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ORIGINAL ARTICLE

Controlled Hypotension: A Comparison Between Magnesium Sulphat and Remifentanil in Middle Ear Surgery

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Objective: This prospective, randomized study was designed to compare remifentanil and magnesium sulphate during middle ear surgery in terms of controlled hypotension.

Materials and Methods: Fourty patients undergoing middle ear surgery were enrolled in the study. Patients were randomized into two groups of 40 to receive remifentanil (Group R) or magnesium sulphate (Group M) infusion. Propofol 2 mg kg−1 was administered to induce anaesthesia, which was maintained using sevoflurane. Group R received a continuous infusion of remifentanil infusion 0.5 microg/kg IV during induction of anaesthesia and then it was titrated about 0.250 microg kg−1min−1 during the operation, whereas Group M received an i.v. magnesium sulphate bolus of 50 mg kg−1 followed by a 15 mg kg−1 h−1 continuous infusion to maintain a mean arterial pressure (MAP) between 60 and 70 mm Hg. Haemodynamic variables,SpO_2, surgical conditions, and adverse effects were recorded.

Results: Controlled hypotension was well maintained in all groups. MAP, systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and heart rate were higher in Group M than in Group R. Surgical conditions, and side effects were not different between the two groups.

Conclusion: Remifentanil when combined with sevoflurane provided more adequate controlled hypotension and proper surgical conditions for middle ear surgery than magnesium.

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Introduction

Controlled hypotension is used to achieve a bloodless operative field which is needed for successful middle ear microsurgery [1]. Although the primary premise for the use of controlled hypotension is to limit intraoperative blood loss, an additional benefit may be improved visualization of the surgical field [1,2]. Vasodilators (nitroprusside, nicardipine, and nitroglycerine), alpha adrenergic agonists (clonidine and dexmedotomidine), beta-adrenergic antagonists (propranolol and esmolol), alpha- and beta-adrenergic antagonists (labetolol), and high doses of potent inhaled anaesthetics (halothane, isoflurane, and sevoflurane) have been used to control hypotension during middle ear surgery [1]. Remifentanil known to induce good surgical conditions by controlling hypotension during tympanoplasty [2].

I.V. magnesium sulphate may be a good agent for deliberate hypotension because magnesium intervenes in the activation of membrane Ca ATPase and Na–K ATPase involved in transmembrane ion exchanges during depolarization and repolarization phases, and thus act as a stabilizer of cell membrane and intracytoplasmic organelles [3]. In addition, magnesium sulphate acts as a vasodilator by increasing the synthesis of prostacyclin, as well as inhibiting angiotensin converting enzyme activity. Magnesium sulphate has small, dose-dependent myocardial depressant effect [4].

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A few comparative study has been performed on the use of magnesium sulphate or remifentanil for controlled hypotension during middle ear surgery. We hypothesized that magnesium sulphate would be as effective as remifentanil for hypotension. We therefore investigated the efficacies of magnesium sulphate and remifentanil in terms of controlled hypotension and other complications during middle ear surgery.

Materials and Methods

In this randomized and prospective trial, 40 adults undergoing middle ear surgery under general anaesthesia, ASA physical status I or II, aged 20–65. were enrolled. This study was approved by the Institutional Ethics Committee and written informed consents were obtained from all patients. Exclusion criteria were renal, hepatic, or cardiovascular diseases, neuromuscular disease, atrioventricular conductance disturbance, allergic reactions to study drugs, and chronic treatment with calcium channel blockers, opioids, or non-steroidal anti-inflammatory drugs.

Patients were allocated to receive either magnesium sulphate (Group M) or remifentanil (Group R) using a computerized random number generator. Anaesthetic induction was started with propofol 2 mg kg^{-1} i.v. and study drugs were administered using an infusion pump system. Group M patients received an i.v. bolus injection of magnesium sulphate 50 mg kg^{-1} in saline over 10 min during the induction of anaesthesia, and then 15 mg kg^{-1} h^{-1} by continuous infusion until the end of the operation. Patients in Group R were administered with remifentanil infusion 0.5 microg/kg IV during induction of anaesthesia and then the effect-site concentration of remifentanil was titrated about 0.250 microg kg^{-1} min^{-1} during the operation. After loss of eyelid reflex, patients were ventilated with 2.5 MAC sevoflurane, and atracurium 0.5 mg kg^{-1} was given to facilitate tracheal intubation. Anaesthesia was maintained with sevoflurane and mean arterial pressure (MAP) between 60 and 70 mm Hg during the operation. Patients were ventilated with oxygen and medical air.

MAP, SAP, DAP, heart rates (HRs), SpO_2 measured at the following time points: before anaesthetic induction, before induction, induction first min, intubation first min, after intubation, at 10, 20, 30, 40, 50, 60 min, extubation and after 5min extubation. If hypertension or tachycardia over 20% of the preoperative value occurred during anaesthesia it was assumed to be due to insufficient analgesia and an i.v. bolus of fentanyl 1 µg kg^{-1} was given. If hypotension under 60 mm Hg or bradycardia under 20% of the preoperative HR occurred, ephedrine 5 mg (for hypotension) or atropine 0.5 mg (for bradycardia) was given i.v. At the end of the procedure, sevoflurane, magnesium sulphate, and/or remifentanil infusions were stopped. The duration of hypotension and total amounts of remifentanil and magnesium sulphate administered were recorded. Surgical conditions were assessed by the surgeon using a six-point category scale (0–5: 0, uncontrolled bleeding; 5, no bleeding, virtually bloodless field) [5].

The sample size was calculated to be 20 (α=0.05 and β=0.2) to achieve 80% power to detect a 30% difference in MAP between the two groups. Data obtained in this study were evaluated using SPSS v.12.0. Information on anaesthesia and surgery and incidence variables were compared using t-test or $\chi 2$ test as appropriate. The Kolmogorov-Smirnov test was used to examine the assumption of normality; continuous, normally distributed data were compared using Mann-Whitney U test. To compare the data (MAP, HR) at each time point, t-test was used. Values are expressed as counts or as mean (SD). p-values of <0.05 were considered statistically significant.

Results

Patient characteristics in both groups were described in Table 1. Demografic variables were no different in study groups. Additional intraoperative fentanyl and nitroglyserin was necessary in M group.

Group M showed higher MAP, SAP, DAP than Group R (Figure 1, Table 2). Heart rate values were higher in group M before induction than Group R (Figure 2). SpO_2 values weren't different (Figure 3). Ephedrine was not used intraoperatively in both groups. There were no respiratory and circulatory complications in either group.

Table 1. Demographic datas in groups.

	Group R (n=40) Mean (SD)	Group M (n=40) Mean (SD)
Age (yr)	36.8 (17.0)	42.0 (11.4)
Gender (M/F)	22/18	23/17
Body weight (kg)	73.2 (11.6)	74.8 (12.1)
Height (cm)	169.7 (7.6)	170.2 (7.5)
ASA (I/II)	25/15	27/13
Fentanyl used intraoperatively (patient)	0	3
Nitroglyserin used intraoperatively (patient)	0	8

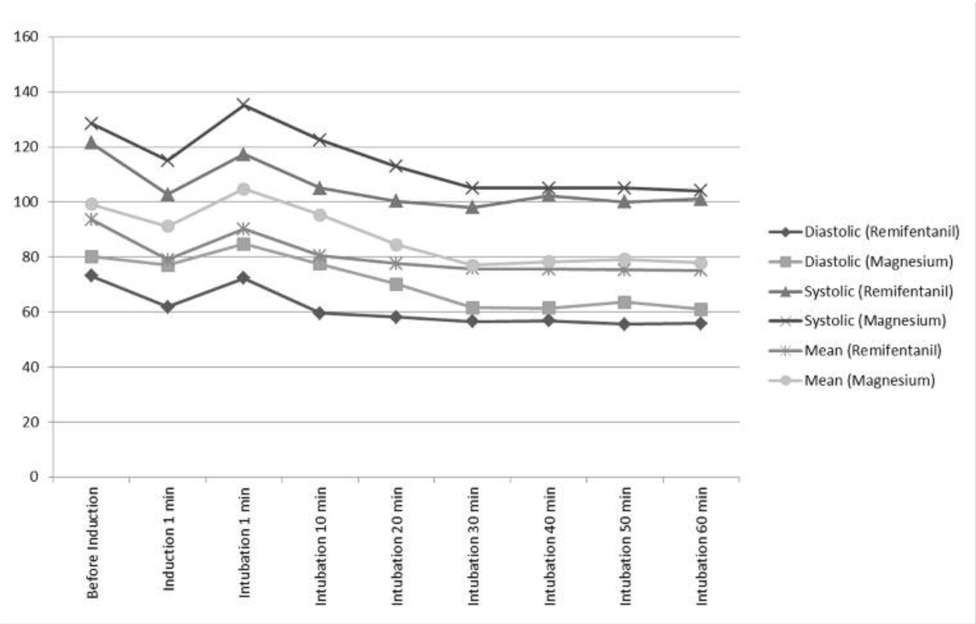

Figure 1. Systolic arterial pressure. Diastolic arterial pressure. Mean arterial pressure.

Table 2. Surgical conditions, operation time and side effects in groups.

	Group R (n=40)	Group M (n=40)
Operation time (min)	100.9 (43.7)	105.9 (56.6)
Surgical conditions		
0	0	0
1	0	0
2	3	4
3	14	10
4	20	23
5	3	3
Rescue antiemetics (patients)	17	14
Shivering	5	3

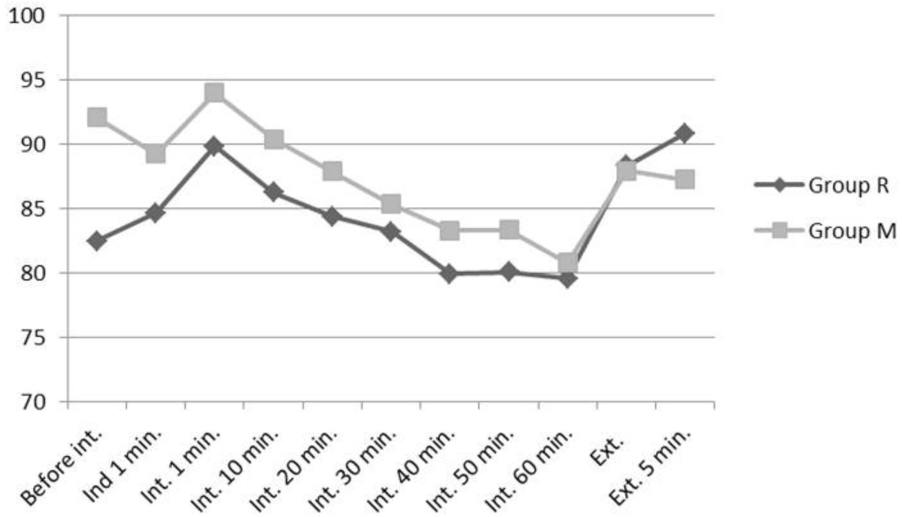

Figure 2. Heart rate

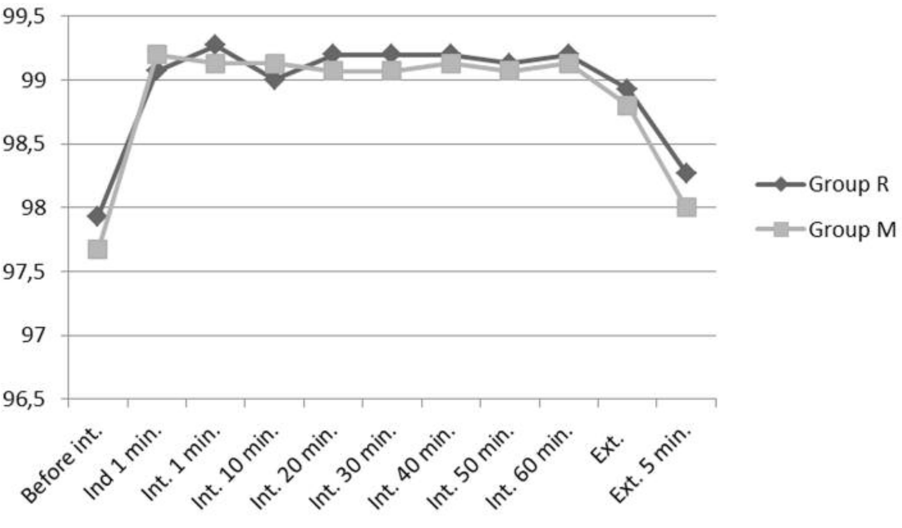

Figure 3. SpO_2 values

Surgical conditions, duration and side effects were not different between the two groups (Table 3).

Discussion

This study shows that when combined with sevoflurane, remifentanil and magnesium sulphate produced intraoperative conditions and haemodynamics during middle ear surgery. However, our results demonstrate that remifentanil has more advantages during surgery and that its usage was associated with more stable perioperative haemodynamics (smaller increases in MAP, SAP, DAP and HR) than magnesium sulphate. In the present study, the majority of patients in both groups had a surgical condition score of 3–5, indicating at least a good operative field.

Table 3. Hemodynamic values in groups.

	Group	N	Mean	SD	p
Before ind.SAP	R	20	121.53	13.69	0.078
	M	20	128.53	15.51	
Before ind.DAP	R	20	73.20	12.89	0.089
	M	20	80.13	10.40	
Before ind.MAP	R	20	93.60	14.75	0.097
	M	20	99.27	10.37	
ind.1.minSAP	R	20	102.80	16.22	0.097
	M	20	115.13	20.90	
ind.1. min.DAP	R	20	61.87	12.57	0.013*
	M	20	77.07	15.75	
ind.1. min.MAP	R	20	79.07	11.93	0.038*
	M	20	91.13	17.45	
ent.1. min.SAP	R	20	117.40	14.53	0.005*
	M	20	135.27	12.68	
ent.1. min.DAP	R	20	72.27	13.35	0.004*
	M	20	84.80	8.95	
ent.1. min.MAP	R	20	90.13	10.59	0.001*
	M	20	104.80	9.58	
Ent.10. min.SAP	R	20	105.00	11.83	0.001*
	M	20	122.47	12.60	
Ent.10. min.DAP	R	20	59.53	10.89	0.001*
	M	20	77.40	11.17	
Ent.10. min.MAP	R	20	80.40	9.98	0.001*
	M	20	95.27	11.32	
Ent.20. min.SAP	R	20	100.40	14.22	0.04*
	M	20	112.87	12.20	
20.min.DAP	R	20	58.20	11.66	0.009*
	M	20	70.20	13.11	
20.min.MAP	R	20	77.60	10.69	0.135
	M	20	84.53	11.75	
30.min.SAP	R	20	98.00	14.18	0.146
	M	20	105.13	10.99	
30.min.DAP	R	20	56.53	11.74	0.152
	M	20	61.53	8.08	
30.min.MAP	R	20	75.73	10.84	0.519
	M	20	77.07	7.46	
40.min.SAP	R	20	102.33	11.02	0.299
	M	20	105.00	12.22	
40.min.DAP	R	20	56.93	9.90	0.221
	M	20	61.40	10.05	
40.min.MAP	R	20	75.67	8.90	0.418
	M	20	78.33	9.16	
50.min.SAP	R	20	100.13	10.34	0.14
	M	20	105.00	9.96	
Ent.50.min.DAP	R	20	55.53	10.88	0.071*
	M	20	63.53	10.76	
Ent.50.min.MAP	R	20	75.27	7.67	0.183
	M	20	79.13	9.09	
Ent.60.min.SAP	R	20	101.13	10.46	0.253
	M	20	104.13	11.93	
Ent.60.min.DAP	R	20	55.87	10.23	0.134
	M	20	61.07	10.52	
Ent.60.minMAP	R	20	75.13	8.18	0.406
	M	20	77.87	9.53	
ekst SAP	R	20	116.93	12.88	0.12
	M	20	125.53	19.40	
ekst DAP	R	20	68.20	13.45	0.349
	M	20	74.13	14.05	
ekst MAP	R	20	87.73	13.19	0.213
	M	20	93.60	17.23	
Ekst 5min. SAP	R	20	114.07	8.57	0.056
	M	20	124.93	22.21	
Ekst.5min. DAP	R	20	67.93	11.79	0.254
	M	20	72.40	13.94	
Ekst.5min. MAP	R	20	85.40	7.89	0.164
	M	20	91.87	16.27	

SAP; *Systolic arterial pressure,* ***DAP;*** *Diastolic arterial pressure,* ***MAP;*** *Mean arterial pressure*
*** *p<0.001 Statistically significant.*

Controlled hypotension is used to decrease intraoperative blood loss. Remifentanil, an ultra-short-acting µ-agonist opioid receptor, has recently been reported to provide appropriate surgical conditions during surgery with controlled hypotension [6-9]. Magnesium sulphate is a non-competitive NMDA receptor antagonist, and has been investigated as a possible adjuvant for intra- and postoperative analgesia [10]. In addition, magnesium sulphate is used as a vasodilator to control hypertension, and thus, reduce blood loss during endoscopic sinus surgery [4].

Magnesium sulphate was chosen as it is a vasodilator with minimal myocardial depression [3]. It produces a dose-dependent depressant effect on cardiac contractility and it has been shown that the depressant effect of magnesium on cardiac function is offset by lowering of the peripheral vascular resistance, thus maintaining cardiac pump function [11]. A study using magnesium sulphate during sevoflurane anaesthesia at doses of 30, 60 and even more than 120 mg kg^{-1} concluded that magnesium did not have a deleterious effect on atiroventricular (AV) conduction time and surface ECG during 1 minimal alveolar concentration (MAC) of sevoflurane; and recommended the use of high doses of magnesium sulphate in patients with cardiac arrhythmia and hypertension during sevoflurane anaesthesia [12]. Magnesium causes an increase in cerebral blood flow velocity [13], which would be beneficial in a hypotensive anaesthesia technique.

The use of different doses of magnesium to produce deliberate hypotension has been studied. In a study of patients undergoing cerebral-aneurysm clipping [3], an initial magnesium sulphate dose of 40 g h^{-1} was used until MAP of 70 mm Hg was reached, followed by 20 g h^{-1} until the target MAP was reached, and then 10 g h^{-1} for the remaining time [3]; however, anaesthesia had been maintained with a total i.v. technique using fentanyl and midazolam. Lower serum magnesium concentrations were found in a study [14] of patients undergoing major oral and maxillofacial surgery, where magnesium was given at a rate of 40 g h^{-1} after induction until the MAP reached 55[5] mm Hg, followed by a maintenance dose of 5 g h^{-1} until 30 min before the end of surgery, without loss of the hypotensive effect. This study [14] also compared deliberate hypotension induced by sodium nitroprusside with that produced by magnesium sulphate. The magnesium sulphate infusion showed poorer control of arterial pressure and had a slower onset, taking 28 [12] min to reach the desired MAP. As in our study, there was no rebound hypertension or reflex tachycardia associated with magnesium sulphate infusion.

In a study [15] in which controlled hipotension mg and remifentanil were compared, MAP values were found same in both groups. As for our study, we have found out that while both drugs decrease MAP, SAP, and DAP values, hemodinamia remains more stable in the periods of intubation, and ekstubation in remifentanil group. In the same study, it has been reported that no extra drug was applied to either group for the control of hemodinami. With regard to our study, extra drug was required in mg group. It is believed that the differences in both groups result from the characteristics of the patients. We are, also, of the opinion that comparative studies are to be carried out for the effectiveness of mg.

As magnesium is known as a central nervous system depressant, In the present study, anaesthesia was maintained during surgery with sevoflurane. Furthermore, the low solubility of sevoflurane makes it a good agent for rapid induction and fast emergence from anaesthesia with reduced airway irritability. In this study that is why we thought that we did not see delayed awakeness at our patients. In addition, a previous investigation showed that although sevoflurane has a hypotensive effect, it does not alter cerebral blood flow, whereas propofol has less protective effect on inner ear microcirculation [16]. Many studies have concluded that magnesium sulphate reduces anaesthetic and analgesic requirements for surgery [17]. And It is well known that magnesium sulphate potentiates the neuromuscular block induced by non-depolarizing neuromuscular blocking agents, and thereby reduces neuromuscular blocking agent consumption [18,19]. In our study we could not eveluate the consumtion of anaesthetics and analgesics and we did not assess neuromuscular block. It may be useful to eveluate these parameters in the future.

In summary, it appears that both magnesium sulphate and remifentanil can induce adequate hypotensive anaesthesia in patients undergoing middle ear surgery. However, remifentanil was found to be associated with a more favourable course during surgery.

References

1.Dikmen B, Sahin F, Ornek D, Pala Y, Kilci O, Horasanli E, Canturk M. Dexmedetomidine for Controlled Hypotension In Middle Ear Surgery with Low-FlowAnesthesia Int. Adv. Otol. 2010; 6:331-336

2-Aydin GB, Ozlu O, Alacakir H, Aksoy M. Controlled hypotension: remifentanil or esmolol duringtympanoplasty. Mediterr. J. Otol 2008; 4: 125-31

3- Crozier TA, Radke J, Weyland A, et al. Haemodynamic and endocrine effects of deliberate hypotension with magnesium sulphate for cerebral-aneurysm surgery. Eur J Anaesthesiol 1991;8:115-21.

4- Elsharnouby NM, Elsharnouby MM Magnesium sulphate as a technique of hypotensive anaesthesia. Br J Anaesth 2006; 96: 727-31.

5- Fromme GA, Mackenzie RA, Gould AB Jr, Lund BA, Offord KP. Controlled hypotension for orthognatic surery. Anesth Analg 1986; 65: 683-6.

6- Degoute CS, Ray MJ, Manchon M, Dubreil C, Bansillon V. Remifentanil and controlled hypotension; comparison with nitroprusside or esmolol during tympanoplasty. Can J Anaesth 2001; 48: 20-7.

7- Degoute CS,Ray MJ, Gueugniaud PY, Dubreuil C. Remifentanil induces consistent and sustained controlled hypotension in children during middle ear surgery. Can J Anaesth 2003; 50: 270-6.

8- Fodale V, Schifilliti D, Pratico C, Santamaria LB. Remifentanil and the brain. Acta Anaesthesiol Scand 2008; 52: 319-26.

9- Guntz E, Dumont H, Roussel C,et al. Effects of remifentanil on N-methyl-d-aspartate receptor: an electrophysiologic study in rat spinal cord. Anesthesiology 2005; 102:1235-41.

10- Levaux C, Bonhomme V, Dewandre PY, Brichant JF, Hans P. Effect of intra-operative magnesium sulphate on pain relief and patient comfort after major lumbar orthopaedic surgery. Anaesthesia 2003; 58: 131-5.

11- Nakaigawa Y, Akazawa S, Shimizu R, et al. Effects of magnesium sulphate on the cardiovascular system, coronary circulation, myocardial metabolism in anaesthetized dogs. Br J Anaesth 1997; 79: 363-8.

12- Akazawa S, Shimizu R, Nakaigawa Y, Ishii R, Ikeno S, Yamato R. Effects of magnesium sulphate on atrioventricular conduction times and surface electrocardiogram in dogs anaesthetized with sevoflurane. Br J Anaesth 1997; 78: 75-80.

13- Ludbrook GL, James MF, Upton RN. The effect of magnesium sulfate on cerebral blood flow velocity, cardiovascular variables, and arterial carbon dioxide tension in awake sheep. J Neurosurg Anesthesiol 1999; 11: 96-101.

14- Sanders GM, Sim KM. Is it feasible to use magnesium sulphate as a hypotensive agent in oral and maxillofacial surgery? Ann Acad Med Singapore 1998; 27:780-5.

15- Ryu JH, Sohn IS, Do SH. Controlled hypotension for middle ear surgery: a comparison between remifentanil and magnesium sulphate. Br J Anaesth. 2009; 103: 490-5.

16- Albera R, Ferrero V, Canale A, De Siena L, Pallavicino F, Poli L. Cochlear blood flow modifications induced by anaesthetic drugs in middle ear surgery: comparison between sevoflurane and propofol. Acta Otolaryngol 2003; 123: 812-6.

17- Steinlechner M, Dworschak B, Birkenberg G, et al. Magnesium moderately decreases remifentanil dosage required for pain management after cardiac surgery. Br J Anaesth 2006; 96: 444-9.

18- Ryu JH, Kang MH, Park KS, Do SH. Effects of magnesium sulphate on intraoperative anaesthetic requirements and postoperative analgesia in gynaecology patients receiving total intravenous anaesthesia. Br J Anaesth 2008; 100: 397-403.

19- Kussman B, Shorten G, Uppington J, et al. Administration of magnesium sulphate before rocuronium: effects on speed of onset and duration of neuromuscular block. Br J Anaesth 1997; 79:122-4.