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Original Research Article

COMPARATIVE STUDY OF DEXMEDETOMIDINE AND MAGNESIUM SULPHATE IN ATTENUATION OF PRESSOR RESPONSE DURING EXTUBATION IN LAPAROSCOPIC CHOLECYSTECTOMY

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ABSTRACT

Background: Cardiovascular stress response to extubation can result in elevated heart rate and mean arterial blood pressures which can be detrimental. The objective is to study and compare the efficacy of Dexmedetomidine 0.7mcg/kg versus Magnesium sulphate 30mg/kg in attenuating the pressor response to tracheal extubation.

Materials and Methods: 60 patients aged between 20-50yrs of both sexes scheduled for elective laparoscopic cholecystectomy procedures belonging to ASA Grade1 and ASA Grade II were included in study, divided into 2 groups of 30 each, in randomized double blinded manner. A detailed history, complete physical examination and necessary investigations are done for all patients. Group D patients received 0.7mcg/kg of Inj Dexmedetomidine in 100ml Normal Saline[0.9% sodium chloride] Over 10 minutes duration at the time of port site skin closure. Group M patients received 30mg/kg Inj magnesium sulphate in 100ml Normal Saline[0.9% sodium chloride] Over 10 minutes duration at the time of port site skin closure.

Results: Dexmedetomidine group had a better quality of extubation compared to MgSO4 group. Ramsay sedation score post-operative period were statistically significant between the dexmedetomidine and MgSO4 groups, with the latter showing more sedative effect than former. There was no statistically significant difference found between two groups with respect to Duration of emergence of extubation. In our study other complications like bradycardia, hypotension, respiratory depression, bronchospasm and laryngospasm were not observed in any of the patients in both the groups.

Conclusion: Dexmedetomidine administered in the dose of 0.7mcg/kg body weight before tracheal extubation, was more effective in maintaining the hemodynamic stability, facilitated smooth tracheal extubation with no side effects and had a better quality of recovery as compared to Magnesium Sulphate administered in the dose of 30mg/kg body weight.

Keywords: Attenuation, Stress Response, Extubation; Dexmedetomidine; Magnesium Sulphate; Laparoscopic Cholecystectomy.

INTRODUCTION

During general anaesthesia laryngoscopy, tracheal intubation and extubation are the critical events which provoke transient but marked sympatho-adrenal response that manifests as hypertension and tachycardia. Additionally, in laparoscopic surgery, CO2 is routinely utilised to create carboperitoneum, which causes increased plasma level of catecholamine and vasopressin. Elevation of intra-abdominal pressure with raised diaphragm is known to cause various adverse effects on the cardiovascular system such as decreased cardiac output, elevated arterial pressure, and increased systemic and

pulmonary vascular resistance leading to hypertension and tachycardia.[1]

Endotracheal extubation is the trans-tracheal removal of endotracheal tube from trachea via the nose or mouth. Tracheal extubation is the discontinuation of an artificial airway when the indications for its placement like airway obstruction, airway protection, suctioning of airway, ventilatory failure and hypoxemia no longer exists. For a smooth extubation, there should not be any straining, movement, coughing, breath holding or laryngospasm. [2]

In regards to difficulty in extubation many problems have been discussed like, bronchospasm, laryngospasm, stridor, airway obstruction, tracheal collapse, laryngeal oedema, supraglottic oedema, retroarytenoid oedema, subglottic oedema, vocal cord paralysis, pulmonary oedema associated with upper airway obstruction. At the same time, airway irritation appearing during tracheal extubation may cause cough or difficulties in breathing and may contribute to an increase in blood pressure.[3]

A better understanding of the problems of tracheal extubation and devising appropriate management strategy to tide over these crisis helps us to avoid these complications and provide better patient care and safety.

LAPAROSCOPY is considered "the golden standard" in treating symptomatic gallstones. Because its benefits are superior to open cholecystectomy. It has the benefits such as small incision, improved cosmetic aspects, less postoperative pain, and quick recovery time to normal activities

In laparoscopic cholecystectomy, initial Trendelenberg position, creation of carbo-peritoneum, systemic absorption of CO2 and reverse Trendelenberg position cause patho-physiological changes in various systems of the body leading to increase in plasma levels of nor epinephrine, epinephrine and plasma renin activity.[4]

The most commonly used gas for insufflation is carbon dioxide and is usually administered at a rate of 1–2 ml/min. As it is a highly soluble gas, it is readily absorbed into the circulation through the peritoneum, causing hypercapnia and acidosis. Insufflation, causes an increase in intra-abdominal pressure (IAP), the diaphragm is pushed upwards causing stiffness of the chest wall, causing the total volume of the lungs to be reduced. Hence the pulmonary compliance is decreased to 35–40%.[5, 6]

Hypercarbia has direct and indirect sympatho-adrenal stimulating effects on cardiovascular functions. The physiological effects of intra-peritoneal carbon dioxide insufflation combined with variations in patient positioning can have a major impact on cardio-respiratory function.[7]

Dexmedetomidine, a newer drug in this class is a highly selective alpha 2 adrenergic agonist. It has a selective anxiolytic and analgesic actions as well. It is known to exhibit dose dependant attenuation of stress response to intubation without causing significant respiratory depression.[8]

It has a sympatholytic effect, similar to clonidine, causing decrease in the concentration of norepinephrine. This further decreases the BP and the HR. Thus it may be theoretically appropriate for reducing airway and circulatory reflexes during emergence from anaesthesia. Effects on hemodynamics are mediated by inhibition of central sympathetic outflow.[9]

Magnesium sulphate is a non-competitive NMDA (N-methyl- D-aspartate) receptor antagonist, Magnesium is well known to block the release of catecholamine from both adrenergic nerve terminals and the adrenal glands and IV Magnesium Sulphate inhibits catecholamine release associated with laparoscopy. Magnesium is also known to produce vasodilatation by directly acting on blood vessels, and in high doses, attenuates vasopressin mediated vasoconstriction.[10,11]

With this background, this study was conceptualized to analyse the outcome of dexmedetomidine with that of intravenous Magnesium sulphate on the recovery profiles during endotracheal extubation.

MATERIALS AND METHODS

The proposed study is a double blinded study and was conducted in the department of Anaesthesiology, Adichunchanagiri Institute of Medical Sciences and Research Centre, B.G.Nagara, Mandya District between January 2019- June 2020 with permission from the ethical committee of the institute.

Data was sourced from 60 adult patients, of both sexes in a randomized prospective manner undergoing elective Laparoscopic cholecystectomy surgery.

Inclusion Criteria:

- Written informed consent
- The patients of both sexes with the age group from 20 to 50 years.
- ASA Grade 1 and Grade II
- Study group consisted of 60 patients scheduled for Laparoscopic cholecystectomy procedure under general anaesthesia.

Exclusion criteria:

- Patients refusal
- Patients aged <20yrs, >50yrs
- ASA physical status III and IV
- Emergency surgical interventions.

Patients having any significant systemic disorders, IHD, Hypertensive heart disease, diabetes mellitus, bronchial asthma, patients with previous myocardial infarction, patients with known drug allergy, patients with cerebrovascular insufficiency or associated with co-morbid disease and smoker will be excluded from the study.

Sixty patients aged between 20-50yrs of both sexes scheduled for elective laparoscopic cholecystectomy procedures belonging to ASA Grade1 and ASA Grade II were included in study. The study population was divided into 2 groups comprising of 30 patients in each group.

- Group D - The patients received 0.7mcg/kg of Inj Dexmedetomidine in 100ml Normal Saline[0.9% sodium chloride]Over 10 minutes duration at the time of port site skin closure (n=30)
- Group M-The patients received 30mg/kg of Inj magnesium sulphate in 100ml Normal Saline[0.9% sodium chloride]Over 10 minutes duration at the time of port site skin closure (n=30)

Pre-anaesthetic evaluation was done on the evening before the surgery after obtaining informed written consent. A routine pre-anaesthetic examination was conducted assessing

- General condition of the patient
- Nutritional status, weight and height of the patient.
- A detail examination of vital organ systems including respiratory system, cardiovascular system, central nervous system, renal system, hepatic system.

Induction of anaesthesia:

Anaesthesia was induced with Inj Propofol 2mg/kg and endotracheal intubation was facilitated with Inj succinylcholine 1.5mg/kg. After confirming bilateral equal air entry, the endotracheal tube was secured.

Anaesthesia was maintained using 66% nitrous oxide and 33% oxygen. After the patients recovered from Inj succinylcholine further neuromuscular blockade was maintained with non-depolarizing muscle relaxant Inj vecuronium bromide with a loading dose of 0.04mg/kg and a top up dose of Inj Vecuronium 0.01mg/kg intermittently and intermittent isoflurane 0.5-1%was used during maintenance.

At the end of the surgery, percentage of oxygen saturation (SPO2), heart rate, systolic and diastolic blood pressure, mean arterial pressure[MAP], ECG, end tidal carbon-di-oxide, were recorded. These served as baseline values. As the surgeon started closing the port site, study drugs were infused over 10 minutes. Group D - patients received 0.7mcg/kg of Inj Dexmedetomidine in 100ml Normal Saline [0.9% sodium chloride]. Group M- patients received 30mg/kg of Inj magnesium sulphate in 100ml Normal Saline [0.9% sodium chloride].

Then the patients received neuro muscular block reversal agent (Inj. Neostigmine 0.05mg/kg IV and Inj Glycopyrrolate 0.01mg/kg IV) and patients were extubated once the respiratory efforts were adequate andpatient started to regainconsciousness.

- Heart rate (HR) in beats per min (bpm)
- Oxygen saturation (SPO2).
- Systolic blood pressure (SBP) in mmHg.
- Diastolic blood pressure (DBP) in mmHg.
- Mean Arterial Pressure [MAP].
- continuous ECG monitoring in lead II
- End tidal carbon dioxide [ETCO2]

The above parameters were recorded as follows:

- At the end of surgery which serves as baseline.
- At the time of administration of study drug.
- 3min and 5 min after administration of study drug.
- At the time of extubation
- After extubation at 1 min, 3 min, 5 min, 10 min, 15 min.

The following parameters were recorded in all the patients.

Sedation was evaluated using Ramsay sedation scale at 5 mins after extubation.

Sample Size Estimation: The sample size was decided in consultation with the statistician and was based on initial pilot study observations, indicating that approximately 23 patients should be included in each group in order to ensure a power of 0.80.

Statistical analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test or Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs. P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS

This section of the dissertation is devoted for the presentation of results of the present study which was conducted at Adichunchanagiri Institute Of Medical Sciences, Mandya. 60 patients aged 20-50yrs of both sexes belonging to ASA Grade I and II were randomly selected and divided into 2 groups comprising of 30 patients in each group.

Group D - 0.7mcg/kg of Inj Dexmedetomidine in 100ml Normal Saline [0.9% sodium chloride]

Group M- 30mg/kg of Inj magnesium sulphate in 100ml Normal Saline [0.9% sodium chloride].

Table 1: Distribution of subjects according to sex among the groups

	Group		Total
	D	M	
Female	16	22	38
	53.3%	73.3%	63.3%
Male	14	8	22
	46.7%	26.7%	36.7%
Total	30	30	60
	100.0%	100.0%	100.0%

The P Value is 0.108, there was no statistically significant difference found between two groups with respect to distribution of sex.

Table 2: Comparison of mean age between two groups

	Mean	Std. Deviation	P Value
Group D	36.10	10.001	0.697
Group M	35.13	9.092	

In group D Mean age was 36.10+10yrs. In group M Mean age was 35.13+9.09yrs.The P value was 0.697.There was no statistically significant difference found between two groups with respect to distribution of age.

Table 3:- Distribution of subjects according to Pre-op diagnosis among the groups

	Group		Total
	D	M	
Cholelithiasis	27	28	55
	90.0%	93.3%	91.7%
GB polyp	3	2	5
	10.0%	6.7%	8.3%
Total	30	30	60
	100.0%	100.0%	100.0%

In Group D90% of the subjects had Cholelithiasis and 10% of the subjects had GB polyp. In Group M 93.3% of the subjects had Cholelithiasis and 6.7% of the subjects had GB polyp.The P Value was 0.640, there was no statistically significant difference found between two groups with respect to Pre-op diagnosis.

Table 4: Comparison of mean weight between two groups

	Mean	Std. Deviation	P Value
Group D	63.43	10.947	0.07
Group M	68.63	11.355	

The P value was 0.07. There was no statistically significant difference found between two groups with respect to weight.

There was a statistically significant difference found between two group with respect to heart rate at 3min after administration of study drug with P value being 0.041,5min after administration of drug, P value was less than 0.01, At time of extubation, after extubation 0min, 1min, 3min, 5min, 10min, 15min, P value was less than 0.01 which were all statistically significant. Group D showed significant decrease in heart rate compared to group M.

There was a statistically significant difference found between group D and group M with respect to Systolic blood pressure. At 5min after administration of drug with P value was 0.011, At time of extubation P Value was less than 0.01, after extubation at 0min and 1 min P value was less than 0.01, 5min after extubation P value was 0.023, 10min after extubation P value was less than 0.01, 15min after extubation P value was less than 0.01, which were all statistically significant. Group D showed significant decrease in systolic blood pressure compared to group M.

There was a statistically significant difference found between group D and group M with respect to Diastolic blood pressure. At5min after administration of drug the P value was less than 0.01, At time of extubation P value was less than 0.01, after extubation at 0min and 1min P value was less than 0.01,at 3min P value was 0.033, at 5min P value was less than 0.01 ,at 10min P value was less than 0.01, at 15min P value was less than 0.01, which were all statistically significant, with group D showing significant decrease in mean Diastolic pressure when compared to group M.

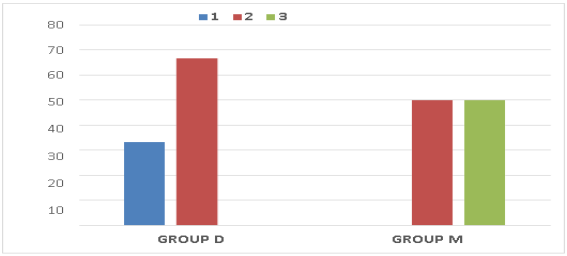

Figure 1: Graph showing Distribution of subjects according to Ramsay sedation scaleamong the groups

P Value 0.035, there was a statistically significant difference found between two groups with respect to quality of extubation. Quality of extubation was better in Group D than Group M.

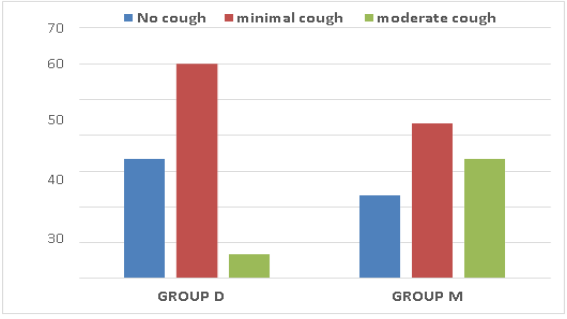

Figure 2: Graph showing Distribution of subjects according to quality of extubation among the groups.

There was a statistically significant difference found between two group with respect to Mean arterial pressure (MAP). At 5min after administration of study drug P value was less than 0.01, At time of extubation P value was less than 0.01, after extubation at 0min and 1min P value was less than 0.01, at 3min P value was 0.046, at 5min P value wasless than 0.01, at 10min P value was less than 0.01, at 15min P value was less than 0.01, which were all statistically significant. Group D showing significant decrease in Mean arterial pressure compared to that of Group M. The results were statistically not significant between two group in regards to oxygen saturation. P Value <0.001, there was a statistically significant difference found between two groups with respect to Ramsay sedation scale. In Group M sedation was more compared to group D.

Table 5: Comparison of mean Duration of emergence of extubation between two groups

	Mean	Std. Deviation	P Value
Group D	9.17	1.315	<0.001
Group M	12.03	2.236	

There was statistically significant difference found between two groups with respect to Duration of emergence of extubation with P value being less than 0.001 with Group D showing lesser duration of emergence compared to that of Group M.

DISCUSSION

Several drugs have been tried to obtund the hemodynamic extubation response but all have variable side effects that may affect the quality of short-term recovery.

Dexmedetomidine and Magnesium Sulphate are associated with control of the hemodynamic changes mentioned above and stressful airway responses.

This was a prospective, randomised, double blind study carried out in Adichunchanagiri Institute of Medical Sciences to analyze the effects of Dexmedetomidine versus Magnesium Sulphate, variations in hemodynamic and recovery responses during tracheal extubation.

This study was conducted in 30 patients belonging to ASA I AND II, between the age group of 20 to 50 years of age of both sexes who were posted for elective laparoscopic cholecystectomy surgeries.

Group D - The patients received 0.7mcg/kg of Inj Dexmedetomidine in 100ml Normal Saline [0.9% sodium chloride] Over 10 minutes duration at the time of port site skin closure (n=30).

Group M-The patients received 30mg/kg of Inj magnesium sulphate in 100ml Normal Saline [0.9% sodium chloride] Over 10 minutes duration at the time of port site skin closure (n=30).

Parameters observed included Oxygen saturation (SPO2),Heart rate (HR) in beats per min (bpm),Systolic blood pressure (SBP) in mmHg, Diastolic blood pressure (DBP) in mmHg, Mean Arterial Pressure [MAP], continuous ECG monitoring in lead II, End tidal carbon dioxide [ETCO2], At the end of surgery served as baseline, At the time of administration of study drug, 3min and 5 min after administration of study drug, At the time of extubation, After extubation at 0min, 1 min, 3 min, 5 min, 10 min, 15 min.

Dexmedetomidine 0.5µg/kg[83] and magnesium sulphate 25mg/kg[12] are the lowest possible doses studied for this purpose with significant effect, whereas maximum dose of dexmedetomidine studied for this purpose is 1mcg/kg which showed significant bradycardia and hypotension,whereas the maximum dose of Magnesium sulphate studied for this purpose with significant effect is 50mg/kg,[12,13] which showed significant side effects such as hypotension, increase in duration of emergence.

Hence in our study we have used Dexmedetomidine 0.7mcg/kg and magnesium sulphate 30mg/kg to know the effects on attenuation of pressor response during extubation.

In our study, we observed that the heart rate increased in Magnesium Sulphate group as compared to their baseline values. But, the Dexmedetomidine group was associated with a lesser incidence of increase in heart rate as compared to that of Magnesium Sulphate.

This is in conjunction with observation done by TANDON et al,[14] who observed that HR records were significantly lower in groups receiving Dexmedetomidine compared to group receiving Magnesium Sulphate with P value being less than 0.01.

Systolic Blood Pressure: Dexmedetomidine Group showed significant decrease in systolic blood pressure with respect to its baseline values compared to Magnesium sulphate group.

This is in conjunction with the observation done by Vudithe K, et al,[15] who observed that On comparing Magnesium sulphategroup with Dexmedetomidine group, significant difference (p<0.01) in SBP was observed at all the time intervals after drug administration, post extubation.

Diastolic Blood Pressure: In our study, we observed that the diastolic blood pressure variations between Dexmedetomidine and Magnesium Sulphate were statistically significant.

The findings are concurrent with the study conducted by TANDON N et al,[14] who observed that diastolic blood pressure were significantly decreased in group receiving Dexmedetomidine than group receiving Magnesium Sulphate with P value being less than 0.05.

Mean Arterial Pressure: In our study, we observed that Dexmedetomidine had a better control over mean arterial pressure as compared to that of Magnesium Sulphate and it remained statistically significant.

So, the findings are similar to the study conducted by PASSAINT FH, AMANY HS et al,[16] who observed that MAP values difference were more when compared the Dexmedetomidine group with ($p<0.001$), that of Magnesium sulphate group.

Extubation Quality Score: In our study, patients in Dexmedetomidine group extubated smoothly with minimal cough when compared to Magnesium sulphate group. Moreover, in the Dexmedetomidine group, 6.7 % of the patients had moderate cough whereas,in the Magnesium Sulphate group, 33.4% of the patients had moderate cough during extubation.

Hence, in our study, the quality of extubation is better with Dexmedetomidine when compared with Magnesium Sulphate which is in concurrence with the study conducted by VUDITHE K, et al,[15] who observed in their study that83.33% of patients in Dexmedetomidine group had no coughing, while 66.66% of patients in Magnesium sulphate group had no cough. Minimal coughing was observed in 16.66% of patients in Dexmedetomidine group and 26.66% of patients in group. Moderate coughing was observed in 6.66% of patients in Magnesium sulphate group. Thus statistical analysis shows there was lower extubation score in Dexmedetomidine group compared to Magnesium sulphate group.

Adverse Effects: Sedation in our study was assessed using Ramsay Sedation Scale. Significant number of patients in Magnesium Sulphate group were drowsy [25%] but responded to oral commands [score of 3] when compared with patients in the Dexmedetomidine group with P value being less than 0.001 which was statistically significant.

This observation was similar to the findings of Srivastava K et al,[13] who observed that,higher sedation score (score 2, 3) was seen in Magnesium sulphate group [30mg/kg]as compared to Dexmedetomidine group[0.5mcg/kg]

In our study, bradycardia, hypotension, bronchospasm, laryngospasm were not observed in any patients.

CONCLUSION

Dexmedetomidine administered in the dose of 0.7mcg/kg body weight before tracheal extubation, was more effective in maintaining the hemodynamic stability, facilitated smooth tracheal extubation with no side effects and had a better quality of recovery as compared to Magnesium Sulphate administered in the dose of 30mg/kg body weight.

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