Section: Anesthesiology

Original Research Article

COMPARATIVE STUDY OF INTRAVENOUS DEXMEDETOMIDINE AND INTRAVENOUS MAGNESIUM SULFATE FOR ATTENUATION OF CARDIOVASCULAR STRESS RESPONSE DURING LAPAROSCOPIC APPENDICECTOMY UNDER GENERAL ANAESTHESIA

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Abstract

Background: Laryngoscopy and intubation and pneumoperitoneum incur a reflex sympathetic discharge which causes a hemodynamic response characterized by tachycardia, rise in blood pressure. This study was to compare the effects of preoperative intravenous magnesium sulphate (MgSo4) and dexmedetomidine on the hemodynamic changes in response to laryngoscopy and intubation and to pneumoperitoneum in cases of laparoscopic appendicectomy. **Materials and Methods:** A randomized, prospective, double blinded interventional comparative study was conducted on 140 patients undergoing laparoscopic appendicectomy. Patients were randomized into 2groups, having 70 patients, to receive magnesium sulphate (30mg/kg) and dexmedetomidine (1mcg/kg) 5 mins before intubation. Baseline readings of heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and after intubation at 0, 3, 5, 10mins of intubation were recorded. Baseline readings of HR, SBP, DBP, MAP and at 0,5,10,30 minutes of pneumoperitoneum were also recorded. **Result:** Heart rate (post intubation) at 3 mins in group D was 73.47 ± 6.89 and in group M 83.46 ± 6.40 which was significant with p value 0.001. Similarly heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure at 0,3,5mins in group D was significant in comparison to group M. Whereas mean arterial pressure at 10 mins was comparable among both groups and hence insignificant. Similarly stress response due to pneumoperitoneum was measured with heart rate, SBP, DBP, MAP at baseline and at 0,1,5,10,30 minutes and found significant in group D except values at 30 minutes. **Conclusion:** From the study it was found that incidence of bradycardia and sedation was more in dexmedetomidine group whereas incidence of nausea, vomiting and hypotension was more in magnesium sulfate group but was statistically not significant. Elevated pressor response was seen in magnesium sulphate group which was statistically significant. It was concluded that Intravenous dexmedetomidine 1µg/kg was better than intravenous magnesium sulfate 30mg/kg given before intubation for attenuation of the cardiovascular stress responses to laryngoscopy and endotracheal intubation and stress response to pneumoperitoneum in cases of laparoscopic appendicectomy.

INTRODUCTION

Direct laryngoscopy and endotracheal intubation cause stress response mainly due to the activation of sympathetic nervous system. Both the procedures cause an increased surge in heart rate, blood pressure and in vulnerable patients may cause hazardous effects like cerebrovascular accidents, angina pectoris and even myocardial infarction.[1] The hemodynamic and respiratory alterations associated with laparoscopic surgery are caused by increased intra-abdominal pressure brought over by pneumoperitoneum. Laparoscopy is associated with increase in serum catecholamine levels during pneumoperitoneum. During laparoscopic appendicectomy, the trendelenburg position may cause decrease in venous return hence decreasing cardiac output. The most relevant hemodynamic changes are decrease in venous return secondary to inferior venacava compression and increase in central venous pressure and arterial blood pressure in absence of heart rate changes.[2,3]

Perioperative ischemia is associated with a significant increase in postoperative morbidity and mortality. Modern anesthesia practices therefore aim to prevent sympathetic discharge and provide hemodynamic stability perioperatively. Methods used for reducing the stress response to laryngoscopy are deepening the plane of anaesthesia with inhalational and intravenous anaesthetic agents and decreasing the total duration of laryngoscopy to less than 15 seconds.[4] Usage of drugs like lidocaine, opioids, vasoactive drugs like sodium nitropruside, calcium channel blockers, beta blockers, alpha 2 agonists like clonidine and dexmedetomidine and magnesium sulphate in attenuation of stress response due to laryngoscopy has been quite in practice.[4]

Venugopal S et al,[5] studied dexmedetomidine in attenuating hemodynamic response to intubation and found that premedication with dexmedetomidine at dose of 1mcg/kg attenuated the pressor response associated with laryngoscopy and tracheal intubation. The attenuation occured within 5 minutes following laryngoscopy and endotracheal intubation and became maximum by 10 minutes. Krishna chaitanya et, al,[6] compared intravenous 50% magnesium sulphate 30mg/kg and dexmedetomidine 1 mcg/kg for changes in hemodynamic parameters and found that both attenuated the systolic, diastolic, mean blood pressure but magnesium sulphate failed to attenuate increase in the heart rate. So this study was undertaken with dexmedetomidine and magnesium sulfate intravenously to compare the efficacy in attenuating cardiovascular stress response to intubation and pneumoperitoneum in laparoscopic appendicectomy.

MATERIALS AND METHODS

This randomized double blind control study was carried out at SRM Medical College and Hospital Bhawanipatna from March 2024 to July 2024 in the department of anaesthesia. The sample size was calculated to be 128, divided into two groups with each group containing 64 persons. Considering 10% dropouts, sample size was 140. So the effective sample size was calculated to be 70 in each group. Patients from both sexes of ASA grade I and II, age 18 to 60 years, BMI < 30kg/m2 with mallampati class I and II undergoing elective laparoscopic appendicectomy under general anesthesia were included in the study. Patients with anticipated difficult airway, with comorbidity like CKD and hypertension, history of allergy to drugs, BMI>30 Kg/m2 and pregnant patients were excluded from the study.

Routine investigations like complete blood count, urine analysis, serum electrolytes, urea and creatinine, fasting blood glucose, liver enzymes and an ECG were done. Written informed consent was duly signed by the patients. After proper pre-anaesthetic check alprazolam 0.5mg and ranitidine 150mg was given orally on the night before surgery and were kept nil per oral for 8 hours before surgery. Both patients and the observers to note the vitals were unaware of the drug administered as infusion.

Patients were premedicated with inj midazolam (0.05mg/kg), inj ondansetron(0.1mg/kg), inj nalbuphine (0.2mg/kg), inj. glycopyrrolate (0.005mg/kg). Group M patients were administered 30mg/kg of 50% magnesium sulphate in 100 ml of normal saline over 15 minutes, 5 min before intubation. Group D patients received intravenous dexmedetomidine 1mcg /Kg in 100 ml of normal saline over 15 minutes, 5 min before intubation. Patients were induced with injection of propofol 2mg/kg followed by rocuronium 1mg/kg to facilitate intubation. Total duration of intubation was noted. Duration of laryngoscopy more than 25 seconds was excluded from the study. Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure before intubation and at 0, 1, 3, 5 and 10 minutes after intubation and at 0,1,5,10,30 minutes after pneumoperitoneum were noted. Surgeons were advised to keep intra-abdominal pressure within 15 mm Hg and to maintain throughout the surgery. Anaesthesia was maintained with O2, N2O, isoflurane and inj. rocuronium. Patients were monitored for any adverse effects like bradycardia, hypotension during intraoperative and postoperative period, nausea, vomiting and level of sedation by modified Ramsay sedation score.

Statistical Analysis: Data was entered in Microsoft excel format. After baseline characteristics all data was analysed using SPSS statistical software version 22. Demographic variables were represented using descriptive statistics. Continuous data was expressed as mean±standard deviation and analysed in terms of student's t-test. Categorical data was expressed in proportion and measured in terms of Chi-square test.

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RESULTS

Table 1: Demographic characteristics of study population.

Demographic Data			Group D(MEAN ± SD)	Group M(MEAN ± SD)	P-value
Age			35.8 ± 6.74	36.78 ± 7.41	0.41
BMI			21.53 ± 1.34	21.66 ± 1.28	0.56
SEX	Male		38	39	1.0
	Female		32	31	
ASA grade	I		29	30	0.8
	II		41	40	
MALLAMPATI SCORE		1	41	38	0.6
		2	29	32	
Duration of laryngoscopy			14.44 ± 2.63	14.62 ± 2.74	0.68

Table 2: Comparison of HR (intubation) between 2 groups

TIME (MIN)	Group D	Group M	P-value
PRE OP	83.63±7.59	83.94±7.18	0.8
(Before intubation)	75.53 ± 8.58	75.03 ± 8.86	0.73
0 MIN	82.84 ± 8.18	90.46 ± 9.10	0.001
1 MIN	75.74 ± 8.50	84.33 ± 8.91	0.001
3 MIN	73.47 ± 6.89	83.46 ± 6.40	0.001
5 MIN	69.60 ± 5.56	77.37 ± 6.44	0.001
10 MIN	68.54 ± 6.1	71.17 ± 6.89	0.019
BASELINE (BEFORE PNEUMOPERITONEUM)	76.01 ± 8.312	75.37 ± 8.760	0.657
0 MIN (AFTER PNEUMOPERITONEUM)	83.16 ± 8.217	90.46 ± 9.1	0.001
1 MIN	76.36 ± 8.506	84.33 ± 8.919	0.001
5 MIN	74.17 ± 6.88	83.46 ± 6.408	0.001
10 MIN	70.11± 6.826	77.36 ± 6.438	0.001
30 MIN	68.97 ± 6.169	71.20 ± 6.888	0.046

Table 3: Comparison of SBP (intubation) between 2 groups.

TIME (MIN)	Group D	Group M	P-value
PRE OP	129.5±8.95	129.86±9	0.81
(Before intubation)	123.46 ± 9.8	125.26 ± 8.6	0.25
0 MIN	129.10 ± 9.03	134.11 ± 9.32	0.002
1 MIN	124.14 ± 8.9	129.50 ± 8.62	0.001
3 MIN	118.39 ± 9.28	126.89 ± 8.82	0.001
5 MIN	113.09 ± 8.04	120.09 ± 7.9	0.001
10 MIN	113.6 ± 7.03	117.49 ± 6.70	0.002
BASELINE (BEFORE PNEUMOPERITONEUM)	124.01± 9.644	125.29 ± 8.693	0.414
0 MIN (AFTER PNEUMOPERITONEUM)	129.63 ± 9.381	134.10 ± 9.311	0.005
1 MIN	124.97± 9.231	129.50 ± 8.624	0.003
5 MIN	118.77 ± 8.901	126.89 ± 8.826	0.001
10 MIN	113.96 ± 8.006	120.09 ± 7.940	0.001
30 MIN	114.59 ± 7.152	117.49 ± 6.702	0.015

Table 4: Comparison of DBP (intubation) between 2 groups.

TIME (MIN)	Group D	Group M	P-value
PRE OP	82.57±6.5	82.97±6.56	0.71
(Before intubation)	75.77 ± 7.26	76.24 ± 7.47	0.706
0 MIN	82.10 ± 6.92	87.84 ± 6.74	0.001
1 MIN	76.84 ± 6.98	82.76 ± 7.35	0.001
3 MIN	73.31± 6.32	79.30± 6.60	0.001
5 MIN	69.49 ± 5.95	74.17± 6.61	0.001
10 MIN	67.56 ± 5.49	69.75± 5.23	0.016
BASELINE (BEFORE PNEUMOPERITONEUM)	76.07 ± 6.939	76.24 ± 7.473	0.888
0 MIN (AFTER PNEUMOPERITONEUM)	82.43 ± 7.058	87.84 ± 6.743	0.001
1 MIN	77.00 ± 6.587	82.76 ± 7.351	0.001
5 MIN	73.97 ± 6.082	79.30 ± 6.66	0.001
10 MIN	69.89 ± 5.953	74.17 ± 6.618	0.001
30 MIN	69.49 ± 5.39	69.76 ± 5.23	0.784

Table 5: Comparison of MAP (intubation) between 2 groups

TIME (MIN)	Group D	Group M	P-value
PRE OP	98.74±7.83	99.14±7.77	0.76
(Before intubation)	87.74 ± 7.55	88.06 ± 7.33	0.8
0 MIN	98.50 ± 8.15	104.53 ± 7.73	0.001
1 MIN	92.59 ± 5.85	98.07 ± 6.10	0.001
3 MIN	88.73 ± 6.56	93.11 ± 6.74	0.001
5 MIN	84.97 ± 6.61	88.69 ± 7.45	0.002

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10 MIN	81.79 ± 6.93	83.75 ± 6.25	0.079
BASELINE (BEFORE PNEUMOPERITONEUM)	87.80 ± 7.369	88.06 ± 7.336	0.836
0 MIN (AFTER PNEUMOPERITONEUM)	98.73 ± 7.901	104.53 ± 7.736	0.001
1 MIN	93.30 ± 5.834	98.07 ± 6.104	0.001
5 MIN	89.19 ± 6.734	93.11 ± 6.745	0.001
10 MIN	85.49 ± 6.668	88.69 ± 7.455	0.008
30 MIN	82.41 ± 6.952	83.76 ± 6.254	0.232

Table 6: Adverse effects

Adverse effects	Group D	Group M	P-value
Sedation	15.7 %	12.85%	0.629
Bradycardia	8.5%	5.71%	0.512
Hypotension	4.28%	7.14%	0.47
Nausea	10%	12.8%	0.59
Vomiting	4.28%	7.14%	0.46

Adverse effects such as bradycardia and hypotension, nausea, vomiting and sedation are present in both the groups but are comparable showing p value insignificant.

DISCUSSION

The hemodynamic response to laryngoscopy and pneumoperitoneum can cause significant change of vitals in case of elderly, haemodynamically unstable patients or even in normal patients. Control of perioperative stress response is an integral part of anaesthesia. The demographic characteristics like age, weight, ASA status of the study population was similar in both the two groups with no statistically significant difference. The mean age in dexmedetomidine group was 35.8±6.74 years and in magnesium sulphate group were 36.78±7.41 years. The mean BMI in magnesium sulphate group was 21.56 ± 1.28 and in dexmedetomidine group was 21.53 ± 1.34. Mallampatti grading of patients were comparable in both group. Total duration of laryngoscopy in magnesium sulphate group was 14.82±5.88 seconds and in dexmedetomidine group was 13.92±6.02 seconds. The duration of surgery was also comparable among both groups with mean value 80.53±14.93 mins in group D and 81.79±13.76 mins in group M.

In Group M, magnesium sulphate 30mg/kg in 100ml normal saline and in group D, dexmedetomidine 1 µg/kg diluted in 100ml normal saline were used. The drugs were administered 5 minutes prior to intubation. In the Study done by Krishna chaitanya6, Magnesium sulphate 30mg/kg and dexmedetomidine 1 µg/kg were used. Both the drugs were effective in controlling the blood pressure but dexmedetomidine was more effective in controlling the heart rate. Patients in both groups were hemodynamically stable and reduced the requirements of opioids, muscle relaxants and volatile anesthetics agents. Recovery in both the groups was uneventful. Azin honarmand,[7] studied using different doses of magnesium sulphate i.e. 30 mg/kg, 40 mg/kg and 50 mg/kg. Hypotension was seen more in group who received 50mg/kg. No significant difference in extubation time between 3 groups. Venugopal et al,[5] used iv dexmedetomidine 1 µg /kg in attenuation of stress response during intubation. Attenuation occured within 5 minutes following laryngoscopy and intubation and became maximum by 10 minutes. In this study the haemodynamic parameters reached near base line values after 5 to10 minutes of intubation.

Though the p-value for heart rate was statistically significant, the mean value for heart rate in magnesium sulphate group did not change more than 15 beats/minute. Heart rate returned to normal within 5 minutes interval. This showed that Magnesium sulphate was also effective in attenuating the cardiovascular stress response to laryngoscopy, intubation and postpneumoperitoneum. Krishna chaitanya et al,[6] observed decrease in heart rate more with dexmedetomidine compared to magnesium sulphate. Heart rate variability was significant in dexmedetomidine compared to magnesium sulphate ($p<0.05$). Though the p value was statistically significant, the mean values for heart rate in magnesium sulphate group did not change more than 10 beats/minute and heart rate returned to normal within 5 minutes. Venugopal et al,[5] used 1 µg/kg iv dexmedetomidine and showed better suppression of mean heart rate when compared to the control group ($p=0.000$) which was statistically significant. Rashi kadam et al,[9] also infused magnesium sulphate 30mg/kg, 5 minutes prior to intubation and observed significant fall in heart rate in magnesium group at 1, 3, 5 and 10 minutes after intubation ($p <0.001$) than the placebo group.

Systolic blood pressure was found to be significant in group D while compared to group M (p value <0.05) showing that dexmedetomidine was better than magnesium sulfate but magnesium sulfate was quite effective in reducing stress response of intubation and post pneumoperitoneum variability of SBP remained within 20 mm Hg of baseline values. Krishna chaitanya et al,[6] observed no significant difference among magnesium sulphate and dexmedetomidine infusion at 0, 1, 3, 5, and 10 minutes for systolic blood pressures. Rajdip hazra et al,[10] used dexmedetomidine 0.5µg/kg, 5 min prior to induction and normal saline as control and observed statistically significant decrease in blood pressure in dexmedetomidine group compared to control group. Kalkeri et al,[11] used dexmedetomidine 1µg/kg, 5 min prior to induction and normal saline as control

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and observed statistically significant decrease in blood pressure when compared to control group.

Diastolic blood pressure was found to be significant in group D while compared to group M (P value <0.05) showing that dexmedetomidine was better than magnesium sulfate but magnesium sulfate was quite effective in reducing stress response of intubation and pneumoperitoneum as variability of DBP remained within 20 mm Hg of baseline values. Rashi kadam et al,[9] used magnesium sulphate 30mg/kg 5 min prior to induction. The average diastolic blood pressure in study group in first 5min after intubation was significantly less (p <0.05) compared to control group. Saraf et al,[12] used Dexmedetomidine 0.6µg/kg and he observed significant decrease in diastolic blood pressure than control group.

Mean blood pressure was found to be significant in group D while compared to group M (P value <0.05) showing that dexmedetomidine was better than magnesium sulfate but magnesium sulfate was quite effective in reducing stress response of intubation as variability of MBP remained within 20 mm Hg of baseline values. Krishna chaitanya et al,[6] used magnesium sulphate 30 mg/kg and dexmedetomidine 1 µg/kg and no statistically significant (p>0.05) difference between mean arterial pressures were found for both the drugs at 0, 1, 3, 5 and 10 minutes interval. The results were in contrast with our study as we got statistically significant difference among both groups except at 10 mins duration values. Rajan sunil et al,[13] used iv Magnesium sulphate 50mg/kg body weight 10 min before induction and 1.5mg/kg lignocaine 90sec before intubation and there was a decrease in mean arterial pressure from induction at 0, 1, 3, 5, and 10 minutes interval but no significant difference between the groups. K. montazeri et al,[14] did a randomised control study using iv magnesium sulphate 30mg/kg body weight 10 min before inducing the patient and there was significant decrease in mean arterial blood pressure. The results were comparable to our study.

James MF et al,[15] and D Jee et al,[16] used MgSO4 in a dose of 60 mg/kg and 50 mg/kg respectively and confirmed the efficacy of intravenous MgSO4 in controlling the hemodynamic response to critical incidences like laryngoscopy, intubation, pneumoperitoneum and extubation comparable to our study as magnesium sulfate helped in attenuation of the stress response during intubation and pneumoperitoneum. Shruthi P Kamble et al,[17] compared magnesium sulphate 50 mg/kg with clonidine 1 mcg/kg in laparoscopic cholecystectomy and concluded that the response was better with Magnesium 50 mg/kg in attenuating hemodynamic response to pneumoperitoneum. Bryskin and Weldon,[8] used a combination of dexmedetomidine and magnesium sulphate for hemodynamic control during laparoscopic resection of pheochromocytoma and reported that cardiovascular stability was achieved with the above combination.

In our study we observed bradycardia in 4 patients in magnesium sulphate group but 6 out of 70 patients developed bradycardia in dexmedetomidine group which was treated with 0.6mg inj atropine. Azin honarmand7 used different doses of Magnesium sulphate (Group i: 30 mg/kg, Group ii: 40 mg/kg, Group iii: 50 mg/kg). There was no difference in the incidence of bradycardia or hypotension in his study. This study showed that fall in heart rate was seen in both magnesium sulphate and dexmedetomidine group, but the cases were more in dexmedetomidine group but statistically insignificant. Similarly nausea was found in 7 patients in group D (10%), 9 patients in group M(12.8%), vomiting in 3 patients in group D(4.28%) and 5 patients in group M(7.14%), sedation in 11 patients in group D(15.7) and in 9 patients in group M(12.85%), hypotension in 3 patients in group D(4.28) and in 5 patients in group M(7.14%). Incidence of bradycardia and sedation was more in dexmedetomidine group whereas incidence of nausea, vomiting and hypotension was more in magnesium sulfate group but was statistically not significant.

CONCLUSION

Intravenous dexmedetomidine 1µg/kg was better than intravenous magnesium sulfate 30mg/kg when administered before intubation for attenuation of the cardiovascular stress responses to laryngoscopy, endotracheal intubation and stress response to pneumoperitoneum in cases of laparoscopic appendicectomy.

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