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

Neelima Tandon¹, Shikha Goyal²

ABSTRACT

Introduction: The anaesthetic 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 and 15 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 Exubtation 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 disease², cerebrovascular disease³ 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.³ Basali et al reported 57% incidence of post craniotomy hypertension.⁴ Different drugs and techniques has been used to attenuate the pressor response such as narcotic analgesics⁵, local anaesthetics⁶, calcium channel blockers⁷ and adrenoceptor blockers⁸,⁹ but none has been found completely successful.

Dexmedetomidine, a highly selective α₂ adrenoceptor agonist decreases the sympathetic outflow and noradrenergic activity thereby counteracting haemodynamic fluctuation occurring at the time of extubation due to increased sympathetic stimulation.¹⁰ 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.¹¹ 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.¹² It inhibits many calcium mediated responses like the release of catecholamine from both adrenal glands and adrenergic nerve terminals in response to sympathetic stimulation.¹³ Intravenously administered magnesium sulphate is capable of attenuating the adverse haemodynamic response associated with endotracheal intubation¹⁴. 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 preanesthetic 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 (SpO2).

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 O2 by face mask during recovery period. Values for HR, SBP and DBP were recorded just before the study drug administration(A0) which taken as baseline value for comparison and 3, 5 min after the study drug administration(A1 and A2) and at extubation (E), 3, 5, 10 and 15 min after extubation (E1, E2, E3, E4, E5).

At the end of study, quality of extubation was recorded with extubation quality scorea (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).

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Respiratory rate and SpO2 were recorded at 3, 5, 10 and 15 min after extubation.

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After extubation, patients were also observed for sedation by Ramsay sedation score a: 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 χ2 (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 and 5 min after study drug administration (p<0.05) which became highly significant during extubation and 3 and 5 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 and 15 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 and 10 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 SpO2 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
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.\textsuperscript{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 haematomata following craniotomies which is a devastating consequence and has an incidence of 0.8% -2.2%.\textsuperscript{19} Dexmedetomidine, an alpha-2 adrenergic agonists have been introduced to clinical anaesthesia for their sympatholytic, sedative, anaesthetic sparing and haemodynamic stabilizing properties.\textsuperscript{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.\textsuperscript{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, C = Control, S= Systolic BP, D= Diastolic BP.

Aksu R et al\textsuperscript{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.\textsuperscript{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.\textsuperscript{22,23} Mg\textsuperscript{2+} inhibits the release of acetylcholine from the vagus nerve so it initially produces tachycardia. Mg\textsuperscript{2+} 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.\textsuperscript{16} After extubation heart rate was higher in group C as compared 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\textsuperscript{23} and James MF et al.\textsuperscript{23} 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\textsuperscript{26} and Jain D et al.\textsuperscript{12} In their study it has been shown a significant reduction in blood pressure during extubation with use of dexmedetomidine.

Nooraei N et al\textsuperscript{27} supported the fact that use of magnesium during extubation with use of dexmedetomidine. study it has been shown a significant reduction in blood pressure.\textsuperscript{16} After extubation heart rate was higher directly and also indirectly by sympathetic ganglia blockade and by Guler G et al\textsuperscript{18}, Turan G et al\textsuperscript{26} adverse effect among 3 groups. This correlate with study done by Sharma VB et al\textsuperscript{8} and Guler G et al.\textsuperscript{18} Our study observed insignificant difference in 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\textsuperscript{8} and Guler G et al.\textsuperscript{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-aminobutyric acid system resulting in anxiolysis and sedation.\textsuperscript{12} Our findings are well supported by Bindu B et al.\textsuperscript{29} Our study observed insignificant difference in incidence of adverse effect among 3 groups. This correlate with study done by Guler G et al\textsuperscript{18}, Turan G et al\textsuperscript{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.

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