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EFFECT OF MAGNESIUM SULFATE AND DEXMEDITOMIDINE AS ADJUVANTS ON REQUIREMENT OF ANESTHETIC AGENTS IN TOTAL INTRAVENOUS ANESTHESIA- A RANDOMISED PLACEBO CONTROLLED TRIAL

Anaesthesiology

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ABSTRACT

INTRODUCTION Total intravenous anesthesia (TIVA) is a technique of general anesthesia which uses a combination of agents given exclusively by intravenous route. The advantages include greater hemodynamic stability, predictable and rapid recovery.Magnesium sulfate is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist with analgesic and sedative properties. Dexmeditomidine is a highly specific alpha-2-adrenergic receptor agonist. Both decreases sympathetic tone, attenuates stress responses to anesthesia and surgery. This randomized placebo controlled single blind study was designed to compare the effects of intravenous magnesium sulfate and dexmeditomidine with Conox-guided TIVA, in observing the anesthetic requirements, intraoperative hemodynamics and postoperative recovery.

OBJECTIVE

- **Research Question:**Can administration of magnesium sulfate or dexmeditomidine as adjuvant reduce the requirement of anesthetic agents in TIVA?
- **Aim and Objective:**

Primary outcome: Requirement of anesthetic agents.
Secondary outcome: Hemodynamic stability and recovery indices.

METHODOLOGY

After ethical committee approval, CTRI registration and informed consent, a randomised single blind study was conducted in 100 patients posted for laparoscopic cholecystectomy, of which 81 completed analysis. The mean of anesthetic drugs required as observed in an earlier publication with 95% confidence level and 80% power, the minimum sample size was 27 in each group. They were allocated to 3 groups of 27 each based on computer generated numbers by block randomization. Patients received study drug prior to induction. Uniform anesthetic regime was followed in all patients. Intraoperative requirement of anesthetic agents and hemodynamic parameters were observed. Results on continuous measurements were expressed as Mean±SD while that of categorical measurements-number %. Significance was assessed at 5% level of significance ($p<0.05$). Chi square test and one way analysis of variance (ANOVA) was used and if significant, post hoc Bonferonni test adopted for pairwise comparison.

RESULTS

All demographic variables (age, sex, ASA physical status) were comparable between the groups except for duration of surgery and BMI, i.e, significant difference in group B (duration of surgery: $p=0.001$, BMI: $p=0.009$). There was statistically significant reduction in propofol induction dose in group A ($p=0.023$, mean dose=90.37±26.67mg).There was no significant difference in requirements of fentanyl and atracurium between the groups. There was significant reduction in SBP in group A at 20mins intraoperative period ($p=0.023$). There was no significant difference in SBP at other time points between the groups. There was significant reduction in DBP in group A at intubation ($p=0.002$), intraoperative period ($p=0.007$), after surgery ($p=0.003$) and at extubation ($p=0.006$). HR showed statistically significant reduction in group A throughout the surgery (intubation $p=0.004$, intraoperative period $p=<0.001$, after surgery $p=<0.001$ and extubation $p<0.001$). There was significant reduction in MAP in group A in the intraoperative period ($p=0.017$), after surgery ($p=0.037$) and at extubation ($p=0.015$). There was statistically significant difference in recovery time ($p<0.001$), orientation time ($p<0.001$) and extubation time ($p<0.001$).

CONCLUSION

We conclude pretreatment with 0.5µg/kg of dexmeditomidine and its maintenance infusion of 0.3µg/kg/hour was better than magnesium sulfate as adjuvant in optimizing TIVA requirements and providing hemodynamic stability in laparoscopic cholecystectomy.

KEYWORDS

TIVA; dexmeditomidine; magnesium sulfate; randomised controlled trial; hemodynamics; laparoscopy.

INTRODUCTION

Total intravenous anesthesia (TIVA) is a technique of general anesthesia which uses a combination of agents given exclusively by intravenous route. The advantages include greater hemodynamic stability, predictable and rapid recovery.Magnesium sulfate is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist with analgesic and sedative properties. Dexmeditomidine is a highly specific alpha-2-adrenergic receptor agonist. Both decreases sympathetic tone, attenuates stress responses to anesthesia and surgery.Laparoscopic cholecystectomy is considered the gold standard of treatment for symptomatic cholelithiasis. The benefits include reduced blood loss, smaller incision, reduced pain, shortened recovery time,reduced exposure of internal organs to possible external contaminants and better postoperative pain profiles. Carbon dioxide (CO2) induced pneumoperitoneummay result in adverse cardiovascular effectssuch as abrupt elevation of mean arterial pressure, systemic vascular resistance, and decreased cardiac output because of the release of both catecholamines and vasopressin. Many drugs have been developed for the attenuation of these vasopressor responses, and include opioids, beta blockers, lidocaine, magnesium, and a2 agonists. As none of the above methods were proved to be ideal, the search of an ideal agent to attenuate the hemodynamic responses is still continuing.

This randomized placebo controlled single blind study was designed to compare the effects of intravenous magnesium sulfate and dexmeditomidine with Conox-guided TIVA, in observing the anesthetic requirements, intraoperative hemodynamics and postoperative recovery.

OBJECTIVES

- **Research Question:** Can administration of magnesium sulfate or dexmeditomidine as adjuvants reduce the requirement of anesthetic agents in TIVA?
- **Aim and Objective:**

Primary outcome: Requirement of anesthetic agents.
Secondary outcome: Hemodynamic stability and recovery indices.

METHODOLOGY

Study Design: Randomized placebo controlled single blind study.

Study Population: Low risk adult patients who underwent laparoscopic cholecystectomy for maximum duration of 2hrs in Jubilee mission medical college and research institute, Thrissur over a period of one year from 24/4/19-24/4/20.

INCLUSION CRITERIA:

1. Adult patients 20 to 70 years of age.
2. American society of anesthesiologists (ASA) physical status I and II.
3. Scheduled for elective laparoscopic cholecystectomy (maximum duration 2hrs)

EXCLUSION CRITERIA:

Patients with the following conditions are excluded from the study

1. Obesity (BMI>30)
2. Pregnancy
3. Hepatic, renal, respiratory disorders.
4. Seizure disorder , endocrinal, hematological disorders
5. Prior neuromuscular disease
6. Any degree of heart block
7. Chronic use of opioids
8. Prior treatment with calcium channel blockers and beta blockers.
9. Patients receiving magnesium supplementation.

SAMPLE SIZE:

The mean of anesthetic drugs required as observed in an earlier publication of "Advanced Pharmaceutical Bulletin- Comparative evaluation of dexmeditomidine and magnesium on propofol consumption, hemodynamics and postoperative recovery in spine surgery Mar17(2016)", with 95% confidence level and 80% power, the minimum sample size comes to 27 in each group.

$$\text{Sample size(n)} = (S_1^2 + S_2^2)\frac{[Z_{1-\alpha/2} + Z_{1-\beta}]^2}{(\bar{x}_1 - \bar{x}_2)^2} \qquad (n=27)$$

RANDOMISATION.

We generated 100 computer generated random samples (Using "**Random UX**" computer application) to account for any loss during the study period.

Of which 5 had seizure disorder, 3 were on calcium channel blockers, 6 were on beta blockers, 3 of them didn't consent for study and 2 patients were excluded as laparoscopy was later converted to open procedure.

Hence 81 samples were randomly allocated into 3 groups in 1:1:1 ratio by block randomisation such that each group contained 27 each.

The participant was blinded about the study drug administered.

STUDY PROCEDURE:

The institutional ethical committee approval was obtained (ref no: 51/18/IEC/JMMC&RI) and the study was registered under the Clinical trial registry India (CTRI/2019/04/018757). With written informed consent, patients were randomised into either groups A, B or C by computer generated randomisation chart.

The participant is blinded about the study drug administered.

- Group A - Dexmeditomidine loading dose of 0.5mcg/kg in 100ml Normal Saline before induction over a period of 15mins and maintenance of 0.3mcg/kg/hr in a 20cc syringe pump throughout the surgery.
- Group B - Magnesium sulfate loading dose 40mg/kg in 100ml Normal saline (NS) before induction over a period of 15mins and maintenance of 10mg/kg/hr in a 20cc syringe pump throughout the surgery.
- Group C - (control group) - Receives same volume of Normal saline.

Monitoring of ECG, pulse oximetry and blood pressure was established before starting study drug. Electrodes were applied to the patient's forehead for monitoringConox (Smart Anesthesia Monitoring). Neuromuscular transmission was monitored using train-of-four (TOF) Supramaximal stimulations.

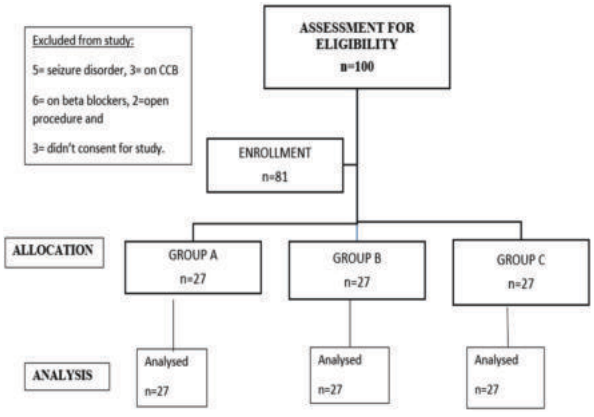
The loading dose of the study drug was administered 20 minutes prior to induction.Anesthesia was induced with inj. Midazolam 0.03mg/kg, inj. Fentanyl 2mcg/kg and inj. Propofol given at 1mg/kg, then waited for 20secs. If qCON>60 , additional doses of Propofol were given at 0.25mg/kg until qCON was below 60 followed by Atracurium 0.5mg/kg and intubation completed with appropriate size cuffed ET tube. Anesthesia was maintained with Oxygen- Air, Propofol infusion and the study drug to achieve a target qCON between 40 and 60.Atracurium was repeated when train of four(TOF) supramaximal stimulation produced 1 or more twitches.Intravenous (i.v) injection (inj) of fentanyl was given:

1. Every hour at 0.5mcg/kg
2. When hypertension (MAP>20%) or tachycardia, with qCON between 40 & 60, provided other causes of hypertension were ruled out.

Hypotension (MAP<30%) was managed with a fluid bolus of 200ml of RL, after ruling out its other causes .If not responding, injmephenteramine 6mg i.v was administered. Bradycardia (HR<50) treated with atropine 0.6mg i.v.After skin closure, all infusion drugs were stopped and neuromuscular blockade reversed with inj. Neostigmine 40mcg/kg and inj. Glycopyrolate 10mcg/kg, when TOF showed 4 twitches, followed by tracheal extubation.

The time elapsed between stoppage of propofol infusion and a qCON value of 80 was considered as the recovery time.The time elapsed between stoppage of propofol infusion and response to verbal commands was defined as orientation time. The time elapsed between stoppage of propofol infusion and extubation was defined as extubation time.

CONSORT FLOW DIAGRAM



ANALYSIS AND INTERPRETATION

STATISTICAL METHOD:

- Descriptive and inferential statistical analysis had been carried out in the present study.
- Results on continuous measurements were expressed as mean± standard deviation (minimum-maximum), while that on categorical measurements as number (%).
- Comparison of continuous measurements between the groups were assessed by one way analysis of variance (ANOVA) and of categorical measurements by Chi square test.
- If significant further pairwise analysis was done using post hoc Bonferonni test.
- Significance was assessed at 5% level of significance.

A 'p' value of less than 0.05 was considered statistically significant.

Statistical Software: The standard computer software IBM SPSS version 25 - was used for analysis of data.

Microsoft word and Excel were used to generate graphs and tables.

RESULTS

A total of 100 patients were included in our study of which, 19 were excluded as they didn't satisfy the inclusion criteria.

The remaining 81 were randomly allocated to the three groups A, B and C in 1:1:1 ratio by block randomization.

ANESTHETIC REQUIREMENT:

Table 1: Propofol induction dose

Groups	N	Propofol Induction Dose(mg)		p Value
		Mean	SD	
A	27	90.37	26.67	0.023[ab,ac]
B	27	100.74	23.68	
C	27	99.63	13.72	

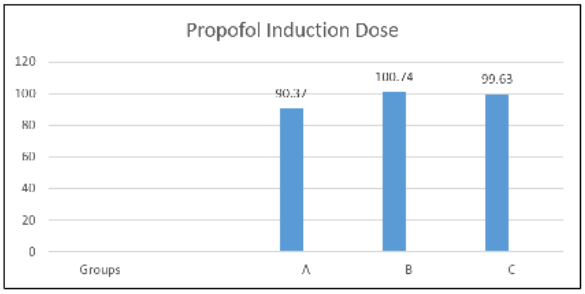


Figure 1: Propofol induction dose

Out of 27 patients in group A, the mean of propofol induction dose is 90.37±26.67mg, while in group B, it is 100.74±23.68mg and that in group C, is 99.63±13.72mg.Thus there is significant difference within the groups as p<0.05(p=0.023. In pairwise comparison, groups A, B and A, C are statistically significant.

Table 2: Propofol maintenance dose

Groups	N	Propofol Maintenance Dose(mg)		p Value
		Mean	SD	
A	27	256.30	80.67	0.573
B	27	280.37	78.47	
C	27	253.33	35.08	

Out of 27 patients in group A, the mean of propofol maintenance dose is 256.30±80.67mg, while in group B, it is 280.37±78.47mg and that in group C, it is 253.33±35.08mg.Thus there is no significant difference in propofol maintenance dose within the groups as p>0.05.

Table 3: Fentanyl maintenance dose

Groups	N	Fentanyl Maintenance Dose)		p Value
		Mean	SD	
A	27	22.59	19.48	0.133
B	27	32.67	21.43	
C	27	31.85	12.41	

Out of 27 patients in group A, the mean of fentanyl maintenance dose is 22.59±19.48 g while in group B, it is 32.67±21.43 g and that in group C, 31.85±12.41 g Thus there is no significant difference within the groups as p>0.05.

Table 4: Atracurium maintenance dose

Groups	N	Atracurium Maintenance Dose(mg)		p Value
		Mean	SD	
A	27	9.00	4.88	0.447
B	27	9.85	3.92	
C	27	8.81	3.48	

Out of 27 patients in group A, the mean atracurium maintenance dose is 9±4.88mg, while in group B, it is 9.85±3.92mg and that in group C, it is 8.81±3.48mg.Thus there is no significant difference within the groups as p>0.05.

HEMODYNAMIC VARIABLES:

Table 5: Systolic blood pressure

SBP(mmHg)	A	B	C	p Value
	Mean ± SD	Mean ± SD	Mean ± SD	
Preoperative	138.52 ± 13.14	137.30 ± 15.79	133.96 ± 10.18	0.429
After Study Drug	135.26 ± 13.88	135.52 ± 16.50	133.07 ± 10.16	0.774
After Induction	128.59 ± 12.25	131.04 ± 16.22	130.52 ± 11.00	0.778
After Intubation	132.52 ± 12.81	134.44 ± 15.22	137.93 ± 8.49	0.278
Intraoperative 10mins	125.18 ± 11.08	131.14±15.38	132 ±10.89	0.104
Intraoperative 20mins	125.77±10.72	133.96±14.56	132.33±9.35	0.030[ab]
Intraoperative 30mins	128.18±9.98	134.81±12.76	131.77±10.41	0.097
Intraoperative 40mins	129.62±8.53	134.28±10.55	131.76±9.95	0.252
Intraoperative 50mins	131.93±7.07	135.12±9.70	137.44±5.54	0.273
Intraoperative 60mins	131.20±6.98	135.10±9.50	133.42±4.07	0.371
Intraoperative 70mins	134.33±7.64	134.68±9.17	129.33±0.57	0.595
Intraoperative 80mins	135.80±6.76	134.68±9.76	139	0.886
Intraoperative 90mins	139±12.72	139.66±8.72	-	0.925
Intraoperative 100mins	136.50±12.02	139.63±10.05	-	0.698
After Surgery	130.52 ± 7.86	136.22 ± 12.76	134.56 ± 8.68	0.105
After Extubation	135.52 ± 9.17	140.11 ± 12.36	139.41 ± 8.34	0.205

Figure 2: SBP

Out of 27 patients in group A, the mean SBP in preoperative period is 138.52 ± 13.14mmHg, while in group B, it is 137.30 ± 15.79mmHg and in group C, it is 133.96 ± 10.18mmHg. There is no significant difference between the groups as p>0.05. Out of 27 patients in group A, the mean SBP after study drug is 135.26 ± 13.88mmHg, while in group B it is 135.52 ± 16.50mmHg and in group C, it is 133.07 ± 10.16mmHg. There is no significant difference between the groups as p>0.05. Out of 27 patients in group A ,the mean SBP after induction is 128.59 ± 12.25mmHg, in group B is 131.04 ± 16.22mmHg and in group C is 130.52 ± 11.00mmHg.There is no significant difference between the groups as p>0.05.

Out of 27 patients in group A, the mean SBP after intubation is 132.52 ± 12.81mmHg, while in group B is 134.44 ± 15.22mmHg and that in group C is 137.93 ± 8.49mmHg.There is no significant difference between the groups as p>0.05. SBP observed at 10mins interval in the intraoperative period.

Out of 27 patients in group A, the mean SBP at 20mins of intraoperative period is 125.77±10.72mmHg, while in group B, it is 133.96±14.56mmHg and in group C, it is 132.33±9.35mmHg. There is significant difference in this time interval between the groups as p<0.05. (p=0.03). In pairwise comparison group A and B are statistically significant. There is no significant difference in the remaining intraoperative period between the groups as p>0.05. Out of 27 patients in group A, the mean SBP after surgery is 130.52 ± 7.86mmHg, while in group B it is 136.22 ± 12.76mmHg and in group C, it is 134.56 ± 8.68mmHg.There is no significant difference between the groups as p>0.05.

Out of 27 patients in group A, the mean SBP after extubation is 135.52 ± 9.17mmHg, while in group B it is 140.11 ± 12.36mmHg and in group C it is 139.41 ± 8.34mmHg.There is no significant difference between the groups as p>0.05.

Table 6: Diastolic blood pressure

DBP(mmHg)	A	B	C	p Value
	Mean ± SD	Mean ± SD	Mean ± SD	
Preoperative	88.44 ± 10.29	86.63 ± 9.39	79.67 ± 6.58	0.001[ac,bc]
After Study Drug	81.15 ± 8.09	79.70 ± 8.80	78.44 ± 4.50	0.408
After Induction	77.30 ± 7.26	75.11 ± 6.70	77.63 ± 4.56	0.284

After Intubation	79.44 ± 7.18	81.89 ± 6.67	85.33 ± 3.08	0.002[ab]
Intraoperative 10mins	76.25 ± 6.10	81.03 ± 7.90	76.88 ± 5.56	0.019[ab]
Intraoperative 20mins	75.29 ± 7.04	80.81±6.26	78.22±5.28	0.007[ab]
Intraoperative 30mins	76.14±6.08	81.18±5.58	78.07±5.53	0.007[ab]
Intraoperative 40mins	76.54±4.99	80.24±5.98	80.03±4.70	0.026[ab]
Intraoperative 50mins	79.73±3.36	80.35±5.40	81.88±2.84	0.503
Intraoperative 60mins	79.14±5.18	82.63±6.77	80.57±4.85	0.258
Intraoperative 70mins	80.22±6.07	83.31±4.41	82.66±2.30	0.301
Intraoperative 80mins	77.40±5.72	80.16±5.23	86	0.331
Intraoperative 90mins	72±2.82	78.09±4.20	-	0.079
Intraoperative 100mins	69±1.41	77.18±5.45	-	0.066
After Surgery	75.41 ± 6.55	80.52 ± 6.50	80.19 ± 4.45	0.003[ab,ac]
After Extubation	81.04 ± 6.49	86.15 ± 6.24	85.04 ± 5.25	0.006[ab]

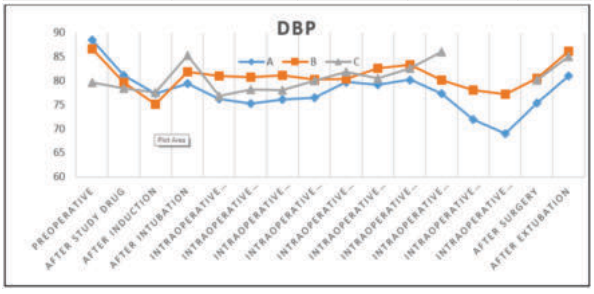


Figure 3: DBP

Out of 27 patients in group A, the mean DBP in preoperative period is 88.44 ± 10.29mmHg, while in group B it is 86.63 ± 9.39mmHg and in group C it is 79.67 ± 6.58mmHg. There is significant difference between the groups as p<0.05. In pairwise comparison groups A, B and B, C are statistically significant. Out of 27 patients in group A, the mean DBP after study drug is 81.15 ± 8.09mmHg, while in group B it is 78.44 ± 4.50mmHg, and in group C it is 78.44 ± 4.50mmHg. There is no significant difference between the groups as p>0.05. Out of 27 patients in group A, the mean DBP after induction is 77.30 ± 7.26mmHg, while in group B it is 75.11 ± 6.70mmHg and in group C it is 77.63 ± 4.56mmHg. There is no significant difference between the groups as p>0.05.

Out of 27 patients in group A, the mean DBP after intubation is 79.44 ± 7.18mmHg, while in group B it is 81.89 ± 6.67mmHg and in group C it is 85.33 ± 3.08mmHg. There is significant difference between the groups as p<0.05(p=0.002). In pairwise comparison group A and B are statistically significant. DBP was observed at 10mins interval in the intraoperative period.

Out of 27 patients in group A, the mean DBP at 10min of intraoperative period is 76.25 ± 6.10mmHg, while in group B is 81.03 ± 7.90mmHg and in group C is 76.88 ± 5.56mmHg. There is significant difference between the groups as p<0.05. (p=0.019). In pairwise comparison group A and B are statistically significant. Out of 27 patients in group A, the mean DBP at 20min of intraoperative period 75.29 ± 7.04mmHg, while in group B is 80.81±6.26mmHg and in group C is 78.22±5.28mmHg. There is significant difference between the groups as p<0.05. (p=0.007). In pairwise comparison group A and B are statistically significant. Out of 27 patients in group A, the mean DBP at 30min of intraoperative period 76.14±6.08mmHg, while in group B is 81.18±5.58mmHg and in group C is78.07±5.53 mmHg. There is significant difference between the groups as p<0.05. (p=0.007) In pairwise comparison group A and B are statistically significant. Out of 27 patients in group A, the mean DBP at 40min of intraoperative period 76.54±4.99mmHg, while in group B is 80.24±5.98mmHg and in group C is 80.03±4.70mmHg. There is significant difference between the groups as p<0.05. (p=0.026) In pairwise comparison group A and B are statistically significant.

There is no significant difference in the remaining intraoperative period between the groups as p>0.05.

Out of 27 patients in group A, the mean DBP after surgery is 75.41 ± 6.55mmHg, while in group B is 80.52 ± 6.50mmHg and in group C it is 80.19 ± 4.45mmHg. There is significant difference between the groups as p<0.05. (p=0.003).) In pairwise comparison groups A, B and A, C are statistically significant.

Out of 27 patients in group A, the mean DBP after extubation is 81.04 ± 6.49mmHg, while in group B is 86.15 ± 6.24mmHg and in group C it is 85.04 ± 5.25mmHg. There is significant difference between the groups as p<0.05. (p=0.006).) In pairwise comparison group A and B are statistically significant.

Table 7: Heart rate

HR(/min)	A	B	C	p Value
	Mean ± SD	Mean ± SD	Mean ± SD	
Preoperative	78.81 ± 9.48	84.74 ± 9.43	76.15 ± 6.78	0.002[ab,bc]
After Study Drug	76.59 ± 9.58	81.59 ± 8.70	75.33 ± 6.40	0.018[bc]
After Induction	71.56 ± 8.90	77.81 ± 7.45	74.44 ± 6.50	0.014[ab]
After Intubation	74.85 ± 9.18	81.59 ± 7.50	81.04 ± 7.32	0.004[ab,ac]
Intraoperative 10mins	70.81±6.89	79.29±7.31	75.74±6.15	<0.001[abac]
Intraoperative 20mins	71.18±6.65	78.66±6.72	75.62±6.39	<0.001[abac]
Intraoperative 30mins	71.59±6.42	79.51±6.33	76.92±7.80	<0.001[abac]
Intraoperative 40mins	70.12±5.39	80.52±6.53	76.19±7.06	<0.001[abac]
Intraoperative 50mins	70.53±6.46	81.40±6.93	77.11±8.11	<0.001[ab]
Intraoperative 60mins	69.42±5.10	81.52±5.53	77.85±7.28	<0.001[abac]
Intraoperative 70mins	69.66±6.50	81.15±5.01	77.33±6.50	<0.001[ab]
Intraoperative 80mins	68.80±5.80	83.66±3.44	85	
Intraoperative 90mins	66.50±6.36	80.45±3.23	-	
Intraoperative 100mins	67±8.48	81.63±4.50	-	
After Surgery	73.52 ± 6.59	82.19 ± 6.73	78.11 ± 6.62	<0.001[ab,ac]
After Extubation	76.52 ± 6.46	85.67 ± 6.55	81.89 ± 7.75	<0.001[ab,ac]

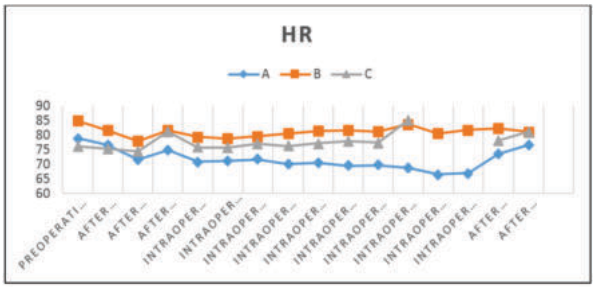


Figure 4: HR

Out of 27 patients in group A, the mean HR in preoperative period is 78.81 ± 9.48/min, while in group B it is 84.74 ± 9.43/min and in group C it is 76.15 ± 6.78/min. There is significant difference between the groups as p<0.05. (p=0.002). In pairwise comparison groups A, B and B, C are statistically significant. Out of 27 patients in group A, the mean HR after study drug is 76.59 ± 9.58/min, while in group B it is 81.59 ± 8.70/min and in group C it is 75.33 ± 6.40/min. There is significant difference between the groups as p<0.05. (p=0.018). In pairwise comparison group B and C are statistically significant.

Out of 27 patients in group A, the mean HR after induction is 71.56 ± 8.90/min, while in group B it is 77.81 ± 7.45/min and in group C it is 74.44 ± 6.50/min. There is significant difference between the groups as p<0.05. (p=0.014).). In pairwise comparison group A and B are statistically significant. Out of 27 patients in group A, the mean HR after intubation is 74.85 ± 9.18/min, while in group B it is 81.59 ± 7.50/min and in group C it is 81.04 ± 7.32/min. There is significant difference between the groups as p<0.05. (p=0.004) In pairwise comparison groups A, B and A, C are statistically significant. There is significant difference in intraoperative HR at 10mins interval between

the groups as p<0.05. (p=<0.001) The mean HR at 10mins in group A is 70.81±6.89/min, while in group B is 79.29±7.31/min and in group C is 75.74±6.15/min. In pairwise comparison groups A, B and A, C are statistically significant. The mean HR at 20mins in group A is 71.18±6.65/min, in group B is 78.66±6.72/min and in group C is 75.62±6.39/min. In pairwise comparison groups A, B and A, C are statistically significant. The mean HR at 30mins in group A is 71.59±6.42/min, while in group B is 79.51±6.33/min and in group C is 76.92±7.80/min. In pairwise comparison groups A, B and A, C are statistically significant. The mean HR at 40mins in group A is 70.12±5.39/min, while in group B is 80.52±6.53/min and that in group C is 76.19±7.06/min. In pairwise comparison groups A, B and A, C are statistically significant. The mean HR at 50mins in group A is 70.53±6.46/min, while in group B is 81.40±6.93/min and that in group C is 77.11±8.11/min. In pairwise comparison group A and B are statistically significant. The mean HR at 60mins in group A is 69.42±5.10/min, while in group B is 81.52±5.53/min and that in group C is 77.85±7.28/min. In pairwise comparison groups A, B and A, C are statistically significant. The mean HR at 70mins in group A is 69.66±6.50/min, while in group B is 81.15±5.01/min and that in group C is 77.33±6.50/min. In pairwise comparison group A and B are statistically significant. Out of 27 patients in group A, the mean HR after surgery is 73.52 ± 6.59/min, while in group B is 82.19 ± 6.73/min and in group C it is 78.11 ± 6.62/min. There is significant difference between the groups as p<0.05. In pairwise comparison groups A, B and A, C are statistically significant. Out of 27 patients in group A, the mean HR after extubation is 76.52 ± 6.46/min, while in group B is 85.67 ± 6.55/min and in group C it is 81.89 ± 7.75/min. There is significant difference between the groups as p<0.05. In pairwise comparison groups A, B and A, C are statistically significant.

Table 8: Mean arterial pressure

MAP(mmHg)	A	B	C	p Value
	Mean ± SD	Mean ± SD	Mean ± SD	
Preoperative	79.63 ± 7.60	79.93 ± 8.12	76.81 ± 4.97	0.207
After Study Drug	76.56 ± 7.06	78.15 ± 8.30	75.85 ± 4.63	0.454
After Induction	73.41 ± 6.40	75.04 ± 7.25	75.22 ± 4.90	0.506
After Intubation	76.11 ± 6.85	79.63 ± 7.20	78.07 ± 4.42	0.126
Intraoperative 10mins	72.81±5.74	77.62±7.35	75.59±4.71	0.017[ab]
Intraoperative 20mins	71.92±4.89	76.33±7.02	75.66±3.74	0.017[ab,ac]
Intraoperative 30mins	71.51±5.15	76.70±6.98	75.51±3.75	0.002[ab,ac]
Intraoperative 40mins	71.41±4.72	76.72±6.30	75.92±4.11	0.001[ab,ac]
Intraoperative 50mins	73.53±4.25	75.26±5.42	78.22±4.29	0.083
Intraoperative 60mins	73.92±4.23	76.68±5.90	77±3.46	0.244
Intraoperative 70mins	76±3.53	77.36±6.10	75.33±3.51	0.727
Intraoperative 80mins	74.80±5.44	78.16±6.16	80	0.529
Intraoperative 90mins	75.50±2.12	78.09±5.64	-	0.547
Intraoperative 100mins	77.50±6.36	78.81±6.38	-	0.793
After Surgery	75.15 ± 6.06	79.22 ± 6.83	77.89 ± 4.23	0.037[ab]
After Extubation	77.85 ± 6.09	82.52 ± 6.64	80.44 ± 4.30	0.015[ab]

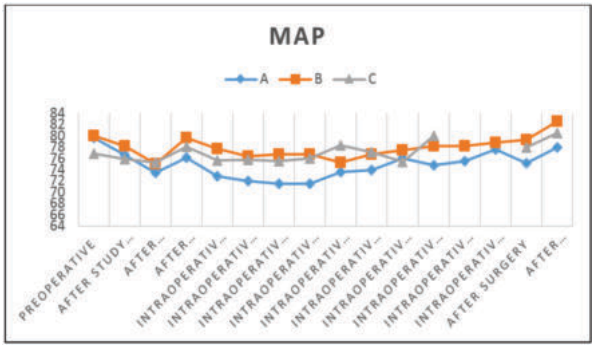


Figure 5: MAP

Out of 27 patients in group A, the mean MAP in preoperative period is 79.63 ± 7.60mmHg, while in group B it is79.93 ± 8.12mmHg and in group C it is 76.81 ± 4.97mmHg. There is no significant difference between the groups as p>0.05.

Out of 27 patients in group A, the mean MAP after study drug is 76.56 ± 7.06mmHg, while in group B it is 78.15 ± 8.30mmHg and in group C it is 75.85 ± 4.63mmHg. There is no significant difference between the groups as p>0.05

Out of 27 patients in group A, the mean MAP after induction is 73.41 ± 6.40mmHg, while in group B it is 75.04 ± 7.25mmHg and in group C it is 75.22 ± 4.90mmHg. There is no significant difference between the groups as p>0.05

Out of 27 patients in group A, the mean MAP after intubation is 76.11 ± 6.85mmHg, while in group B it is 79.63 ± 7.20mmHg and in group C it is 78.07 ± 4.42mmHg. There is no significant difference between the groups as p>0.05

Out of 27 patients in group A, the mean MAP at 10min of intraoperative period is 72.81±5.74mmHg, while in group B is 77.62±7.35mmHg and in group C is 75.59±4.71mmHg. There is significant difference between the groups as p<0.05. (p=0.017). In pairwise comparison group A and B are statistically significant. Out of 27 patients in group A, the mean MAP at 20min of intraoperative period is 71.92±4.89mmHg, while in group B is 76.33±7.02mmHg and in group C is 75.66±3.74mmHg. There is significant difference between the groups as p<0.05. (p=0.017) In pairwise comparison groups A, B and A, C are statistically significant. Out of 27 patients in group A, the mean MAP at 30min of intraoperative period is 71.51±5.15mmHg, while in group B is 76.70±6.98mmHg and in group C is 75.51±3.75mmHg. There is significant difference between the groups as p<0.05. (p=0.002) In pairwise comparison groups A, B and A, C are statistically significant. Out of 27 patients in group A, the mean MAP at 40min of intraoperative period is 71.41±4.72mmHg, while in group B 76.72±6.30 is mmHg and in group C is 75.92±4.11mmHg. There is significant difference between the groups as p<0.05. (p=0.001) In pairwise comparison groups A, B and A, C are statistically significant.

There is no significant difference in the remaining intraoperative period between the groups as p>0.05.

Out of 27 patients in group A, the mean MAP after surgery is 75.15 ± 6.06, while in group B is 79.22 ± 6.83 and in group C it is 77.89 ± 4.23. There is significant difference between the groups as p<0.05. (p=0.037). In pairwise comparison group A and B are statistically significant.

Out of 27 patients in group A, the mean MAP after extubation is 77.85 ± 6.09, while in group B 82.52 ± 6.64 and in group C it is 80.44 ± 4.30. There is significant difference between the groups as p<0.05. (p=0.015). In pairwise comparison group A and B are statistically significant.

RECOVERY INDICES

Table 9: Recovery time

Groups	N	Recovery Time(mins)		p Value
		Mean	SD	
A	27	2.64	0.43	<0.001[abc]
B	27	3.32	0.63	
C	27	2.14	0.30	

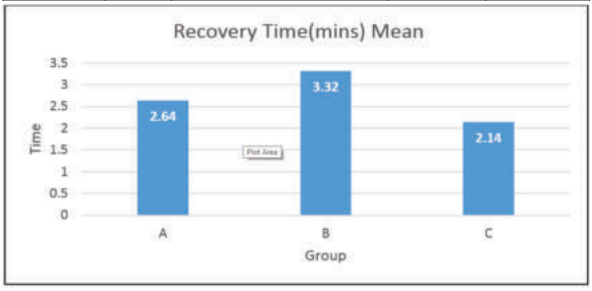


Figure 6: Recovery time

Out of 27 patients in group A, the mean recovery time is 2.64±0.43mins, while in group B is 3.32±0.63mins and in group C is 2.14±0.30mins. There is significant difference between the groups as p<0.05. (p=<0.001). In pairwise comparison groups A, B and C are statistically significant.

Table 10: Orientation time

Groups	N	Orientation Time(mins)		p Value
		Mean	SD	
A	27	2.89	0.39	<0.001[abc]
B	27	3.53	0.62	
C	27	2.28	0.31	

Out of 27 patients in group A, the mean orientation time is 2.89±0.39mins, while in group B is 3.53±0.62mins and in group C is 2.28±0.31mins. There is significant difference between the groups as p<0.05. (p=<0.001). In pairwise comparison groups A, B and C are statistically significant.

Figure 7: Orientation time

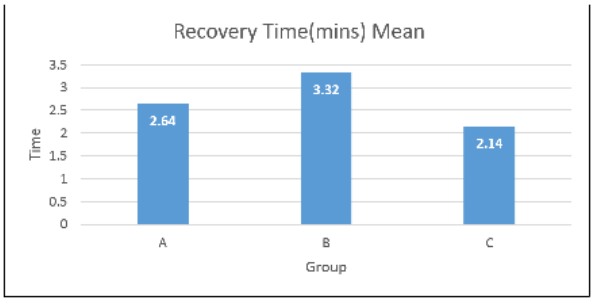


Figure 8: Extubation time

Groups	N	Extubation Time(mins)		p Value
		Mean	SD	
A	27	3.01	0.40	<0.001[abc]
B	27	3.78	0.68	
C	27	2.40	0.31	

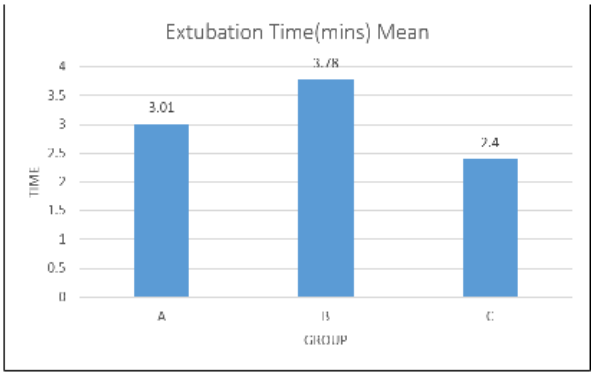


Figure 9: Extubation time

Out of 27 patients in group A, the mean extubation time is 3.01±0.40mins, while in group B is 3.78±0.68mins and in group C is 2.40±0.31mins. There is significant difference between the groups as p<0.05. (p=<0.001). In pairwise comparison groups A, B and C are statistically significant.

DISCUSSION

We conducted this prospective randomised study in an attempt to observe whether administration of dexmeditomidine and magnesium sulfate to a commonly administered anesthetic regimen reduces anesthetic requirement and improves hemodynamic stability.

In our study, all demographic variables (age, sex, ASA physical status) were comparable between the three groups except for duration of surgery and BMI. The mean duration of surgery in group A was 76.30±20.40mins, while in group B was 93.89±25.77mins and in C, 67.41±12.19mins. Thus there is significant difference between the groups (p=0.001). Similarly, the mean BMI in group A was 24.08± 1.51kg/m, while in B was 24.66±2.40kg/m and in C, 23.12±1.32kg/m², i.e. statistically significant (p=0.009).i.e. statistically significant (p=0.009).

The primary objective in this study was requirement of anesthetic agents. Propofol induction dose in group A (Dexmeditomidine) was 90.37±26.67mg while mean propofol maintenance dose was 256.30±80.67mg. The mean fentanyl maintenance dose was 22.59±19.48 ug and the mean atracurium maintenance dose was 9±4.88mg. It was well tolerated, and no serious side effects or adverse reactions occurred. While in group B (Magnesium sulfate), propofol induction dose was 100.74±23.68mg, the mean propofol maintenance dose was 280.37±78.47mg. The mean fentanyl maintenance dose was 32.67±21.43 ug and the mean atracurium maintenance dose was 8.81±3.48mg.

Thus there is statistically significant difference in propofol induction dose (p=0.023) between the groups and it was least in group A. There was no significant difference in requirement of fentanyl and atracurium between the groups.

The secondary objective in our study was hemodynamic stability and recovery indices. In our study, pretreatment with dexmeditomidine 0.5 ug/kg attenuated the cardiovascular response to tracheal intubation after induction of anesthesia. The mean SBP in group A at intubation was 132.52 ± 12.81mmHg while in group B was 134.44 ± 15.22mmHg and in group C was 137.93 ± 8.49mmHg. Intraoperative SBP was monitored every 10mins. At 20mins, SBP in group A was 125.77±10.72mmHg, while in B was 133.96±14.56mmHg and in C was 132.33±9.35mmHg. Thus significant statistically (p=0.030) .There was no significant difference in SBP at other time points between the groups.

DBP at intubation in group A was 79.44 ± 7.18mmHg, while in group B was 81.89 ± 6.67mmHg and in C was 85.33 ± 3.08mmHg, i.e statistically significant(p=0.002). Also there was significant difference in DBP in the intraoperative period wherein group A (p=0.007) had more tight control of DBP during CO2 insufflation. At extubation too DBP was well controlled in group A (p=0.006). The mean DBP at extubation in group A was 81.04 ± 6.49mmHg, while in B was 86.15 ± 6.24mmHg and in C was 85.04 ± 5.25mmHg. Considering MAP, there was no significant difference at intubation between the groups. During intraoperative period, there was significant difference in group A(p=0.017). While at extubation, MAP in group A was 77.85 ± 6.09mmHg, in B was 82.52 ± 6.64mmHg and in C was 80.44 ± 4.30mmHg. There was significant difference between the groups (p=0.015) and group A had stable MAP throughout the surgery in contrast to groups B and C. In our study, there was significant reduction in group A with SBP at 20mins intraoperative period, DBP at intubation, intraoperative period and also at extubation. Also MAP was significantly controlled at intraoperative period and at extubation in group A.HR showed statistically significant difference between the groups. HR at intubation in group A was 74.85 ± 9.18/min, while in B was 81.59 ± 7.50/min and in C was 81.04 ± 7.32/min. There was significant difference in group A with respect groups B and C (p=0.004). Similarly during intraoperative period(p<0.001) and at the time of extubation(p<0.001), group A had more controlled heart rate in contrast to groups B and C. The mean HR at extubation in group A was 76.52 ± 6.46/min, while in B was 85.67 ± 6.55/min and in C was 81.89 ± 7.75/min.

The mean recovery time in group A was 2.64±0.43mins, while in group B was 3.32±0.63mins and in group C it was 2.14±0.30mins. The mean orientation time in group A was 2.89±0.39mins, while in group B was 3.53±0.62mins and in group C, 2.28±0.31mins. The mean extubation time in group A was 3.01±0.40mins, while in group B was 3.78±0.68mins and in group C was 2.40±0.31mins. There was statistically significant difference between the groups (p<0.001) and group C took the least time for extubation.

No incidence of delayed recovery. No adverse cardiovascular effects from the drugs were noted in the present study. There was no event of awareness suggesting adequate depth of anesthesia.

CONCLUSION

This randomised controlled study was conducted with an aim to evaluate the effects of dexmeditomidine and magnesium sulfate in optimising TIVA requirement and improving intraoperative hemodynamics.

We conclude dexmeditomidine infusion reduced requirement of propofol andresulted in a steady and smooth reduction in mean blood pressure and heart rate,with no episodes of severe hypotension or bradycardia. Thus we accept our alternate hypothesis.

There were no incidences of delayed recovery/ intraoperative awareness.