Comparison of Dexmedetomidine and Magnesium Sulphate in Attenuation of Airway and Pressor Responses during Extubation in Patients Undergoing Craniotomies

Neelima Tandon[1], Shikha Goyal[2]

ABSTRACT

Introduction: The anaesthatic technique for intracranial neurosurgery must provide cardiovascular stability during extubation period. This study was conducted to compare the effect of dexmedetomidine and magnesium sulphate in attenuation of haemodynamic and airway responses during endotracheal extubation in patients undergoing craniotomies for intracranial space occupying lesion (ICSOL).

Material and Methods: Ninety patients of ASA grade I and II, age 18 -50 yrs scheduled for craniotomy for nonvascular ICSOL were studied after randomization into 3 groups with 30 patients in each group. Group D, M and C received an IV infusion of dexmedetomidine 0.5µg/kg, magnesium sulphate 30 mg/kg and normal saline 100 ml respectively over 10 min at the time of skin closure in a double blind manner. Heart rate, systolic and diastolic blood pressure were recorded just before drug administration, 3 and 5 min after drug administration, during extubation and at 3, 5, 10 and 15 minutes after extubation. Respiratory rate, oxygen saturation were analyzed at 3, 5, 10 and15 min after extubation. Extubation quality rated on a 5 point scale and postoperative sedation on Ramsay sedation scale. Any laryngospasm, bronchospasm, desaturation, respiratory depression, vomiting, hypotension, bradycardia was noted.

Results: Heart rate, systolic and diastolic blood pressure increased during emergence time in all the three groups but these parameters were significantly lower in group D than group C ($p<0.01$) and M ($p<0.05$) and significantly lower in group M than group C. Twenty seven patients had extubation score 1 in group D as compared to 19 and 18 patients in group C and M respectively ($p<0.05$). Sedation score of most patients was 3 in group D and 1 in group M and C ($p<0.01$). There were no significant differences in the prevalence of adverse events among the 3 groups.

Conclusion: Dexmedetomidine 0.5µg/kg is more effective than magnesium sulfate 30 mg/kg in controlling haemodynamic and airway reflexes during endotracheal extubation in craniotomy.

Keywords: Airway, haemodynamic reflexes, dexmedetomidine, extubation, Magnesium sulfate, craniotomies

INTRODUCTION

Tracheal extubation is an important event in course of general anaesthesia which causes a modest (10% to 30%) and transient (lasting approximately 5 to 15 min) increase in heart rate and blood pressure.[1] Extubation is associated with reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. These changes are transient and probably of no consequences in healthy individual going for general surgery, but has a major concern for patients with coronary artery disease[2], cerebrovascular disease[3] and in hypertensive patients.[4] In patients undergoing general anaesthesia for intracranial space occupying lesions (ICSOL), haemodynamic changes and in particular arterial hypertension may increase the risk of postoperative intracranial edema and haemorrhage.[5] Basali et al reported 57% incidence of post craniotomy hypertension.[6]

Different drugs and techniques has been used to attenuate the pressor response such as narcotic analgesics[7], local anaesthetics[8], calcium channel blockers[9] and adrenoceptor blockers[10,11] but none has been found completely successful.

Dexmedetomidine, a highly selective α_2 adrenoceptor agonist decreases the sympathetic outflow and noradrenergic activity thereby counteracting haemodynamic fluctuation occurring at the time of extubation due to increased sympathetic stimulation.[12] It is increasingly being used as a sedative for monitored anaesthesia care (MAC) because of its analgesic properties, "cooperative sedation" and lack of respiratory depression.[13]

Recently the importance of magnesium in anaesthetic practice has been highlighted. Magnesium is naturally occurring calcium antagonist and noncompetitive antagonist of N-methyl D-aspartate (NMDA) receptor.[14] It inhibits many calcium mediated responses like the release of catecholamine from both adrenal glands and adrenergic nerve terminals in response to sympathetic stimulation.[15] Intravenously administered magnesium sulphate is capable of attenuating the adverse haemodynamic response associated with endotracheal intubation[16].

This study was planned to evaluate and compare the beneficial effects of intravenous dexmedetomidine and magnesium sulphate in attenuation of haemodynamic responses and airway reflexes during extubation period in craniotomies for ICSOL under general anaesthesia.

MATERIAL AND METHODS

The present study was approved by the ethics committee of the institution. This study was conducted as prospective, randomized, placebo controlled, double blind study.

Ninety patients of ASA grade I and II**,** age group 18 to 50 years of either sex admitted for craniotomies for nonvascular ICSOL under general anaesthesia were included for study. Patients

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with cardiopulmonary diseases, hepatic dysfunction, renal dysfunction, psychiatric illness, pregnant and lactating patients and any patient who required postoperative ventilation were excluded from study.

After taking written informed consent from patients preanaesthetic assessment of all the selected patients were done with complete history and physical examination. Routine investigations like complete blood count, blood sugar, blood urea, serum creatinine, chest X-ray and ECG were done.

Patients were randomized into 3 groups of 30 patients each via sealed envelope technique.

Group C (control): 100 ml normal saline IV infusion over a period of 10 min.

Group D: 0.5 µg/kg inj. dexmedetomidine in 100 ml normal saline slow IV infusion over 10 min.

Group M: 30 mg/kg inj. magnesium sulphate in 100 ml normal saline slow IV infusion over 10 min.

Study drugs were given at the time of skin closure.

Patients were kept nil orally for 6 hours before procedure. All patients were uniformly premedicated with inj. glycopyrrolate 0.2 mg IM 30 min before shifting to operation theatre.

Upon arrival of the patient in the operation theatre, intravenous access with 18 G cannula was established. Patients were monitored by heart rate (bpm), systolic and diastolic blood pressure (mmHg), respiratory rate and oxygen saturation (SpO_2). All the drugs administered by a person who not involved in study to avoid bias. Patients were medicated with inj. pentazocine IV 0.5 mg/kg followed by preoxygenation with 100% oxygen for 3 minutes. Induction of general anaesthesia was done with inj. thiopentone sodium 5 mg/kg. Endotracheal intubation was facilitated with intravenous succinylcholine 1.5 mg/kg and ventilation with 100% oxygen for 1 minute. General anaesthesia was maintained with nitrous oxide and oxygen (66:33) and isoflurane (0.5-1%) given by Bain's circuit with intermittent dosage of non-depolarizing muscle relaxant IV vecuronium loading dose- 0.04 mg/kg and intermittent dose - 0.01 mg/kg throughout surgical procedure. At the time of skin closure, isoflurane was discontinued and study drug was given in 100 ml saline over a period of 10 minutes. Residual neuromuscular blockage was reversed with inj. neostigmine (0.05 mg/kg) and inj. glycopyrrolate (0.01 mg/kg) IV. Once patient met the signs of adequate reversal extubation was performed and all patients were given O_2 by face mask during recovery period. Values for HR, SBP and DBP were recorded just before the study drug administration(A_0) which taken as baseline value for comparison and 3, 5 min after the study drug administration(A_3 and A_5) and at extubation (E), 3, 5, 10 and 15 min after extubation (E_3, E_5,E_{10},E_{15}). Respiratory rate and SpO_2 were recorded at 3, 5, 10 and 15 min after extubation.

At the end of extubation, quality of extubation was recorded with extubation quality score[8] (Grade 1: No Coughing; Grade 2: Minimal Coughing [1 -2 times]; Grade 3: Moderate coughing [3-4 times]; Grade 4: Severe coughing [5 or more times]), Grade 5: Poor extubation, very uncomfortable (Laryngospasm and coughing > 10 times).

After extubation, patients were also observed for sedation by Ramsay sedation score as[17]: Grade 1: Anxious and agitated or restless or both; Grade 2: Co-operative, oriented and calm; Grade 3: Responsive to command only; Grade 4: Exhibiting brisk response to light tap/auditory stimulus; Grade 5: Exhibiting sluggish response to light tap/auditory stimulus; Grade 6: Unresponsive.

Patients were closely observed for bradycardia (below 20% of basal value), hypotension (below 20% of basal value) and desaturation (<85%) during intra and postoperative period. During postoperative period along with above nausea, vomiting, respiratory depression and shivering were also recorded if occurred. Any complication if occurred was treated with appropriate medications.

STATISTICAL ANALYSIS

The observations were recorded and subjected to statistical analysis using statistics calculator SPSS 17.00 version. Student's t test was used for analysis of quantitative and χ^2 (chi square) test was used to analyze qualitative data. p-value <0.05 was taken statistically significant.

RESULTS

The patients in three groups were comparable for age, sex, weight, duration of anaesthesia (table 1). The difference among 3 groups was insignificant (p>0.05).

Baseline values such as heart rate SBP and DBP were comparable in all 3 groups (p>0.05). We observed a significant difference in heart rate between Group C and M during extubation and at 3, 5, 10 and 15 min after extubation (p<0.05). Whereas on comparing group C with group D, significant (p<0.01) difference in HR was observed at all study time period. On comparing group M with group D, significant difference (p<0.05) in heart rate was present at all time interval.

Our study showed a significant difference in SBP between Groups C and M, at 3 and5 min after study drug administration (p<0.05) which became highly significant during extubation and 3 and5 min after extubation(p<0.01). After that difference became significant at 10 min after extubation. During comparison of group D and C significant difference in SBP (p<0.01) was present at all time interval. While on comparing group M with group D, significant change (p<0.01) in SBP was observed at all time intervals except at 3 and 5 min after study drug administration.

DBP was lower in group D during extubation and 3,5,10 and15 min after extubation (p<0.01).During comparison of group C and M DBP was lower during extubation (p<0.01) which remain lower during 3,5 and10 min after extubation(p<0.05). DBP was significantly lower in group D as compared to M at extubation and remain lower afterward (p<0.05).

No significant difference was observed in respiratory rate and SpO_2 after extubation until end of study among 3 groups.

90% patients in group D had no coughing against 63.33% in group C and 60 % in group M (table 2). Minimal coughing found in 30% patients in group C, 33.33% in group M and 10% in group D. No patient in group D had moderate coughing as compared to 6.66% patient in group C and group M. During statistical analysis there was lower extubation score (score 1 and 2) seen in group D as compared to group C and group M.

No patient in group D was anxious and agitated as compared to 76.66% in group C and 80% in group M. In group C, 23.33% patients were cooperative and oriented as compared to 20% patients in group M and 33.33% patients in group D. In analysis

variables	Group C	Group M	Group D
Age (yrs)	38.26±10.65	34.7±9.01	35.83±10.88
Sex	14:16	16:14	18:12
Weight (Kg)	60.63±9.74	63.4±9.10	63.33±8.98
Duration of anaesthesia (minute)	176.66±38.10	176.83±35.82	175.66±43.12

Table-1: Demographic profile of three groups (mean±SD)

Extubation score				Sedation score		
Score	**Group C**	**Group M**	**Group D**	**Group C**	**Group M**	**Group D**
1	19	18	27	23	24	0
2	9	10	3	7	6	10
3	2	2	0	0	0	20
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	0	0	0	0	0

Table-2: Distribution of Extubation score and Sedation score in three groups

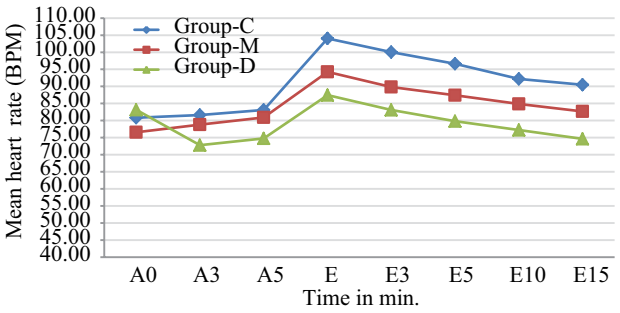

Figure-1: Changes in mean heart rate (beats per min). Measurement points; A_0: During study drug administration, A_3: 3 minutes after drug administration, A_5: 5 minutes after drug administration, E: at the time of extubation, E_3: 3 minutes after extubation, E_5: 5 minutes after extubation, E_{10}: 10 minutes after extubation, E_{15}: 15 minutes after extubation. D = Dexmedetomidine, M = Magnesium sulphate, C = Control

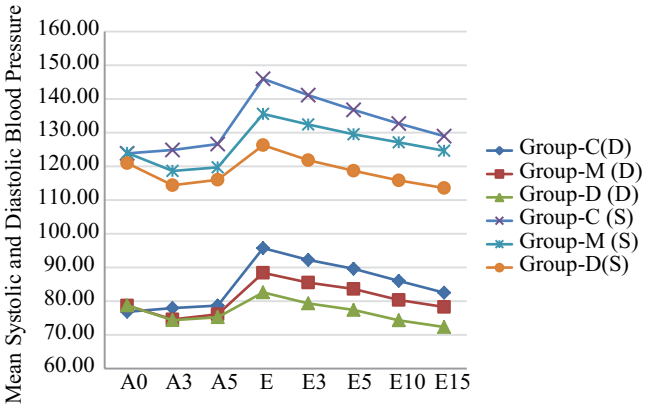

Figure-2: Changes in mean systolic and diastolic blood pressure (mmHg). Measurement points; A_0: During study drug administration, A_3: 3 minutes after drug administration, A_5: 5 minutes after drug administration, E: at the time of extubation, E_3: 3 minutes after extubation, E_5: 5 minutes after extubation, E_{10}: 10 minutes after extubation, E_{15}: 15 minutes after extubation. D = Dexmedetomidine, M = Magnesium sulphate, C = Control, S= Systolic BP, D= Distolic BP.

of sedation score, after extubation there was significantly higher sedation (score 2 and 3) seen in group D on comparing with group C and M.

One and 2 patients had nausea (3.33%) and shivering (6.66%) respectively in control group. Beside these, no untoward side effects like laryngospasm, bronchospasm, respiratory depression, breathholding, desaturation occurred in any group. None of the patients had bradycardia and hypotension in patients of all 3 groups

DISCUSSION

Tracheal intubation and extubation are associated with marked elevation in heart rate and arterial pressure. Coughing is the most common reflex response which occurred due to the presence of endotracheal tube.[18] It can produce increase heart rate, increase blood pressure, increase intraocular pressure, increase intracranial pressure, myocardial infarction and surgical bleeding. Systemic hypertension associated with tracheal extubation may lead to postoperative intracranial haematoma following craniotomies which is a devastating consequence and has an incidence of 0.8% -2.2%.[3] Dexmedetomidine, an alpha-2 adrenergic agonists have been introduced to clinical anaesthesia for their sympatholytic, sedative, anaesthetic sparing and haemodynamic stabilizing properties.[19,20] The ability of magnesium sulphate to inhibit the release of catecholamines has been known for many years. It is effective in attenuating the blood pressure response to tracheal intubation.[16]

This study was designed with aim to evaluate and compare the effects and efficacies of magnesium sulphate and dexmedetomidine on HR, SBP and DBP during extubation. This study was also aimed to observe airway responses during extubation, any untoward effect of study drugs and effect on sedation after extubation.

In this study it was observed that endotracheal extubation led to significant increase in heart rate which remain elevated during and after extubation. Alpha-2 agonist drug e.g. dexmedetomidine and physiological antagonist of calcium channel e.g. magnesium sulphate infusion at the time of skin closure at a dose of 0.5 µg/kg and 30 mg/kg respectively led to a decrease in stress response following extubation. The mean HR was lower in dexmedetomidine as compared to magnesium sulphate but none of patients suffered from bradycardia and did not required dose reduction.

Aksu R et al[21] in their study observed that dexmedetomidine was superior than fentanyl for blunting haemodynamic response. Our results are in accordance with Guler G et al.[18]

Dexmedetomidine activates receptors in the medullary vasomotor centre, reducing noradrenaline turnover and

decreasing central sympathetic outflow resulting in alteration in sympathetic function and decreased heart rate and blood pressure.[22,23]

Mg^{++} inhibits the release of acetylcholine from the vagus nerve so it initially produces tachycardia. Mg^{++} produces vasodilatation directly and also indirectly by sympathetic ganglia blockade and inhibition of release of catecholamine so it leads to decrease in arterial blood pressure.[16] After extubation heart rate was higher in group C as compare to group M. This was probably due to the fact that epinephrine levels in the group M did not increase as high as in control group. This is in conjunction with the study carried by Arar C et al[24] and James MFM et al.[25]

Results in our study has clearly shown that tracheal extubation led to significant increase of SBP and DBP in group C whereas in group M and group D, SBP and DBP remains near to baseline value during extubation. Our results related to dexmedetomidine are in accordance with Turan G et al[26] and Jain D et al.[12] In their study it has been shown a significant reduction in blood pressure during extubation with use of dexmedetomidine.

Nooraei N et al[27] supported the fact that use of magnesium sulphate provides better arterial pressure control than lignocaine during intubation. Panda NB et al[28] studied similar dose as used in our study and found significant reduction in BP during intubation.

Respiratory rate and SpO_2 were comparable among all the 3 groups. Our findings are consistent with the study done by Aksu R et al.[21]

Dexmedetomidine by its analgesic and sedative properties is known to blunt airway responses. Alpha-2 stimulation causes smooth muscle relaxation thereby preventing broncho-constriction. Extubation score 1 (no coughing) was found in 90% patient of group D. Incidence of coughing was more in group C and group M than group D. This is in accordance with study done by Sharma VB et al[8] and Guler G et al.[18]

Significant number of the patients in group D had sedation score 3 while in group C and group M most of the patients belong to sedation score 1. Central stimulation of parasympathetic outflow and inhibition of sympathetic outflow from the locus coeruleus in the brainstem plays an important role in the sedation and anxiolysis produced by dexmedetomidine. Decreased noradrenergic output from the locus coeruleus facilitate for increased discharge of inhibitory neurons including the gamma-amino butyric acid system resulting in anxiolysis and sedation.[22] Our findings are well supported by Bindu B et al.[29]

Our study observed insignificant difference in incidence of adverse effect among 3 groups. This correlate with study done by Guler G et al[18], Turan G et al[26] as they found no significant difference between the dexmedetomidine group and control group in respect to complications.

CONCLUSION

Both intravenous magnesium sulphate and dexmedetomidine attenuate the haemodynamic response during extubation in craniotomies but dexmedetomidine is more effective. It control airway reflexes better, produce smooth extubation and provide adequate sedation postoperatively. No untoward effect were observed with both the study drugs.

REFERENCES

1. Jajoo SS, Chaudhari AR, Singam A, Chandak A. Attenuation of hemodynamic responses to endotracheal extubation: A prospective randomised controlled study between two different doses of Verapamil. International Journal of Biomedical Research. 2013;4:663-9.
2. Paulissian R, Salem MR, Joseph NJ, Braverman B, Cohen HC, Crystal GJ, Heyman HJ. Hemodynamic responses to endotracheal extubation after coronary artery bypass grafting. Anesth Analg. 1991;73:10–5.
3. S Parida, A Badhe. Emergence hypertension in patients undergoing intracranial surgery. The Internet J Anesthesiol. 2008; 22:1.
4. Dogru K, Arik T, Yildiz K, Bicer C, Madenoglu H, Boyaci A. The effectiveness of intramuscular dexmedetomidine on haemodynamic responses during tracheal intubation and anaesthesia induction of hypertensive patients: A randomised, double blind, placebo controlled study. Curr Ther Res Clin Exp. 2007:68;292-02.
5. Bilotta F, Lam AM, Doronzio A, Cuzzone V, Delfini R, Rosa G. Esmolol blunts postoperative hemodynamic changes after propofol-remifentanil total intravenous fast-track neuroanaesthesia for intracranial surgery. Journal of Clinical Anaesthesia. 2008;20:426–430.
6. Basali A, Mascha EJ, Kalfas I, Schubert A. Relation between perioperative hypertension and intracranial hemorrhage after craniotomy. Anesthesiology. 2000;93: 48-54.
7. Nishina K, Mikawa K, Maekawa N, Obara H. Fentanyl attenuates cardiovascular responses to tracheal extubation. Acta Anaesthesiol Scand. 1995;39:85–89.
8. Sharma VB, Prabhakar H, Rath GP, Bithal PK. Comparison of dexmedetomidine and lignocaine on attenuation of airway and pressor responses during tracheal extubation. J Neuroanaesthesiol Crit Care. 2014; 1:50-5.
9. K, Nishina K, Maekawa N, Obara H. Attenuation of cardiovascular responses to tracheal extubation; Verapamil v/s Diltiazem. Anaesthesia and Analgesia. 1996;82:1205-10.
10. Menda F, Koner O, Sayin M, Ture H, Imer P, Aykac B. Dexmedetomidine as an adjunct to anaesthetic induction to attenuate hemodynamic response to endotracheal intubation in patients undergoing fast-track CABG. Annals of Cardiac Anaesthesia. 2010;13:16-21.
11. Talke P, Chen R, Thomas B, Aggarwall A, Gottlieb A, Thorborg P, Heard S, Cheung A, Son SL, Kallio A. The hemodynamic and adrenergic effects of perioperative dexmedetomidine infusion after vascular surgery. Anaesthesia and Analgesia. 2000;90:834-9.
12. D Jain, R Khan, M Maroof. Effect of dexmedetomidine on stress response to extubation. Internet J Anesthesiol. 2008; 21:1.
13. Candiotti KA, Bergese SD, Bokesch PM, Feldman MA, Wisemandle W, Bekker AY, MAC Study Group. Monitored anaesthesia care with dexmedetomidine: a prospective, randomized, double-blind, multicenter trial. Anaesthesia and Analgesia. 2010;110:47-56.
14. Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. Br J Anaesth. 1999;83:302–20.
15. Douglas WW, Rubin RP. The mechanism of catecholamine release from the adrenal medulla and the role of calcium in stimulus-secretion coupling. The Journal of Physiology. 1963;167:288-310.
16. Puri GD, Marudhachalam KS, Chari P, Suri RK. The effect of magnesium sulphate on hemodynamics and its efficacy in attenuating the response to endotracheal intubation in

patients with coronary artery disease. Anesth Analg. 1998; 87:808–11.
17. Ramsay MAE, Savege TM, Simpson BRJ, Goodwin R. Controlled sedation with alphaxalone - alphadolone. British Medical Journal. 1974;2:656–9.
18. Guler G, Akin A, Tosun Z, Eskitascoglu E, Mizrak A and Boyaci A. Single-dose dexmedetomidine attenuates airway and circulatory reflexes during extubation. Acta Anesthesiol Scand. 2005;49:1088–1091.
19. Jaakola ML, Ali-Melkkilä T, Kanto J, Kallio A, Scheinin H, Scheinin M. Dexmedetomidine reduces intraocular pressure, intubation responses and anaesthetic requirements in patients undergoing ophthalmic surgery. British Journal of Anaesthesia. 1992;68:570-5.
20. Panzer O, Moitra V, Sladen RN. Pharmacology of Sedative-Analgesic Agents: Dexmedetomidine, Remifentanil, Ketamine, Volatile Anaesthetics, and the Role of Peripheral Mu Antagonists. Anaesthesiology Clinics. 2011; 29:587-605.
21. Aksu R, Akın A, Biçer C, Esmaoglu A, Tosun Z, Boyaci A. Comparison of the effects of dexmedetomidine versus fentanyl on airway reflexes and hemodynamic responses to tracheal extubation during rhinoplasty: A double-blind, randomized, controlled study. Curr Ther Res. 2009;70: 209-20.
22. Gertler R, Brown HC, Donald H. Mitchell DH, Silvius EN. Dexmedetomidine: a novel sedative-analgesic agent. Proceedings (Baylor University Medical Center) 2001;14:13–21.
23. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs 2000;59:263-8.
24. Arar C, Colak A, Alagol A, Uzer SS, Ege T, Turan N, Duran E, Pamukcu Z. The use of esmolol and magnesium to prevent haemodynamic responses to extubation after coronary artery grafting. Eur J Anaesthesiol. 2007;24:826–31.
25. James MFM, Beer RE, Esser JD. Intravenous magnesium sulfate inhibits catecholamine release associated with tracheal intubation. Anaesthesia and Analgesia 1989; 68:772-6.
26. Turan G, Ozgultekin A, Turan C, Dincer E, Yuksel G. Advantageous effects of dexmedetomidine on haemodynamic and recovery responses during extubation for intracranial surgery. European Journal of Anaesthesiology. 2008;25:816-20.
27. Nooraei N, Dehkordi ME, Radpay B, Teimoorian H, Mohajerani SA. Effects of Intravenous Magnesium Sulfate and Lidocaine on Hemodynamic Variables Following Direct Laryngoscopy and Intubation in Elective Surgery Patients. Tanaffos. 2013;12:57-63.
28. Panda NB, Bharti N, Prasad S. Minimal effective dose of magnesium sulfate for attenuation of intubation response in hypertensive patients. Journal of Clinical Anaesthesia. 2013;25:92–7.
29. Bindu B, Pasupuleti S, Gowd UP, Gorre V, Murthy RR, Laxmi MB. A double blind, randomized, controlled trial to study the effect of dexmedetomidine on hemodynamic and recovery responses during tracheal extubation. J Anaesthesiol Clin Pharmacol. 2013; 29:162–7.

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