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ANAESTHESIOLOGY

"Comparative Evaluation of Dexmedetomidine, Magnesium Sulphate and Control Group to Attenuate Pressor Responses and Airway Reflexes to Intubation during General Anesthesia"

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ABSTRACT Endotracheal intubation is marked by sympathetic stimulation and increase in catecholamine concentration in susceptible individuals. Tracheal extubation can also be associated with detrimental airway and hemodynamic responses. Many drugs are used to attenuate the intubation response. Dexmedetomidine has been shown to be effective in maintaining hemodynamic stability during intubation and extubation without prolonging recovery. Magnesium sulphate decreases the hemodynamic response to airway management, with proven effectiveness. This study evaluated the efficacy and safety of dexmedetomidine and magnesium sulphate to find out safe anaesthetic technique so that pressor response changes and airway reflexes at the time of extubation are not harmful to the patient.

***Materials and Methods*:** This prospective, randomized study was conducted on 100 patients in the Government Medical College and Associated Hospitals, Jammu. The patients enrolled were those undergoing elective surgical procedures under endotracheal anaesthesia, of ASA Grade-I, within the age group of l8-65 years, of either sex. Pulse rate, blood pressure, electrocardiogram and oxygen saturation were recorded during preinduction, just before extubation, and l, 2, 3, 5 and 10 minutes after extubation. Mean arterial pressure at those intervals was calculated. Any laryngospasm, tracheal collapse, laryngeal edema, vocal cord paralysis, pulmonary edema and laryngeal incompetence bronchospasm, or desaturation was recorded. The time for requirement of first analgesic dose post-operatively was noted. The data so collected was analyzed, compared and subjected to statistical analysis.

***Results*:** There was statistically significant rise in mean heart-rate 1 and 2 minutes after extubation in all the groups ($p<0.05$) except in dexmedetomidine group. Mean heart rate decreased to non-significant levels in magnesium sulphate group at 3 minutes, whereas it remained significant in the control group up to 5 minutes. Before extubation and after extubation, mean SBP, mean DBP and mean ABP shot up significantly in the control group.

***Conclusion*:** Dexmedetomidine is more effective as compared to magnesium sulphate in attenuating the rise in heart rate and blood pressure after extubation. There are no adverse effects seen in patients treated with dexmedetomidine.

KEYWORDS : Dexmedetomidine, Magnesium sulphate, Attenuate pressor response, Intubation, Extubation, General Anaesthesia

Introduction

An essential component of general anaesthesia, endotracheal intubation serves in maintenance of the patency of upper airway, proper ventilation, reduction in the risk of aspiration and delivery of the inhalational anaesthetic agents to the patients through breathing circuits. There is marked sympathetic stimulation and increase in catecholamine concentration in susceptible individuals due to tracheal intubation (1). Frequency and degree of hemodynamic changes are significant in patients who are susceptible to systemic hypertension, coronary artery disease, valvular heart disease, cerebrovascular disease and intracranial aneurysm (2).

Tracheal extubation, translaryngeal removal of a tube from the trachea, can also be associated with detrimental airway and hemodynamic responses. Smooth extubation requires the absence of straining, movement, coughing, breath holding and laryngospasm. Many drugs are used to attenuate the intubation response such as intravenous lignocaine, short-acting opioids such as fentanyl and remifentanil, esmolol, labetalol, intratracheal local anesthetic instillation, dexmedetomidine which can be used during extubation also (3).

Adrenergic alpha 2 agonists seem to have the ability to attenuate the pressor response to intubation and extubation (4). Dexmedetomidine, a selective α2 –agonist, has sedative, analgesic as well as sympatholytic properties. It has also been shown to be effective in maintaining hemodynamic stability during intubation and extubation without prolonging recovery. It also helps in attenuating airway reflex response to tracheal extubation (5).

Magnesium sulphate is widely used in order to decrease the hemodynamic response to airway management, with proven effectiveness. It blocks the release of catecholamines from adrenergic nerve terminals and adrenal gland (6).

In the present study, efficacy and safety of dexmedetomidine and magnesium sulphate was evaluated to find out safe anaesthetic technique so that pressor response changes and airway reflexes at the time of extubation are abolished or they occur to the extent when they are not harmful to the patient.

Materials and Methods

This prospective, randomized study was conducted on 75 patients in the Government Medical College and Associated Hospitals, Jammu, after approval from the Institutional Ethical Committee. The patients enrolled were those undergoing elective surgical procedures under endotracheal anaesthesia, of ASA Grade-I, within the age group of l8-65 years, of either sex. A pre-anaesthetic checkup was done one day prior to surgery which included detailed history, thorough clinical examination along with relevant investigations and weight of the patient.

Patients with history of COPD, emergency surgical procedures, pregnant women, morbid obese patients, with pharyngeal mass, preexisting cardiovascular disease and those with significant respiratory, hepatic, renal, heamopoietic, endocrine dysfunctions were excluded from the study. A written and informed consent was taken from all patients included in the study at the time of pre-anaesthetic evaluation.

Patients were allocated to one of the following three study groups using the process of randomization with the help of computer or the table of random numbers. The procedure of randomization involved usage of serially numbered envelopes with the predetermined allocation as below. Each group had 25 patients. Group A patients were given dexmedetomidine 0.5 µg/kg in 100 ml of isotonic saline five minutes before extubation, Group B patients were given magnesium sulphate 30 mg/kg in l00 ml of isotonic saline five minutes before extubation and Group C patients were given 100 ml of isotonic saline five minutes before extubation.

Pulse rate, blood pressure, electrocardiogram and oxygen saturation were recorded for the study at the following intervals: preinduction, just before extubation, and l, 2, 3, 5 and 10 minutes after extubation. Mean arterial pressure at those intervals was calculated. Any laryngospasm, tracheal collapse, laryngeal edema, vocal cord paralysis, pulmonary edema and laryngeal incompetence bronchospasm, or desaturation was recorded. Any post-operative sedation seen was assessed by a five point sedation scoring given by Yeager in 1987: 0 - mildly conversant, 1 - mildly sedated, 2 -

moderately sedated and drowsy, 3 - asleep but arousable, and 4 - asleep not arousable (7). The time for requirement of first analgesic dose post-operatively was noted. The data so collected was analyzed, compared and subjected to statistical analysis.

The data was analyzed with the help of computer software MS Excel and SPSS for windows. Baseline comparability of the patients in all the four groups was ascertained by using Chi-square test/ANOVA as appropriate. Haemodynamic measurements at various intervals were expressed as mean and standard deviation. A p-value of less than 0.05 was considered as statistically significant .All p value reported were two tailed.

Results

In the study, there was no significant difference among the three groups with respect to mean age and mean weight (Table 1). There was statistically significant rise in mean heart-rate 1 and 2 minute after extubation in all the groups ($p<0.05$) except in dexmedetomidine group. Mean heart rate decreased to non-significant levels in magnesium sulphate group at 3 minutes, whereas it remained significant in the control group up to 5 minutes (Table 2). Moreover, just before extubation and after extubation, mean systolic blood pressure, mean diastolic blood pressure and mean arterial blood pressure shot up significantly in the control group (Tables 3, 4, 5).

Discussion

There was statistically no significant difference in mean values of heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure amongst the three groups before intubation. The mean age and mean weight of the patients in all the three groups were statistically comparable. No case of laryngospasm, bronchospasm or desaturation was recorded.

In the dexmedetomidine group, there was increase in heart rate from 85.47±9.94 to 91.80±8.15 and 88.80±6.33 bpm respectively, at preextubation and 1 min after extubation, which were statistically significant ($p<0.05$). Thereafter a decline in the heart rate was observed which was statistically not significant till 3 minutes. At 5 and 10 minutes, heart rate lowered to 72.83 bpm which was statistically significant when compared to preinduction value ($p<0.05$). There was increase in SBP in preextubation, 1, 2 and 3 minutes after extubation which was statistically significant at 1 minutes and non significant at 2, 3 and 5 minutes when compared to preinduction value. However, a decline in SBP was observed at 10 minutes which was statistically significant as compared to the basal value ($p<0.001$). Similar trends were observed with DBP and MAP also. When compared to the control group heart rate, SBP, DBP and MAP were lower in the dexmedetomidine group which was statistically significant ($p <0.001$) at various time intervals of our study, but no intervention was required as this fall in pulse rate was transient and did not affect the blood pressure. The sedation score in all the patients of dexmedetomidine group remained 0 (mildly conversant) signifying no sedation in the post extubation period in the patients receiving dexmedetomidine.

Our observations are in accordance with the findings of Recep *et al.* who reported that dexmedetomidine was not associated with increased HR and SBP after extubation compared with the preextubation values and that none of the patients were sedated after receiving 0.5 µg/kg of dexmedetomidine bolus dose (8). The mechanism by which dexmedetomidine acts is due to reduction of intracellular cyclic adenosine monophosphate (c-AMP) and c-AMP dependent protein kinase activity, resulting in dephosphorylation of ion channels (9).

Recovering from anaesthesia often results in elevating catecholamine concentration following withdrawal of anaesthetics at the culmination of surgery. This response is further aggravated by the laryngeal manipulations occurring at the time of extubation. Dexmedetmidine reduces heart rate and blood pressure (10) and the hemodynamic and catecholamine responses to intubation and extubation (9). Dexmedetomidine induces sedation and analgesia without affecting respiratory status (11). In our study we made use of these properties of dexmedetomidine for providing a smooth transition from the pre-extubation to the post-extubation phase by minimizing the haemodynamic fluctuations.

In the magnesium sulphate group, heart rate increased from 84.23±9.74 to 92.27±7.33 at the preextubation which was statistically significant ($p<0.05$). The heart rate remained increased than the basal values but was statistically not significant at 3 and 5 minutes after extubation. A statistically significant rise in SBP was observed at preextubation ($p<0.001$) in the magnesium group. The increase in the SBP persisted for 1, 2 and 3 minutes after extubation but the difference in SBP was statistically insignificant compared to the baseline value ($p>0.05$). Similar findings were seen with DBP and MAP also. Though there was increase in SBP, DBP and MAP, it was of smaller magnitude and of lesser duration in the magnesium treated group as compared to the control group. Seventeen of the patients in the magnesium sulphate group had sedation score of 2 (moderately sedated and drowsy) and rest 8 had sedation score of 3 (asleep but arousable). These differences were statistically significant as compared to the control group and the dexmedetomidine group but were clinically insignificant. Our study is in accordance to Arar *et al.* (12). Magnesium sulphate inhibits the hemodynamic responses to intubation, as it inhibits catecholamine release from adrenergic nerve endings (13). It also reduces the hemodynamic responses to extubation.

In the magnesium group, the increase in the SBP persisted for 1, 2, 3 and 5 after extubation but the difference in SBP was statistically not significant compared to the baseline value ($p>0.05$). Similar findings were seen with DBP and MAP also.

In the dexmedetomidine group, bradycardia (HR <45 beats/minute) and emesis was not observed in any patient. The time from tracheal extubation and emergence from anaesthesia were similar in all the groups. Postoperative somnolence and respiratory depression were not observed in any patient in any of the study groups.

Conclusion

The study concludes that dexmedetomidine and magnesium sulphate are effective in attenuation of pressor response to extubation. However, dexmedetomidine is more effective in attenuating the rise in heart rate and blood pressure after extubation and is associated with better extubation quality as depicted by lower sedation scores and no adverse effects seen in patients treated with dexmedetomidine.

Table 1. Comparison of mean age and mean weight in the four groups

Groups	Age (in years) Mean ± SD	Weight (in kgs) Mean ± SD
A (Dexmedetomidine)	37.36± 12.99	72.12±13.67
B (Magnesium sulphate)	40.64±12.62	70.84±12.53
C (Control)	35.80±13.47	71.76±17.58
Statistical inference (Anova test)	p = 0.41**	p = 0.95**

**Not significant

Table 2. Comparison of mean heart rate changes in the three groups before and after extubation

Time	Groups					
	A (Dexmedetomidine)		B (Magnesium sulphate)		C (Control)	
	Mean ± SD	p-value	Mean ± SD	p-value	Mean ± SD	p-value
Pre Induction	85.47±9.94	0.001*	84.23±9.74	0.002*	87.12±9.74	0.002*
Pre Extubation	91.80±8.15		92.27±7.33		95.76±14.87	
After Extubation						
1 Min	88.80±6.33	0.099	92.27±7.15	0.002*	104.87±11.17	0.000*
2 Min	85.60±5.97	0.275	88.10±6.94	0.032*	102.27±10.27	0.000*
3 Min	79.17±5.71	0.275	85.40±6.68	0.490	96.60±10.17	0.001*
5 Min	72.83±4.47	0.002*	81.13±6.23	0.066	92.20±9.70	0.026*
10 Min	72.83±6.31	0.000*	78.53±4.23	0.000*	84.20±8.96	0.245

*Significant

Table 3. Comparison of mean systolic blood pressure changes in the three groups before and after extubation

Time	Groups					
	A (Dexmedetomidine)		B (Magnesium sulphate)		C (Control)	
	Mean ± SD	p-value	Mean ± SD	p-value	Mean ± SD	p-value
Pre Induction	120.28± 10.68	0.001*	122.64± 14.89	0.002*	121.36± 9.99	0.002*
Pre Extubation	135.54± 9.20		132.96± 13.20		142.00± 22.55	
After Extubation						
1 Min	140.56± 9.71	0.002*	141.56± 11.37	0.099	163.92± 6.52	0.000*
2 Min	132.36± 7.39	0.321	139.08± 11.72	0.275	162.44± 6.21	0.000*
3 Min	125.92± 5.99	0.491	136.36± 12.42	0.275	157.84± 7.18	0.001*
5 Min	117.76± 6.82	0.067	133.20± 11.51	0.062	153.16± 8.37	0.027*
10 Min	111.64± 9.61	0.000*	124.48± 7.88	0.000*	147.12± 21.32	0.251

*Significant

Table 4. Comparison of mean diastolic blood pressure changes in the three groups before and after extubation

Time	Groups					
	A (Dexmedetomidine)		B (Magnesium sulphate)		C (Control)	
	Mean ± SD	p-value	Mean ± SD	p-value	Mean ± SD	p-value
Pre Induction	72.96±10.48	0.001*	75.72±11.37	0.002*	69.80± 9.59	0.002*
Pre Extubation	75.36±9.31		70.36±12.09		79.44±21.15	
After Extubation						
1 Min	94.36±9.88	0.002*	92.92±10.78	0.099	105.76± 8.10	1.000
2 Min	86.16±8.01	0.321	90.40±10.82	0.271	104.52± 7.10	0.000*
3 Min	80.48±7.84	0.470	87.88±10.94	0.276	102.12± 7.15	0.001*
5 Min	88.64±6.13	0.066	99.08±8.76	0.012*	116.68± 7.38	0.027*
10 Min	69.60±6.59	0.000*	76.52±5.72	0.000*	101.20± 6.46	0.251

*Significant

Table 5. Comparison of mean arterial blood pressure changes in the three groups before and after extubation

	A (Dexmedetomidine)		B (Magnesium sulphate)		C (Control)	
	Mean ± SD	p-value	Mean ± SD	p-value	Mean ± SD	p-value
Pre Induction	91.96±5.92	0.001*	93.32±8.22	0.002*	95.20±5.59	0.002*
Pre Extubation	95.64±12.23		91.23±12.46		100.29± 21.62	
After Extubation						
1 Min	109.80± 9.33	0.002*	109.16± 10.57	0.099	125.12± 6.74	0.000*
2 Min	101.52± 7.35	0.321	106.64± 10.66	0.490	123.80± 6.12	0.000*
3 Min	95.72±6.70	0.257	104.08± 10.98	0.256	120.68± 6.54	0.001*
5 Min	88.64±6.12	0.066	99.08±8.76	0.210	116.68± 7.38	0.027*
10 Min	83.64±6.00	0.000*	92.56±6.00	0.000*	108.16± 8.96	0.254

*Significant

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