Magnesium sulfate decreases the dose of rocuronium for satisfactory double lumen tube placement condition in patients with myasthenia gravis

Shoujun Fei  
Hongkong University Shenzhen Hospital

Hengfu Xia  
Hongkong University Shenzhen Hospital

Xiaowei Chen  
Hongkong University Shenzhen Hospital

Dazhi Pang  
Hongkong University Shenzhen Hospital

Xuebing Xu (✉ xuxuebing@hotmail.com)  
Hongkong University Shenzhen Hospital  https://orcid.org/0000-0002-5042-0578

Research article

Keywords: Magnesium sulfate; double lumen tube; myasthenia gravis; intubation; rocuronium

Posted Date: February 27th, 2019

DOI: https://doi.org/10.21203/rs.2.414/v1

License: © This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Version of Record: A version of this preprint was published on August 31st, 2019. See the published version at https://doi.org/10.1186/s12871-019-0841-4.
Abstract

Background: Titrating a low dose of non-depolarizing neuromuscular blockers for induction of general anesthesia for patients with myasthenia gravis (MG) is a popular accepted practice. This practice may confront with unsatisfactory intubation conditions, especially for double lumen tube (DLT). This double-blind randomised study was to investigate whether magnesium sulfate could decrease the rocuronium demand and improve the DLT placement conditions for MG patients who scheduled for video-assisted thoracoscopic (VATS) thymectomy. Methods: The patients were randomly assigned into the magnesium sulfate or normal saline group. After acquiring the adequate sedative depth, magnesium sulfate(60mg.kg-1) or normal saline(control) was given to the patients in two groups respectively. After that, the same Train of Four (TOF) value was obtained with one or more doses of 0.05 mg.kg-1 rocuronium with 3 minutes interval, then DLT was intubated. The primary and secondary observational outcomes were the cumulative rocuronium dose and the intubation condition for DLT placement respectively. Results: 23 patients in the magnesium sulphate group and 22 patients in the control group completed the study. The amount of rocuronium used to meet the setting value of TOF were 0.10 (0.05)mg.kg-1 and 0.28(0.17) mg.kg-1 in the magnesium sulphate and control group respectively (P<0.0001). Under a similar depth of neuromuscular blockade and sedation, 23 patients in magnesium sulphate group and 16 patients in control group showed excellent intubation condition. The patients in both groups showed similar characteristics of recovery from neuromuscular blockade. Conclusions: Our research showed that magnesium sulfate could decrease the rocuronium demand for satisfactory DLT intubation condition in MG patients.

Background

Myasthenia Gravis (MG) is a chronic neuromuscular disease characterized by skeletal muscle weakness. Maximal thymectomy is one of the treatment options recommended for all patients who have mild to moderate muscle weakness due to myasthenia gravis [1]. There are several different approaches for maximal thymectomy, of which right sided video-assisted thoracoscopic (VATS) thymectomy is gaining popularity [2]. MG patients are highly sensitive to nondepolarizing neuromuscular blockers [3]. When performing general anesthesia for these patients, neuromuscular blocker (NMB) administration is always a controversial issue [3,4]. The use of NMB in MG patients may increase the risk of unsuccessful extubation and postoperative respiratory failure, what's more, in some circumstances, perioperative stress induced exacerbation of MG makes these risks more complicated [4-6]; while the strategy of no NMB may result in unsatisfactory intubation condition and increase the incidence of upper airway injury [7]. In my institution, we routinely titrate small doses of non-depolarizing NMB till Train of Four (TOF), the neuromuscular monitoring parameter, is less than 10% before intubation in MG patients. For VATS thymectomy, this strategy cannot guarantee satisfactory intubation conditions because double lumen tube (DLT) placement demands much better conditions compared with single lumen tube.

Magnesium sulphate is an agent with analgesic, anaesthetic and NMB effects [8,9]. Previous research showed after the adminstration of rocuronium, the period of time required to achieve 95% suppression of
TOF was shortened if pre-treated with magnesium sulphate [10]. Here we investigated whether magnesium sulfate could decrease the rocuronium dose demand and improve the DLT placement conditions in patients with MG.

Methods

The study was approved by the Hospital Institutional Review Board and registered with the Clinical Trial Registry of China (ChiCTR-1800017696).

Consecutive patients diagnosed as MG grade I~II of Osserman classification scheduled to undergo right sided VATS thymectomy were enrolled in this study between May 2016 and May 2018. The diagnosis was confirmed by the presence of circulating antibody to the acetylcholine receptor, typical clinical and laboratory findings (ptosis, diplopia, limb weakness, and a decremental conduction response on electrical stimulation of the nerve supply to the deltoid muscle). Written informed consent was obtained from patients the day before the operation. Exclusion criteria included suspected difficult intubation, BMI >30 kg.m$^{-2}$, age less than 18 or over 60 years old, hepatic or renal dysfunction, cardiovascular dysfunction, neurologic disorder, operational time over 4 hours, intraoperative blood loss over 1000 ml, history of chronic pulmonary disease, chronic medication with calcium channel blocker or magnesium, history of known allergy to magnesium sulphate or any other study drugs, and coexisting autoimmune diseases, such as hyperthyroidism, rheumatoid arthritis, scleroderma or lupus.

The selected patients were randomly assigned to magnesium sulfate or normal saline (control) group. A random sequence was kept within a sealed opaque envelope by an assistant not involved in this study. On the morning of the surgery, the assistant opened a sealed envelope and prepared magnesium sulfate (60mg.kg$^{-1}$ diluted in 50ml normal saline) or 50ml normal saline according to the group allocation. The anaesthetist was blinded to the study drug.

Anticholinesterase medication and/or steroid drug was continued as the patient’s routinely treatment regimen until the morning of surgery. No premedication was given to the patients. Once upon the patient arrived operative room, anesthesia monitoring, including SpO$_2$, ECG, noninvasive blood pressure, bispectral index (BIS™ sensor; Medtronic, Minneapolis, MN, USA) monitoring was applied. Bispectral index was recorded using BISx Power Link™ by Philips Medical Systems (Royal Philips Electronics, Eindhoven, The Netherlands). After checking the patient’s information with the surgeon and operative circulating nurse, an 18 intravenous cannula and a left radial artery line were placed under local anesthesia with 2% lidocaine, and then the noninvasive blood pressure monitoring was changed to invasive continuous blood pressure monitoring. All the monitoring data were retrieved from an automatic anesthesia information system which was linked to the patient’s physiological monitor and was recorded.

Anesthesia was induced with 4µg.kg$^{-1}$ fentanyl and propofol target controlled infusion (TCI) with Marsh model built-in pump (Fresenius Kabi AG, Bad Homburg, Germany) started with effect-site concentration (Ce) 2µg.ml$^{-1}$ and aimed for patient’s unconsciousness with BIS value at 40-60. The patients were...
ventilated with face masks and kept end tidal carbon dioxide between 30-45 mmHg. After BIS value was kept between 40-60 for 10 minutes with relative stabilized propofol concentration, the TOF monitoring at the adductor pollicis muscle (ISx Power Link™ by Philips Medical Systems) was started with electric stimulation (amplitude 50mA, interval time 20 seconds). For TOF monitoring, 2 surface electrodes were placed on cleaned skin overlying the ulnar nerve at the wrist. After the basal TOF was recorded, the observational drug (magnesium sulfate or normal saline) was given in 5 minutes. Five minutes later after observational drug infusion was finished, the TOF was recorded. If the TOF was larger than 10%, 0.05mg.kg⁻¹ rocuronium and repeated dose of rocuronium in a 3 minutes interval was given intravenously until the TOF was less than 10%. After the TOF less than 10%, the DLT was intubated with direct video laryngoscopy. The intubation was performed by an experienced anaesthetist. If the tracheal intubation was not successfully completed within 20 s, it was recorded as a failed attempt. Mean blood pressure (MAP) and heart rate (HR) were recorded before intubation (Pre-intubation), and after intubation (Post-intubation), the maximum values of MAP and HR within 3 minutes after intubation were also recorded.

The intraoperative anesthesia was maintained with propofol TCI and remifentanil 2~4µg.kg⁻¹ according to clinical need and BIS values (40-60). Before skin incision, local anesthesia was performed with 0.5% ropivacaine 10ml. During the operation, we did not give any NMB. After the end of operation, if the TOF was less than 90% or the anaesthetist was not satisfied with recovery of the respiratory function, neostigmine 0.05mg.kg⁻¹ and calcium chloride 1g were given to the patient. 15~30 minutes before the end of operation, 40mg parecoxib was administered for prevention of postoperative pain, and 4mg ondansetron plus 5 mg dexamethasone was administered for prevention of postoperative nausea and vomiting (PONV). During the operation, 5mg.kg⁻¹.h⁻¹ Ringer's lactate solution was given, and no urine catheter was used. Epinephrine was used to maintain blood pressure normal if necessary. All thymectomy was conducted with right sided VATS thymectomy with three holes. Before closing the chest ports, negative suction of chest cavity combined with lung recruitment maneuvers was used to re-expand the right collapsed lung. No postoperative chest duct drainage was left.

The primary observational outcome of this study was the cumulative rocuronium dose during the induction. The secondary outcome was intubation condition for DLT placement. The DLT intubation condition quality was evaluated based on Copenhagen Consensus Conference scoring system: ease of laryngoscopy, vocal cord position and/or movement and response to intubation or cuff inflation (cough or diaphragmatic movement), and further classified as excellent, fair or difficult [11,12]. Other outcomes including intubation stimulation induced MAP and HR change (Post-intubation vs. Pre-intubation), propofol concentration when intubation, time from last dose of rocuronium administration to TOF returned to 90%, the needed time for extubation based on the decision of the anaesthetist (measured from the moment of the end of the operation). After extubation, 0-100mm visual analogue score (VAS) , postoperative Riker sedation and agitation scale and PONV were recorded. For 0-100mm VAS, we classified the patients' postoperative pain intensity as none, mild, moderate, or severe. The following cut points on the pain VAS were determined: no pain (0–4 mm), mild pain (5–44 mm), moderate pain (45–74 mm), and severe pain (75–100 mm) [13]. For Riker sedation and agitation scales, we further divided the
patients into three categories according to the scale: over sedated (scales 1 - 2), non-agitated (scales 3 - 4) and agitated (scales 5 - 7) [14,15].

We estimated the sample size based on the primary outcome (cumulative rocuronium dose used for intubation). In our pilot study, the mean difference of the initial rocuronium dose between magnesium sulfate group and normal saline group was 0.14mg.kg\(^{-1}\) with a pooled variance (SD) of 0.11. To obtain an alpha value of 0.05 and a test power of 80%, about 12 subjects were needed in each group. Anticipating about 20% dropout rate, we roughly estimated that 30 patients were needed.

Continuous variables presented as mean (SD) or number (%) were compared by Student t-test, F-test, Chi-square test or Fisher’s exact test. Categorical variables are presented as the number of patients and were compared by Chi-square test or Fisher’s exact test. A \(P\) value <0.05 was considered significant. Data Analyses were accomplished using MedCalc for Windows, version 11.4.2.0 (MedCalc Software, Mariakerke, Belgium).

**Results**

In total, 61 eligible patients were approached to participate in the study. Nine patients refused to participate, and 3 patients in magnesium sulphate group and 4 patients in control group were excluded for uncompleted observational data collection or for long operational time (Fig 1). Finally, 23 patients who received magnesium sulfate and 22 patients who received normal saline were included in the analysis.

Patients had similar clinical characteristics (sex, age, BMI) including Osserman classification and length of MG history in both groups. All intubation procedures were successful with one attempt. No difference was found between the two groups in operation time (Table 1). There was no incidence of postoperative myasthenic crisis and postoperative prolonged tracheal extubation in any patients. After the operation, all the patients were extubated in the operation room and transferred to ward via postoperative anesthesia recovery unit (PACU).

Magnesium sulphate (60mg.kg\(^{-1}\)) given in 5 minutes did not show obvious effects on the MAP and HR. After the observational drug was given, the TOF value of patients in magnesium sulfate group dropped from 95.7(10.5) to 77.2(29.2), which showed a significant decrease( \(p = 0.095\)); whereas the TOF value of patients in the control group was quite stable (94.7(12.2) vs 95.9(9.58), \(p = 0.211\)). Pretreatment with magnesium sulphate decreased the amount of rocuronium required to meet the setting depth of neuromuscular blockade (TOF<10%). Before intubation, propofol concentration did not show obvious difference in maintaining BIS between 46-60 (Table 2). Under the similar depth of neuromuscular blockade and sedation, patients in the magnesium sulphate group showed more satisfactory intubation condition (Table 2). DLT intubation procedure and stimulation induced significant increase of MAP and HR in control group, whereas no obvious change of MAP and HR was found in magnesium sulphate group (Table 3).
Pretreating with magnesium sulphate did not increase the time from the last dose of rocuronium administration to the TOF returned to 90%, and also did not affect the extubation time from the end of operation (Table 2).

Though there was no difference between two groups in postoperative pain intensity, the patients in control group showed higher postoperative readings on the Riker sedation and agitation scale (Table 2). No PONV cases in either group was reported in PACU.

Discussion

As we knew, the myasthenic patient is extremely sensitive to nondepolarizing NMBs (eg, rocuronium, vecuronium, cisatracurium) [3,16]. Very small dose and residual neuromuscular effect may result in respiratory distress or loss of airway protection during emergence from anesthesia. Owing to the concern of extubation delay and admission into ICU, for MG patients, most anaesthetists prefer to avoid NMB, whereas intubation without NMBs was reported increasing the risk of difficult tracheal intubation and intubation-related complications [4,5].

Though recent evidence had showed that rocuronium combined it's specific antagonist sugammadex might be a good choice for muscle relax management for MG patients [16-18], while sugammadex is quite expensive and still not available in some countries and regions [19]. Thus currently, using a minimal dose of intermediate-acting NMB is a more common choice of tracheal intubation for MG patients [16,17]. Here we found that pre-administration of magnesium sulfate 60mg.kg$^{-1}$ could significantly decrease the rocuronium demand and improve the intubation condition for DLT placement with the same degree of neuromuscular blockade monitored with TOF.

Magnesium had an inhibitory effect on neuromuscular transmission and caused a decrease in muscle fiber membrane excitability. It decreased pre-junctional release of acetylcholine from the motor nerve terminal by decreasing the calcium conductance of presynaptic voltage-dependent calcium channels, and it also reduced sensitivity of the endplate to acetylcholine [20,21]. Magnesium shows significant neuromuscular blockade at high plasma concentrations (5 to 10 mM) or at lower concentrations ($\geq 1$ mM) in the presence of neuromuscular-blocking agents [20,21]. Several studies had showed that magnesium sulphate could decrease the amount of rocuronium required to maintain adequate neuromuscular blockade during different kinds of surgery [22,23]. In our research, after 60mg.kg$^{-1}$ magnesium sulfate was administrated, TOF value in MG patients decreased from 96% to 77%, and further resulted in a significant decrease of the rocuronium demand for targeted TOF.

With the same TOF value, which means the same neuromuscular block degree, the patients in magnesium sulphate group illustrated better intubation condition and less hemodynamic change caused by laryngoscope and tracheal intubation. This may relate to the anti-noxious stimulation effects of magnesium sulfate on the laryngoscope and tracheal intubation [24]. The mechanism of this action is
proved to be inhibition of catecholamine release from adrenal medulla and adrenergic nerve endings [8]. Our results were similar to other research for single lumen tube placement [25,26].

Though some research had showed that magnesium sulphate decreased the intravenous and inhaled anaesthetics for induction [8,27], while in our study, magnesium sulphate did not decrease the propofol concentration targeted for similar sedative depth. This discordance is possibly related to the small sample size in our study, and magnesium sulphate exerts more enhancement effects on neuromuscular blocker than that of on sedative agent.

After being pretreated with magnesium sulfate, an increased speed of onset and a prolongation of the recovery period of neuromuscular blockade has been observed with rocuronium and other non-depolarizing neuromuscular blocking agents [28-30]. Whereas in our research, possibly because the rocuronium dose used for intubation was less in magnesium sulphate group, the time taken for TOF recovery to 90% from the last dose of rocuronium and the extubation time from the end of operation showed no difference between the magnesium sulphate and control groups.

Though there are two meta-analyses which independently concluded that perioperative systemic magnesium sulphate administration could decrease the postoperative pain scores and opioid consumption [31,32], we did not get this result. Compared to other studies, the reason for this difference may be because that we just gave one dose of magnesium sulphate before DLT intubation and did not continuously administer magnesium sulphate during the VATS thymectomy procedure, and also because we provide a comprehensive pain treatment (local anesthesia and intravenous parecoxib were given). The Riker sedation and agitation scale showed that the patients in magnesium sulphate group felt more comfortable and were more cooperative than those in control group. This result was consistent with Abdulatif’s finding that magnesium sulphate decreases the incidence and severity of emergence agitation in children undergoing adenotonsillectomy [33]. In Abdulatif’s research, magnesium sulphate also did not find any beneficial effect on the postoperative pain. There are many factors related to postoperative agitation, and pain is only one of them, therefore the discordance effect of magnesium sulphate on postoperative agitation and pain in our and Abdulatif’s research is acceptable.

When selecting a drug for a specific purpose, one should consider the balance between its efficiency and associated side-effects. Magnesium sulphate (50 - 60 mg.kg) was not associated with serious complications in previous studies [31,32]. In present study, the MAP and HR was quite stable during and after magnesium sulphate infusion. Combined with the advantage of magnesium sulphate on decrease of rocuronium dose and improvement of intubation condition for DLT, we concluded that intravenous magnesium sulphate is an appropriate adjuvant for DLT intubation in MG patients. Although magnesium sulphate had been extensively investigated as an adjuvant for neuromuscular blocker, this is the first study to describe the benefits of magnesium sulphate on DLT placement in MG patients.

There are two limitations in this study. The first is that the patients enrolled in our study were classified Osserman I~II and aged less than 60 years. The effects of magnesium sulphate on these patients may be different to that on those patients of Osserman classification III and over, or aged older than 60, therefore
our conclusion cannot be applied in those types of patients. The second limitation is related to the titration method of rocuronium, the dose of total rocuronium in the control group was larger than that of the magnesium sulphate group; thus the duration of rocuronium administration in the control group was longer than that of the magnesium sulphate group. This duration difference resulted in a difference in total anesthesia time and could be a confounding factor for emergence characteristics of two groups.

Conclusions

In conclusion, magnesium sulfate could decrease the rocuronium demand for DLT placement and improve the intubation condition in patients with MG, and could possibly improve emergence quality without severe complications.

Abbreviations

MG: Myasthenia gravis; VATS: Video-assisted thoracoscopic; NMB: Neuromuscular blocker; TOF: Train of Four; DLT: Double lumen tube; BMI: Body mass index; ECG: Electrocardiogram; BIS: Bispectral index; TCI: Target controlled infusion; Ce: Effect-site concentration; MAP: Mean blood pressure; HR: Heart rate; PONV: Postoperative nausea and vomiting; VAS: Visual analogue score; PACU: Postoperative anesthesia recovery unit; ICU: Intensive care unit; SD: Standard deviation

Declarations

Ethics approval and consent to participate

The study was approved on April 8th, 2016 by the Hospital Institutional Review Board of Hongkong University Shenzhen Hospital and registered with the Clinical Trial Registry of China (ChiCTR-1800017696). We have obtained written informed consents from all of the participants in the study.

Consent for publication

The written consents of publication were obtained from all of the authors.

Availability of data and materials

The raw data and materials are available from the corresponding author upon reasonable request.

Competing interests

There are no competing interests to declare.

Funding

This study was supported by a grant from Science and Technology Innovation Committee of Shenzhen, China (201607030), and a grant from Science and Innovation Fund of Shenzhen, Guangdong,
China(JCYJ20150331142757390).

Authors’ contributions

XB X and SJ F searched the database, designed the study. DZ P helped to invent the main idea of research, collected the data and coordination. HF X and XW C helped in clinical cases and collected the data. XB X and SJ F participated in the data collection and the data analysis. XB X wrote the primary and final manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not Applicable

References

1. Ricciardi R, Melfi F, Maestri M, De Rosa A, Petsa A, Lucchi M, Mussi A. Endoscopic thymectomy: a neurologist’s perspective. Ann Cardiothorac Surg 2016; 5:38-44.
2. Elsayed HH, Gamal M, Raslan S, Abdel Hamid H. Video-assisted thoracoscopic thymectomy for non-thymomatous myasthenia gravis: a right-sided or left-sided approach? Interact Cardiovasc Thorac Surg 2017; 25:651-653
3. Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. Acta Anaesthesiol Scand 2012; 56:17-22
4. Fujita Y, Moriyama S, Aoki S, et al. Estimation of the success rate of anesthetic management for thymectomy in patients with myasthenia gravis treated without muscle relaxants: a retrospective observational cohort study. J Anesth 2015; 29:794-7
5. Della Rocca G, Coccia C, Diana L, et al. Propofol or sevoflurane anesthesia without muscle relaxants allow the early extubation of myasthenic patients. Can J Anaesth 2003; 50:547-52
6. Juel VC. Myasthenia gravis: management of myasthenic crisis and perioperative care. Semin Neurol 2004; 24:75-81
7. Lundstrøm LH, Duez CHV, Nørskov AK, et al. Effects of avoidance or use of neuromuscular blocking agents on outcomes in tracheal intubation: a Cochrane systematic review. Br J Anaesth 2018; 120:1381-1393
8. Herroeder S, Schonherr ME, De Hert SG, Hollmann MW. Magnesium - essentials for anesthesiologists. Anesthesiology 2011; 114: 971–93
9. Aissaoui Y, Qamous Y, Serghini I, Zoubir M, Salim JL, Boughalem M. Magnesium sulphate: an adjuvant to tracheal intubation without muscle relaxation—a randomised study. Eur J Anaesthesiol 2012; 29:391-7
10. Kim MH, Oh AY, Jeon YT, Hwang JW, Do SH. A randomised controlled trial comparing rocuronium priming, magnesium pre-treatment and a combination of the two methods. Anaesthesia 2012; 67: 748-54
11. Fuchs-Buder T, Claudius C, Skovgaard LT, et al. Good clinical research practice in pharmacodynamic studies of neuromuscular blocking agents II: the Stockholm revision. Acta Anaesthesiol Scand 2007; 51:789-808

12. Thwaites AJ, Edmends S, Tomlinson AA, Kendall JB, Smith I. Double-blind comparison of sevoflurane vs propofol and succinylcholine for tracheal intubation in children. Br J Anaesth 1999; 83: 410-414

13. Jensen MP, Chen C, Brugger AM. Interpretation of visual analog scale ratings and change scores: a reanalysis of two clinical trials of postoperative pain. J Pain 2003; 4: 407–14

14. Lepousé C, Lautner CA, Liu L, Gomis P, Leon A. Emergence delirium in adults in the post-anaesthesia care unit. Br J Anaesth 2006; 96:747-53

15. Riker RR, Picard JT, Fraser GL. Prospective evaluation of the sedation-agitation scale for adult critically ill patients. Crit Care Med 1999; 27: 1325–1329

16. Anesthesia for the patient with myasthenia gravis. Available from https://www.uptodate.com/contents/anesthesia-for-the-patient-with-myasthenia-gravis (last updated: Dec 11, 2017)

17. Sungur Z, Sentürk M. Anaesthesia for thymectomy in adult and juvenile myasthenic patients. Curr Opin Anaesthesiol 2016;29:14-9

18. Sungur Ulke Z, Yavru A, Camci E, Ozkan B, Toker A, Senturk M. Rocuronium and sugammadex in patients with myasthenia gravis undergoing thymectomy. Acta Anaesthesiol Scand 2013; 57:745-8

19. Ledowski T, Hillyard S, Kozman A, Johnston F, Gillies E, Greenaway M, Kyle BC. Unrestricted access to sugammadex: impact on neuromuscular blocking agent choice, reversal practice and associated healthcare costs. Anaesth Intensive Care 2012; 40:340-3

20. Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. Br J Anaesth 1999; 83:302-20

21. Del Castillo J, Engbaek L. The nature of the neuromuscular block produced by magnesium. J Physiol 1954; 124: 370–84

22. Gupta K, Vohra V, Sood J. The role of magnesium as an adjuvant during general anaesthesia. Anaesthesia 2006; 61:1058-63

23. Na HS, Lee JH, Hwang JY, Ryu JH, Han SH, Jeon YT, Do SH. Effects of magnesium sulphate on intraoperative neuromuscular blocking agent requirements and postoperative analgesia in children with cerebral palsy. Br J Anaesth 2010; 104: 344-50

24. James MF, Cronjé L. Pheochromocytoma crisis: the use of magnesium sulfate. Anesth Analg 2004; 99:680-6

25. Park SJ, Cho YJ, Oh JH, Hwang JW, Do SH, Na HS. Pretreatment of magnesium sulphate improves intubating conditions of rapid sequence tracheal intubation using alfentanil, propofol, and rocuronium - a randomized trial. Korean J Anesthesiol 2013; 65:221-7
26. Kiraci G, Demirhan A, Tekelioglu UY, et al. A comparison of the effects of lidocaine or magnesium sulfate on hemodynamic response and QT dispersion related with intubation in patients with hypertension. Acta Anaesthesiol Belg 2014; 65:81-6

27. Seyhan TO, Tugrul M, Sungur MO, Kayacan S, Telci L, Pembecl K, Akpir K. Effects of three different dose regimens of magnesium on propofol requirements, haemodynamic variables and postoperative pain relief in gynaecological surgery. Br J Anaesth 2006; 96:247-52

28. TCzarnetzki C, Lysakowski C, Elia N, Tramèr MR. Time course of rocuronium-induced neuromuscular block after pre-treatment with magnesium sulphate: a randomised study. Acta Anaesthesiol Scand 2010; 54:299-306

29. Rodríguez-Rubio L, Solis Garcia Del Pozo J, Nava E, Jordán J. Interaction between magnesium sulfate and neuromuscular blockers during the perioperative period. A systematic review and meta-analysis. J Clin Anesth 2016; 34:524-34

30. Kim SH, So KY, Jung KT. Effect of magnesium sulfate pretreatment on onset and recovery characteristics of cisatracurium. Korean J Anesthesiol 2012; 62:518-23

31. Albrecht E, Kirkham KR, Liu SS, Brull R. Peri-operative intravenous administration of magnesium sulphate and postoperative pain: a meta-analysis. Anaesthesia 2013; 68:79-90

32. De Oliveira GS Jr, Castro-Alves LJ, Khan JH, McCarthy RJ. Perioperative systemic magnesium to minimize postoperative pain: a meta-analysis of randomized controlled trials. Anesthesiology 2013; 119:178-90.

33. Abdulatif M, Ahmed A, Mukhtar A, Badawy S. The effect of magnesium sulphate infusion on the incidence and severity of emergence agitation in children undergoing adenotonsillectomy using sevoflurane anaesthesia. Anaesthesia 2013; 68:1045-52.

### Tables

|                         | Magnesium sulfate group (n=23) | Normal saline group (n=22) | P   |
|-------------------------|-------------------------------|----------------------------|-----|
| Age (year)              | 34.4±11.3§                    | 30.3±9.0§                  | 0.185|
| Body weight             | 55.8±8.0§                     | 60.5±11.0§                 | 0.111|
| BMI (kg.m⁻²)            | 21.7±2.0§                     | 22.2±3.0§                  | 0.577|
| Sex (Male / Female)     | 4 / 19                        | 7 / 15                     | 0.260|
| MG history ≥6 years / <6 years | 6 / 17                       | 8 / 14                     | 0.457|
| Osserman stage(I / IIA / IIB) | 6 / 11 / 6                  | 8 / 6 / 8                  | 0.364|
| Operation time (minutes)| 110.1(31.6)                  | 117.7(24.4)                | 0.370|
Table 2 Anesthesia and emergence data. Data are presented as mean (standard deviation) or number of patients.

|                             | Magnesium sulfate group (n=23) | Normal saline group (n=22) | P     |
|-----------------------------|--------------------------------|-----------------------------|-------|
| Rocuronium dosage (mg.kg\(^{-1}\)) | 0.10 (0.05)                   | 0.28 (0.17)                 | <0.0001* |
| Propofol concentration when intubation | 3.15 (0.36)                   | 3.37 (0.91)                 | 0.267 |
| Intubation condition score (excellent / fair / poor) | 23 / 0 / 0                     | 16 / 5 / 1                  | 0.027* |
| Time of TOF recovered to 0.9 after the last dose of rocuronium | 50.5 (42.4)                    | 47.2 (42.2)                 | 0.881 |
| Time of extubation time from the end of operation | 9.4 (5.6)                      | 10.5 (6.8)                  | 0.561 |
| Postoperative pain intensity (free / mild / moderate) | 15 / 7 / 1                     | 8 / 6 / 6                   | 0.056 |
| Riker sedation and agitation scale in PACU (non-agitated / agitated) | 23 / 0                         | 16 / 6                      | 0.009* |

*Significant at P=0.05
Table 3  MAP and HR before intubation (Pre-intubation) and after intubation (Post-intubation). Data are presented as mean (standard deviation).

|                | MAP (mmHg)       | HR (bpm)       |
|----------------|------------------|----------------|
|                | Magnesium sulfate | Normal saline  | Magnesium sulfate | Normal saline  |
| Pre-intubation  |                  |                |                  |                |
| Group (n=23)   | 65.6(11.7)       | 69.5(12.3)     | 62.0(13.5)       | 59.0(9.2)      |
| Post-intubation | 69.3(12.3)       | 86.2(7.42)     | 66.8(12.7)       | 76.4(17.1)     |
| P              | 0.309            | <0.0001*       | 0.218            | 0.001*         |

*Significant at P=0.05

MAP: Mean arterial blood pressure; HR: heart rate

Figures
Figure 1

Consort flowchart.