 15, 25, 40, 60 and 90 minutes postinjection.

Statistical analysis

Data were collected and analyzed by computer programe "student T test GraphPad software". to compare between different readings for the variable in each group. Data were expressed as mean+SE. Differences were considered non-significance if $P>0.05$ (n.s), Low significance if $P<0.05$ (*), Significance if $P<0.01$ (**) and High significance if $P<0.001$ (***).

Results

Analgesia

At doses of 1, 2 and 4 ml of IT magnesium sulphate in the subgroups Ia, Ib and Ic, onset of analgesia was 1-2 min (1.60+0.54 min), 1-2 min (1.60+0.54 min) and 1-2 min. (1.40+0.54 min.) and lasted for 10-18 min (14.32+3.51 min), 30-57 min (46.60+10.69 min) and 67-89 min (78.20+9.83 min) respectively while normal saline didn't alter sensory perception (**Table 2 and Figure 1**).

Desensitized area

Subarachnoid injection of 1 ml magnesium sulphate in the subgroup Ia resulted in a uniform bilateral analgesia in the triangular flank area which extended cranially from level of the caudal border of the last rib, dorsally it was limited by the level of transverse processes of lumbar vertebrae and ventrally by imaginary line joining the external angle of the ilium to the level of caudoventral border of the last rib.

The desensitized area extended in both subgroups Ib (2 ml) and Ic (4 ml) to include the gluteal region, tail, perineum, udder or scrotum, lateral aspect of the thigh till the level of the stifle joint distally and extended cranially to the level of the first rib.

Limb status

There was an incoordination with shivering in both pelvic limbs after subarachnoid injection of $MgSO_4$ 10% solution in all donkeys in the subgroups Ia, Ib and Ic. However donkeys in subgroup Ia remained in standing position, two animals in subgroup Ib as well as three animals in subgroup Ic showed recumbency 10-15 min. postinjection lasting for 20-25 min.

Pulse rate

In the magnesium sulphate groups there was an increase for the first 5 min, highly significant in both subgroups Ia & Ib and significant in Ic; thereafter the pulse rate showed a gradual decrease until the end of the session.

The control group exhibited a significant increase in the pulse rate after 5 min, returning toward the base line values at the end of the session. (**Table 3 and Figure 2**).

Table 1 Main groups and subgroups of the animals.

Main groups	Sub groups	No. of animals	Drug used	Doses (ml)	Site of injection	Route of injection
Subarachnoid (Group I)	Ia Ib Ic	5 5 5	$MgSO_4$ 10%	1 2 4	Lumbosacral	Intrathecal
Control (Group II)	IIa IIb IIc	3 3 3	Normal Saline	1 2 4		

Table 2 The analgesic effect of subarachnoid $MgSO_4$ 10% in donkeys.

Main groups	Subgroups	Drug used	Doses (ml)	Onset (min)	Duration (min)
Subarachnoid (Group I)	Ia	$MgSO_4$ 10%	1	1.60+0.24	14.32+0.38
	Ib		2	1.60+0.24	46.60+4.78
	Ic		4	1.40+0.24	78.20+4.39
Control (Group II)	IIa	Normal saline	1	----------	----------
	IIb		2	----------	----------
	IIc		4	----------	----------

Respiratory rate

IT magnesium sulphate decreased the respiratory rate (RR) except for an increase at the first 5 min post injection. A similar trend was observed in the control group (**Table 4 and Figure 3**).

Temperature

IT magnesium sulphate resulted in an increase in body temperatures, that was significant in subgroups Ia and Ib, and low significant in subgroup Ic.

In the control group, there was non-significant increase in body temperature in subgroup IIa, low significant decrease in subgroup IIb and significant increase in subgroup IIc (**Table 5 and Figure 4**).

Discussion

Few studies evaluated the efficiency of spinal injection of $MgSO_4$ as an anlgesic agent. Magnesium is an antagonist of the NMDA receptor and its associated ion channels [7,9]. Analgesic effect of Magnesium sulfate ($MgSO_4$) may be attributed to the effect of magnesium as a physiological calcium channel blocker and NMDA receptor antagonist that suppresses NMDA-induced adverse behavioral reactions and autotomy caused by nerve injuries in animals. Magnesium inerferes with neuromusclar transmision by inhibiting release of acetylcholine (Ach) and competitively blocks calcium entry at the motor nerve terminal.

The results of the present work cleared that intrathecal $MgSO_4$ had sensory and motor block effects. This result was in agreement with [10,11] who reported that intrathecal $MgSO_4$ produced sensory and motor effects. Both [12,13] demonstrated that antinociception potentiation and delay in the development of morphine tolerance produced by intrathecal co-infusion of $MgSO_4$ and morphine in rats, suggesting that intrathecal administration of $MgSO_4$ might be a useful adjunct to spinal morphine analgesia [14] recorded that intrathecal injection of $MgSO_4$ in rats produced a state of spinal anesthesia and general sedation.

On the other hand, our results and those of many authers disagreed with [15] who demonstrated that intrathecal $MgSO_4$ administered in rats was unable to produce antinociceptive effecte in rat acute pain models. [16] stated that intrathecal $MgSO_4$ caused motor paralysis but not complete analgesia in rats.

The spinal cord of most donkeys terminates at the junction between the first and second sacral vertebra [17] therefore the access at the lower lumbosacral interspaces is easy and safe. The possibility of subarachnoid injection was great with lumbosacral puncture. This result agreed with [18] who recorded that the subarachnoid cavity is enlarged in the area of the cauda equina in the caudal lumbar and sacral regions to form lumbar cistern from which CSF can be obtained by lumbar puncture.

The rapid onset of analgesia following subarachnoid injection of $MgSO_4$ 10% may be attributed to the peculiar anatomy of the nerve roots within the subarachnoid space where they are not covered a thick protective dural sheets, so that they can be readily anaesthetized [19,20]. In this context, [21] stated that the transfer of substances from the spinal fluid to the intercellular spaces of nervous tissues occurs rapidly. It has been demonstrated that the increase in the $MgSO_4$ dose resulted in an increase in the duration of action as well as increase in the desensitized area in a dose dependent manner. These results agreed with that recorded by [22,23].

The least effect on motor control of the hind limbs following subarachnoid injection of $MgSO_4$ could be attributed to the use of small doses of the drug in addition to the dilution effect of spinal fluid. Also Mg^{2+} has a direct depressant effect on skeletal muscle. Excess Mg^{2+} decrease Ach release by motor-nerve impulses, reduces the sensitivity of the motor end-plate to applied Ach and decrease the amplitude of the motor end-plate potential [24].

The present study showed that the pulse rate initially increased after subarachnoid $MgSO_4$ injection during the first 5 min postinjection. It could be attributed to excitement associated with mechanical control of the animals as well as spinal needle puncture. This was followed by gradual decrease in pulse rate till the end of the experiment. Similar findings were recorded by [14,11,25]. They recorded that Mg^{2+} increased conduction time and lengthened P-R and QRS intervals of the ECG [24] also recorded that Mg^{2+} slows the rate of S-A nodal impulse formation [2] reported that Mg^{2+} reduces myocardial contractile force as it is a calcium antagonist. It also reduces peripheral vascular tone by sympathetic blockade and inhibition of catecholamine release.

Regarding respiratory rate, subarachnoid injection of $MgSO_4$ 10% resulted in a low significant decrease in respiratory rate when compared with its base line values. Our results were in

Table 3 The effect of subarachnoid $MgSO_4$ 10% on pulse rate in donkeys.

Main Group	Sub group	Time of injection (min.)						
		Before	After					
		0	5	15	25	40	60	90
Subarachnoid	Ia	41.80+1.8	57.20+1.85***	57.2+1.85***	53.40+3.4**	40.80+0.58n.s	40.60+0.74n.s	40.2+0.8n.s
	Ib	40.0+1.09	58.0+0.63***	47.4+3.76n.s	40.0+0.00n.s	41.2+0.37n.s	39.0+1.14*	38.8+1.06*
	Ic	40.2+1.56	54.80+1.82**	53.0+1.67**	37.6+1.24**	37.4+1.12*	38.2+1.46n.s	38.6+1.2n.s
Control	IIa	38.33+0.55	49.0+0.96**	40.33+0.55*	39.0+0.36*	39.0+0.36*	37.67+0.42***	37.4+0.31**
	IIb	38.67+1.52	47.33+2.34***	45.67+1.47***	41.0+0.63n.s	38.33+1.05n.s	35.33+0.21n.s	35+0.12n.s
	IIc	38.00+0.73	48.0+0.63***	40.67+0.21*	40.0+0.00*	38.67+0.21n.s	37.33+0.76*	37.2+0.41*

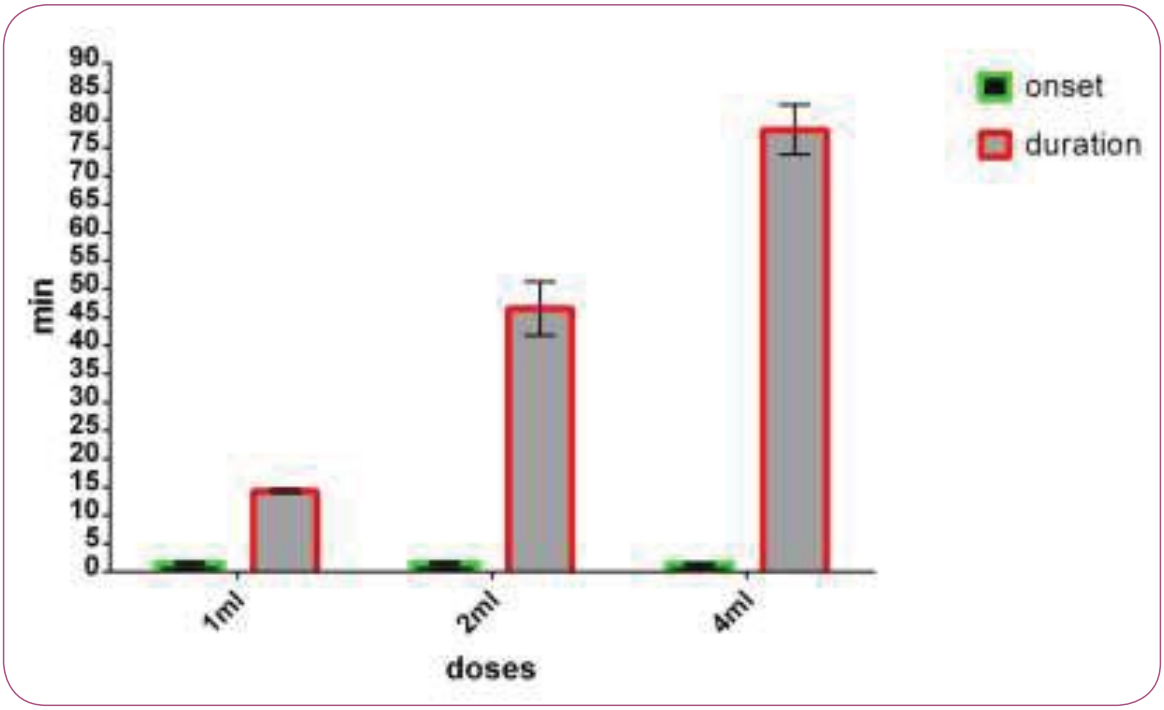

Figure 1 The analgesic effect of subarachnoid $MgSO_4$ 10% in donkeys.

agreement with [14,11,]. The decrease in respiratory rate may be attributed to that Mg^{2+} has respiratory depressant effect due to the neuromuscular block that it produces but it has no effect on centarl respiratory drive [2]. High conc. of Mg^{2+} produce respiratory paralysis was reported by [24].

Lumbosacral subarachnoid injection of $MgSO_4$ 10% resulted in non-significant changes in rectal temperature throughout the experiment when compared with its base line values. Similar finding recorded by [11] neurotoxicity of spinal magnesium sulphate in donkeys should be taken in consideration in further studies.

Conclusion

Lumbosacral subarachnoid injection by 2 and 4 ml of $MgSO_4$ 10% could be considered an effective dose for a rapid onset and discrete duration of analgesia in donkeys, with minimal physiological changes. These preliminary data must be corroborated during surgery, where stimuli coming from peritoneum and visceral organs are much stronger than the pinching of the skin.

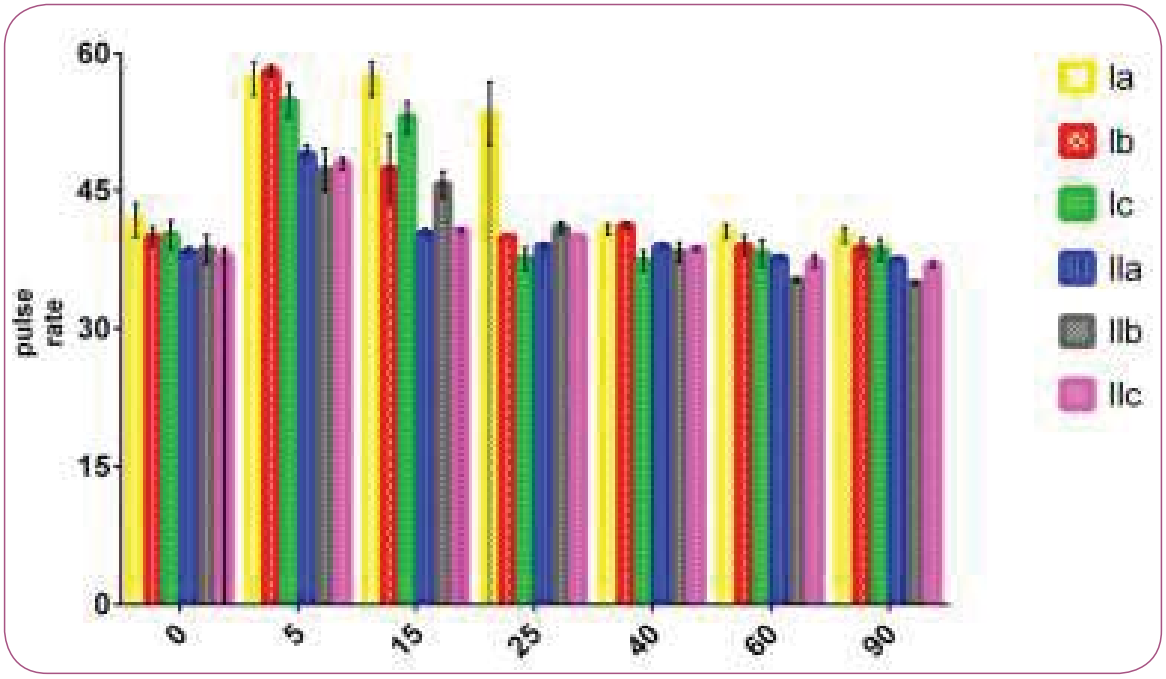

Figure 2 The effect of subarachnoid $MgSO_4$ 10% on pulse rate in donkeys.

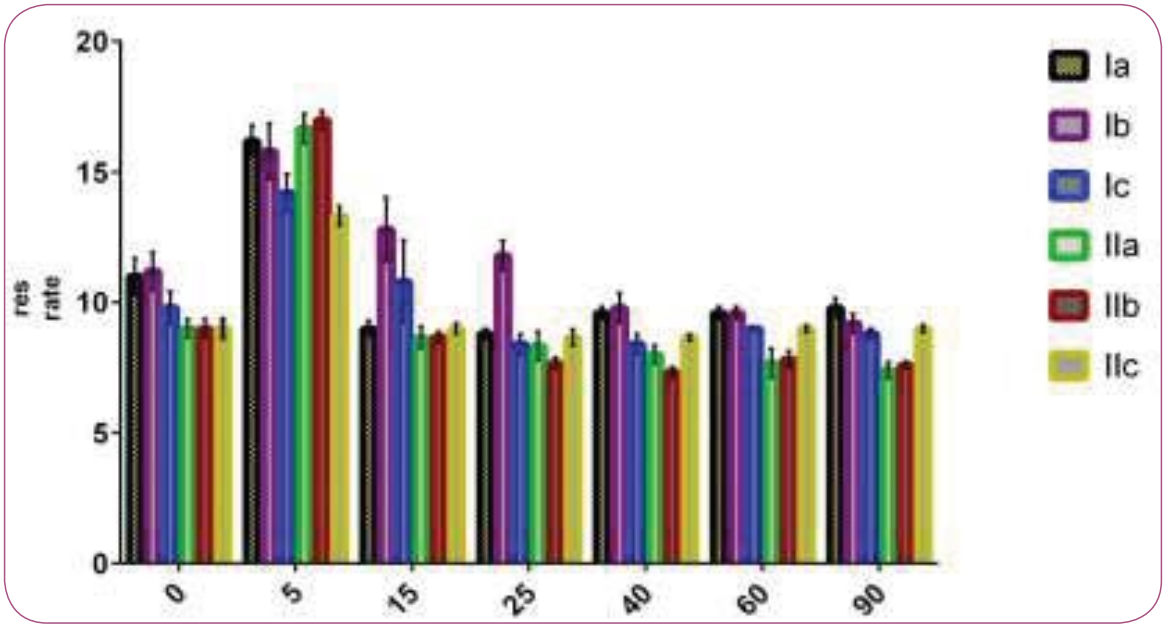

Figure 3 The effect of subarachnoid $MgSO_4$ 10% on respiratory rate in donkeys.

Table 4 The effect of subarachnoid $MgSO_4$ 10% on respiratory rate in donkeys.

Main Group	Sub group	Time of injection (min.)						
		Before	After					
		0	5	15	25	40	60	90
Subarachnoid	Ia	11.0+0.70	16.2+1.3***	9.0 +0.31n.s	8.80+0.2n.s	9.6+0.24n.s	9.6+0.24n.s	9.80+0.37*
	Ib	11.20+0.73	15.8+1.06*	12.8+1.24*	11.8+0.58*	9.80+0.58Ns	9.60+0.24ns	9.20+0.37ns
	Ic	9.80+0.63	14.20+0.73***	10.8+1.59n.s	8.40+0.4*	8.40+0.4*	9.0+0.00n.s	8.8+0.2n.s
Control	IIa	9.0+0.36	16.66+0.57***	8.66+0.42n.s	8.33+0.55*	8.0+0.36*	7.67+0.55*	7.4+ 0.32*
	IIb	9.0+0.36	17.0+0.36***	8.67+0.21ns	7.67+0.21ns	7.33+0.21*	7.83+0.32*	7.6+ 0.13*
	IIc	9.00+0.73	13.33+0.55**	9.0+0.36n.s	8.67+0.21n.s	8.67+0.21n.s	9.0+0.36n.s	9.+ 0.12n.s

Table 5 The effect of subarachnoid $MgSO_4$ 10% on body temperature in donkeys.

Main Group	Sub group	Time of injection (min.)						
		Before	After					
		0	5	15	25	40	60	90
Subarachnoid	Ia	37.38+0.24	37.50+0.24n.s	37.84+0.23n.s	37.58+0.21**	37.62+0.22**	37.66+0.23***	37.72+0.21**
	Ib	37.50+0.26	37.52+0.26n.s	37.51+0.36n.s	37.64+0.22n.s	37.66+0.22*	37.68+0.51**	37.66+0.25**
	Ic	37.22+0.24	37.32+0.34*	37.82+0.44*	37.92+0.43*	37.40+0.27*	37.60+0.37*	37.44+0.26*
Control	IIa	37.30+0.12	37.33+0.17n.s	37.40+0.19n.s	37.43+0.23n.s	37.33+0.56n.s	37.36+0.24n.s	37.11+0.11n.s
	IIb	37.50+0.10	37.56+0.09*	37.63+0.05n.s	37.26+0.09n.s	37.10+0.09*	37.13+0.11*	37+ 0.21
	IIc	37.63+0.05	37.7+0.06n.s	37.70+0.06n.s	37.83+0.02**	37.66+0.05n.s	37.56+0.04*	37.2 + 0.02

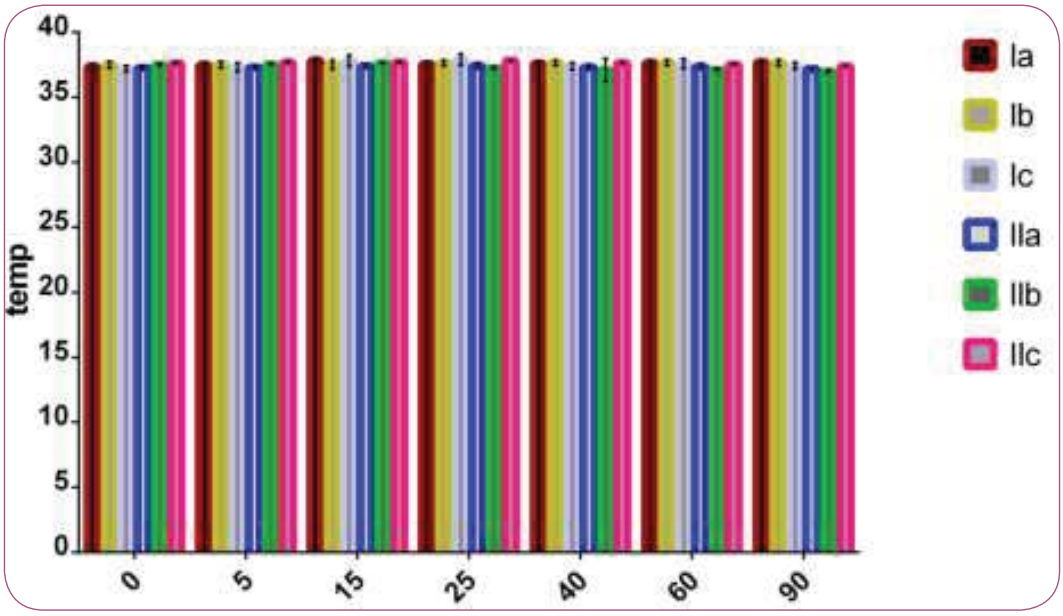

Figure 4 The effect of subarachnoid $MgSO_4$ 10% on body temperature in donkeys.

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