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Comparison of Dexmedetomidine and Magnesium Sulphate in Attenuating Airway and Hemodynamic Response during Extubation in Patients Undergoing Craniotomies - A Randomised Clinical Trial

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Abstract: ***Background: Intracranial neurosurgeries require cardiovascular stability during extubation period. Hence this study was done to compare the effect of dexmedetomidine and magnesium sulphate in attenuation of hemodynamic and airway responses during extubation in patients undergoing craniotomies. Aim & Objective: To compare the efficacy of I.V Dexmedetomidine versus I.V Magnesium sulphate in evaluation of hemodynamic and airway response in patients undergoing craniotomies. Methods and Material: Total 60 patients with ASA Grade 1 &2 aged 18 to 50 years undergoing craniotomies under general anaesthesia were randomly divided into two groups, with each group of 30 patients. Group D: received an infusion of dexmedetomidine 0.5mcg/kg over a period of 10 minutes at the time of skin closure. Group M: received an infusion of magnesium sulphate 30mg/kg over a period of 10 minutes at the time of skin closure. Hemodynamic parameters such as heart rate, systolic and diastolic blood pressure were recorded just before drug administration,3 and 5 minutes after drug administration, during extubation and 3, 5, 10 and 15 minutes after extubation. Respiratory rate, oxygen saturation were analysed at 3,5,10 and 15 minutes 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 were noted. Results: Hemodynamic responses was significantly lower in group D compared to group M. There were no significant differences in the prevalence of adverse events among the two groups. Conclusion: Dexmedetomidine 0.5mcg/kg is more effective than Magnesium sulphate 30mg/kg in controlling hemodynamic and airway reflexes during endotracheal extubation in craniotomy.***

Keywords: Dexmedetomidine, Magnesium sulphate, airway, haemodynamic reflexes, extubation , craniotomies

1. Introduction

Tracheal Extubation is a vital event in general anaesthesia. It is associated with modest and transient increase in heart rate and blood pressure lasting for approximately 5 to 15minutes which is seen in 10% to 30% of patients[1]. These changes have no adverse consequences in healthy patients undergoing 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 intracranial surgeries, hemodynamic changes and in particular arterial hypertension may increase in the risk of postoperative intracranial edema and haemorrhage[5].

Various drugs have been used to attenuate, these pressor response such as narcotic analgesics[6], local anaesthetics, calcium channel blockers[7] and adrenoceptor blockers, etc.

Dexmedetomidine[8],a selective α2 adrenoceptor agonist. It acts by decreasing the sympathetic outflow and noradrenergic activity thereby counteracting hemodynamic fluctuation occurring at the time of extubation, due to increased sympathetic stimulation[9]. It is more commonly used as a sedative due to its analgesic properties, co-operative sedation and lack of respiratory depression.

Recently, magnesium sulphate use in anaesthesia practice has been studied. Magnesium[10], a naturally occurring calcium channel antagonist and non-competitive antagonist of N-methyl D-aspartate (NMDA) receptor. It acts by inhibiting calcium channel mediated release of catecholamine from both adrenal glands and adrenergic nerve terminals in response to sympathetic stimulation. Thus, this study was done to evaluate the efficacy of Dexmedetomidine and Magnesium sulphate in attenuating airway and hemodynamic response during extubation in patients undergoing intracranial surgeries.

2. Aims and Objectives

This study was a prospective randomised clinical trial. The main objective of this study was to evaluate and compare the beneficiary effects of intravenous dexmedetomidine and magnesium sulphate in attenuation of hemodynamic response and airway reflexes during endotracheal Extubation in patients undergoing craniotomies under general anaesthesia.

3. Methods and Materials

After obtaining Institutional Ethical Committee approval, sixty patients posted for elective intracranial surgeries, aged between 18 to 50 years of either sex with ASA Grade 1 and 2 were randomly selected. The exclusion criteria was patients refusal, patients with cardiopulmonary dysfunction, hepatic dysfunction, renal dysfunction,psychiatric disorder, pregnant and lactating mothers, patients who require postoperative ventilation.

After obtaining written and informed consent, pre-anaesthetic assessment of all the selected patients was done with complete history and physical examination. Patients were randomly divided into two groups.

Group D: received an infusion of dexmedetomidine 0.5mcg/kg over a period of 10 minutes at the time of skin closure.

Group M: received an infusion of magnesium sulphate 30 mg/kg over a period of 10 minutes at the time of skin closure.Patients were kept nil orally for 6 hours before procedure.

In the operating room, 18G IV catheter was inserted and 6ml/hour crystalloid was infused.

Non-invasive monitors such as ECG, Systolic blood pressure, diastolic blood pressure, respiratory rate and oxygen saturation(SPO2) were recorded.

After pre-oxygenation with 100% O2 for 3 minutes, anaesthesia was pre-medicated with injection glycopyrrolate, midazolam (0.05mg/kg), fentanyl (2mg/kg).

Induction of general anaesthesia was done with injection thiopentonesodium(5mg/kg) followed by succinyl choline (2mg/kg) to facilitate endotracheal intubation and ventilated with 100% oxygen for 1 minute.

General anaesthesia was maintained with oxygen and nitrogen ratio of 33%:66%, sevoflurane 0.8% MAC and vecuronium bromide loading dose 0.04mg/kg and intermittent dose 0.01mg/kg throughout surgical procedure.

At the time of skin closure, sevoflurane was discontinued, study drug were given in 100 ml saline over 10 minutes.

Residual neuromuscular blockade was reversed with Inj.neostigmine (0.05mg/kg) and Inj.glycopyrrolate (0.01mg/kg) IV. When the signs of reversal were met, extubation was performed and all patients were given 02 by face mask during recovery period.

HR, SBP and DBP were recorded just before the study drug administration and at 3, 5 minutes after the drug administration and during extubation, 3, 5, 10 and 15 minutes after extubation. Respiartory rate and SPO2 were recorded at 3,5. 10 and 15 minutes after extubation.At the end of extubation, quality of extubation was recorded using Extubation quality score[11].

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 cough > 10 times)

After extubation, patients were also observed for sedation by Ramsay sedation score[12].
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

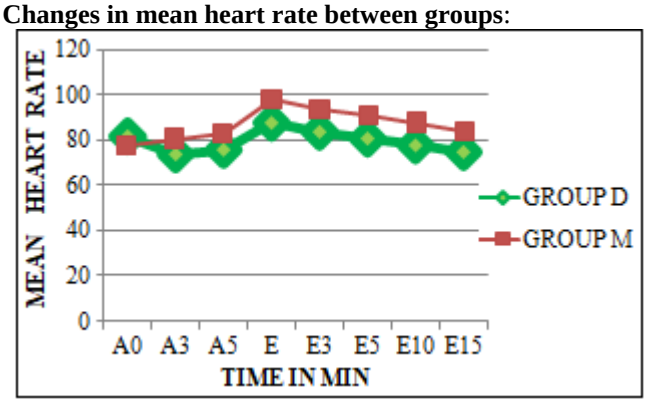
Patients were observed for bradycardia (below 20% of baseline), hypotension (below 20% of baseline) and desaturation (SPO2 <85%) during intra-operative and postoperative period. During postoperative period, along with above findings nausea, vomiting, respiratory depression and shivering were also recorded if any. The observations were recorded and subjected to statistical analysis. p- value <0.05 was taken as statistically significant.

4. Results

Demographic Data

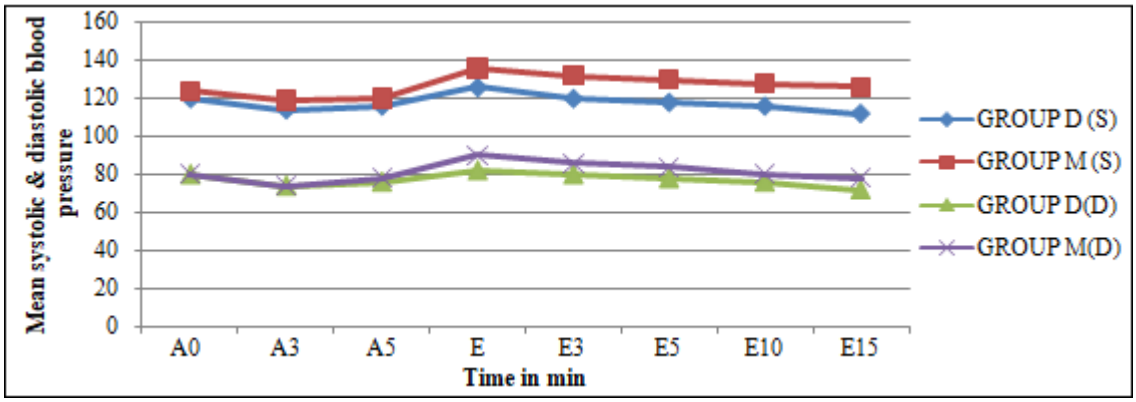
Variable	Group D	Group M
Mean Age(Years)	35.7± 8.01	36.83± 9.08
Sex Ratio (Male: Female)	18:12	16:14
Mean Weight (Kgs)	64.4±9.10	64.3±8.98
Mean Duration of Surgery (Minutes)	177.83±35.82	176.66±43.12

Changes in mean heart rate between groups:



Changes in mean heart rate

Measurements: A0- DURING STUDY DRUG ADMINISTRATION; A3- 3 MIN AFTER DRUG ADMINISTRATION; A5- 5 MIN AFTER DRUG ADMINISTRATION; E- AT THE TIME OF EXTUBATION; E3- 3 MIN AFTER EXTUBATION; E5- 5 MIN AFTER EXTUBATION; E10- 10 MIN AFTER EXTUBATION; E15- 15 MIN AFTER EXTUBATION; D – DEXMEDETOMIDINE; M- MAGNESIUM SULPHATE



Changes in mean systolic and diastolic blood pressure

Measurements: A0- DURING STUDY DRUG ADMINISTRATION; A3- 3 MIN AFTER DRUG ADMINISTRATION; A5- 5 MIN AFTER DRUG ADMINISTRATION; E- AT THE TIME OF EXTUBATION; E3- 3 MIN AFTER EXTUBATION; E5- 5 MIN AFTER EXTUBATION; E10- 10 MIN AFTER EXTUBATION; E15- 15 MIN AFTER EXTUBATION; D – DEXMEDETOMIDINE; M- MAGNESIUM SULPHATE;S- SYSTOLIC BP;D- DIASTOLIC BP

Distribution of Extubation Score and Sedation Score

Score	Extubation Score		Sedation Score	
	Group D	Group M	Group D	Group M
1	25	20	0	20
2	5	8	12	10
3	0	2	18	0
4	0	0	0	0
5	0	0	0	0
6	0	0	0	0

The present study showed a significant ($p<0.05$) difference in heart rate at all the time interval in group M compared to group D.

On comparing group M with group D, significant difference ($p<0.01$) in SBP was observed at all the time intervals except at 3 and 5 min after drug administration.

DBP was significantly lower in group D compared to group M at the time of extubation and remain lower afterward ($p<0.05$)

There was no significant difference in respiratory rate and SPO2 in both the groups.

83.33% of patients in group D had no coughing, while 66.66% of patients in group M had no cough. Minimal coughing was observed in 16.66% of patients in group D and 26.66% of patients in group M. Moderate coughing was observed in 6.66% of patients in group M. Thus statistical analysis shows there was lower extubation score in group D compared to group M.

No patients in group D are anxious and agitated (score 1), as compared to 66.66% of patients in group M. 40% of patients in group D are cooperative and oriented and calm (score 2) as compared to 33.33% in group M. 60% of patients in group D responded to commands only (score 3). Statistical analysis showed higher sedation score (score 2, 3) seen in group D as compared to group M.

There were no side effects like laryngospasm, respiratory depression, desaturation, bradycardia and hypotension observed in either of the groups.

5. Discussion

Tracheal intubation and extubation are associated with significant increase in heart rate and blood pressure. It is most commonly associated with cough[13], which is reflex response to tracheal insertion. Cough in turn leads to marked increase in heart rate, arterial blood pressure, intraocular pressure, intracranial pressure, myocardial ischaemia and surgical site bleeding and hematoma. The incidence of postoperative hematoma was 0.8%- 2.2%[3]. In the present study, it was observed that endotracheal extubation is associated with marked increase in heart rate, which remains elevated during and after elevation. Both the drugs, Dexmedetomidine and Magnesium Sulphate infused at the time of skin closure had been observed to decrease stress response after extubation. The mean heart rate was lower in dexmedetomidine (group D) when compared to magnesium sulphate (group M).

Dexmedetomidine, a highly selective α2 agonist- acts by activating the receptors in the medullary vasomotor centre, thereby reducing noradrenaline turnover and also reduces central sympathetic outflow resulting in alteration in the sympathetic function and thus reduces heart rate and blood pressure[14][15].

Whereas, Mg++ acts by inhibiting the release of acetylcholine from vagus nerve ending, so it initially produces tachycardia[10]. Mg++ produces vasodilation directly and also indirectly by sympathetic ganglion blockade and thus reducing the release of catecholamine and hence decreases the arterial blood pressure. This is in conjunction with Arar C et al[16] and James MFM et al[17].In a study by Aksu R et al[18]., it was observed that dexmedetomidine was superior to fentanyl in attenuating airway reflex response and maintaining hemodynamic stability without prolonging recovery period

Guler G et al[19].,in their study observed that single dose bolus of dexmedetomidine injected before tracheal

extubation, attenuates airway and circulatory reflexes. The present study was comparable with the above studies

After extubation, heart rate was higher in group M as compared to group D. This may be probably due to the fact that epinephrine levels are not inhibited to such level of dexmedetomidine as compared to magnesium sulphate.Results in our study showed that tracheal extubation led to marked increase in SBP and DBP in both groups but returns near to normal baseline during and after extubation. These findings of dexmedetomidine were similar to Turn et al[20] and Jain et al[21]. In these studies, it was observed that there was significant reduction in blood pressure during extubation with use of dexmedetomidine.

Nooraei N et al[22] supported the use of magnesium sulphate provide better arterial control than lidocaine during intubation. In study by Panda NB et al[23], used similar dose as used in our study and found significant reduction in blood pressure during intubation. In the present study, respiratory rate and SPO2 are comparable in both the groups.

Dexmedetomidine by its analgesic and sedative effects is known to blunt airway responses. Alpha-2 stimulation causes smooth muscle relaxation thereby preventing bronchospasm. Extubation score 1 (no coughing) was seen in 83.33% patients in group D where 66.66%in group M. The incidence of cough was more in group M compared to group D. This is similar with study done by Sharma VB et[8] al and Guller G et al[13].

Significant number of patients in group D had a sedation score of 3 while in group M most patients belong to sedation score 1. This finding is observed because dexmedetomidine cause stimulation of parasympathetic outflow and inhibition of sympathetic outflow from locus coeruleus in the brainstem, which plays a pivotal role in the sedation and anxiolysis. This in turn increases the discharge of inhibitory neurons including GABA system resulting in anxiolysis and sedation. This is well supported by Bindu B et al[24].In the present study there is significant difference in the incidence of adverse effects in the two groups.

6. Conclusion

Both intravenous dexmedetomidine and magnesium sulphate are effective in attenuating the hemodynamic response in craniotomies but dexmedetomidine is more effective because of its properties.

1) Smooth extubation
2) Better control of airway reflexes
3) Adequate postoperative sedation

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