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ORIGINAL ARTICLE

A Comparative Study between Infusion of Dexmedetomidine and Infusion of Magnesium Sulfate on Haemodynamic Changes in Laparoscopic Surgeries Under General Anaesthesia – A Prospective, Randomized, Double-Blind Study

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Abstract
Background: The study was undertaken to compare between infusion of Dexmedetomidine and infusion of Magnesium sulfate on haemodynamic changes in laparoscopic surgeries under general anaesthesia – a prospective, randomized, double-blind study
Materials and Methods: 80 patients of ASA grade I and II of both sexes undergoing elective surgery in SPS Hospitals, Ludhiana. They were randomly divided into two groups of forty each. Group M received Magnesium Sulfate 30mg/kg in 100ml NS over 10 mins as loading dose followed by 10mg/kg/h in NS to make 50ml and given as infusion. Group D received Dexmedetomidine 1mcg/kg in 100ml NS over 10mins as loading dose followed by 0.2mcg/kg/h in NS to make 50ml and given as infusion. Haemodynamic parameters were noted every 5 mins starting from the time when patient was shifted to operating room to initial 30 mins of pneumoperitoneum and thereafter every 10 mins till the time of deflation. **Results:** Attenuation of haemodynamic response during pneumoperitoneum was better with Dexmedetomidine group. More number of patients were comfortable with sedation score 2 or 3 (Modified Ramsay Sedation Score) while using Dexmedetomidine group for the first 30 mins than Magnesium Sulfate. No significant adverse effects were noted in both groups.
Conclusion: Dexmedetomidine infusion even at a dose of 0.2mcg/kg/h provides a better attenuation of haemodynamic changes during pneumoperitoneum than Magnesium Sulfate in Laparoscopic surgeries. Dexmedetomidine also provides a better sedation score in terms of benefits versus side effects in patients.

Keywords: Dexmedetomidine, Magnesium sulfate, haemodynamic response, laparoscopic surgeries, pneumoperitoneum.

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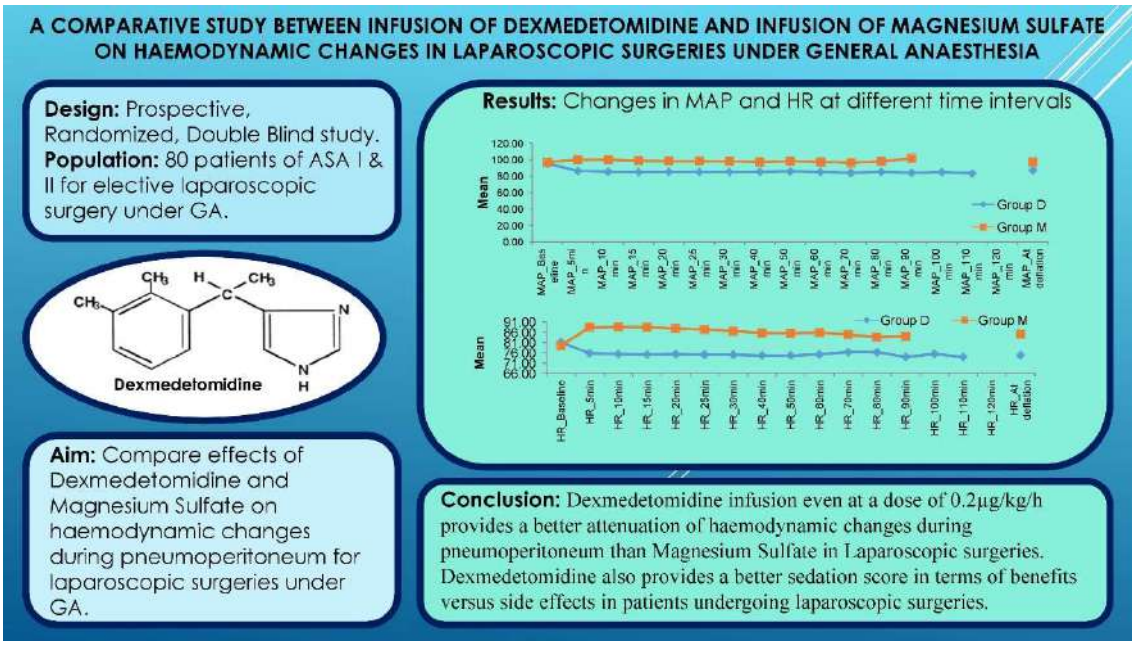
Graphical Abstract



Introduction

Laparoscopic surgeries are one of the most commonly performed surgeries these days. The use of laparoscopy has revolutionized the surgical field with many advantages. There is a reduction of postoperative pain, less postoperative surgical and pulmonary complications, early recovery and reduced hospital stay [1]. The scope of laparoscopic surgeries extends to various gastrointestinal, gynaecological (e.g., diagnostic laparoscopy, ectopic pregnancy), urological (e.g. nephrectomy, prostatectomy) and vascular procedures.

Major step of laparoscopic surgery is pneumoperitoneum creation. Use of carbondioxide for pneumoperitoneum and rise in intra-abdominal pressure (IAP) have various systemic effects [2]. Cardiovascular: This depends on the IAP. At lower IAP of less than 15 mmHg, there is an increase in cardiac output and blood pressure due to augmentation of venous return. However, at higher IAP of more than 15 mmHg, due to the reduction of venous return (compression of inferior venacava), cardiac output and blood pressure fall (Figs. 1 and 2). Changes in respiratory system include increase in airway pressures, decrease in lung volume leading to basal atelectasis and intrapulmonary shunting. Intracranial pressure can increase because of hypercapnia, increased IAP and trendelenberg position, which can be lethal to those with decreased intracranial compliance (Fig. 3).

Adverse effects of pneumoperitoneum might be potentiated by trendelenberg or reverse trendelenberg position. Trendelenberg position will lead to decrease in venous return and reduction in MAP. Pneumoperitoneum will activate of neurohormonal stress response [1] and renin angiotensin aldosterone system [3]. Pressures of more than 15 mmHg are related to vital pathophysiologic effects. The circulatory and ventilatory changes are often appreciated after 5 min of the onset of insufflation of gas, however they reverse over a period of 2 h [4].

Different classes of drugs have been used to reduce haemodynamic changes associated with laparoscopic surgery with variable response. Clonidine an α_2-adrenergic agonist has been studied widely [5,6]. Using α_2-adrenergic agonist can decrease anaesthetic and analgesic requirements, provide better haemodynamic stability without impairment of myocardial or renal blood flow and attenuate neurohumoral "stress response" of major

surgery [7]. These may reduce circulating catecholamine level during surgery. All these properties make Dexmedetomidine an ideal agent for premedication. Magnesium use as a therapeutic agent for conditions like preeclampsia, eclampsia, and torsades de pointes arrhythmias [8].

There are only limited clinical studies which compared effects of Dexmedetomidine and Magnesium Sulfate as premedication followed by infusion in perioperative haemodynamic stability and postoperative sedation. Our study aims in comparing the effect of Magnesium Sulfate and Dexmedetomidine in attenuating haemodynamic responses during pneumoperitoneum in laparoscopic abdominal surgeries.

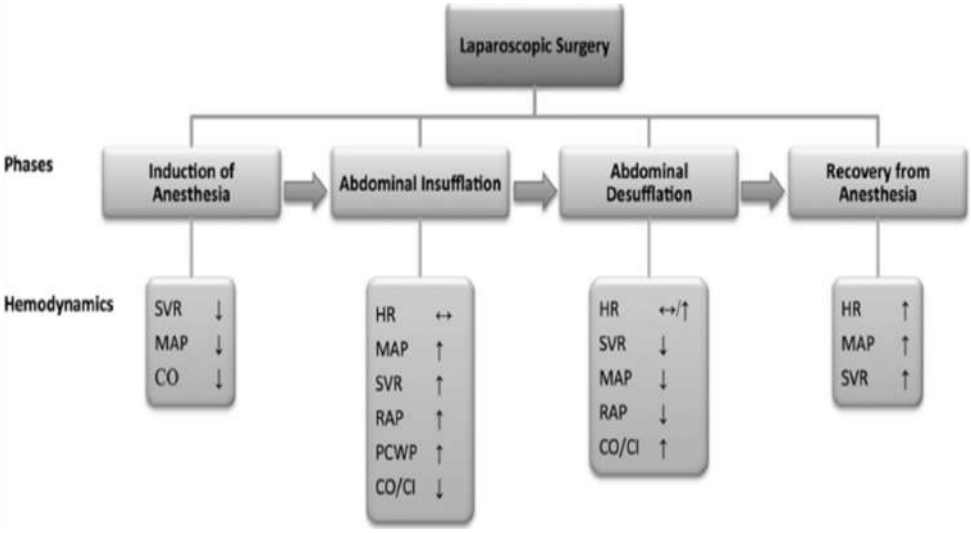


Figure 1: Haemodynamic changes at different phases of laparoscopic surgery [9]

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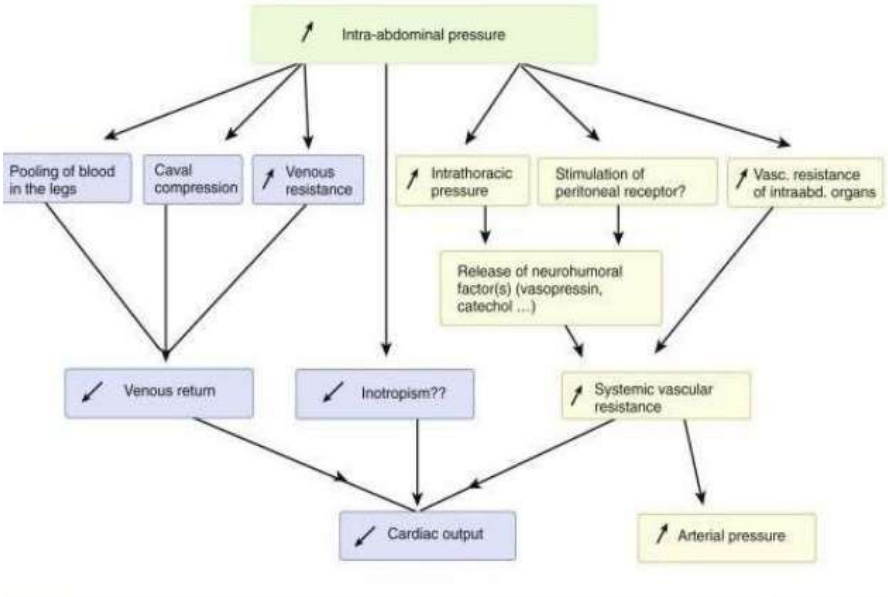

Figure 2: Schematic representation of different mechanism leading to reduced cardiac output [10]

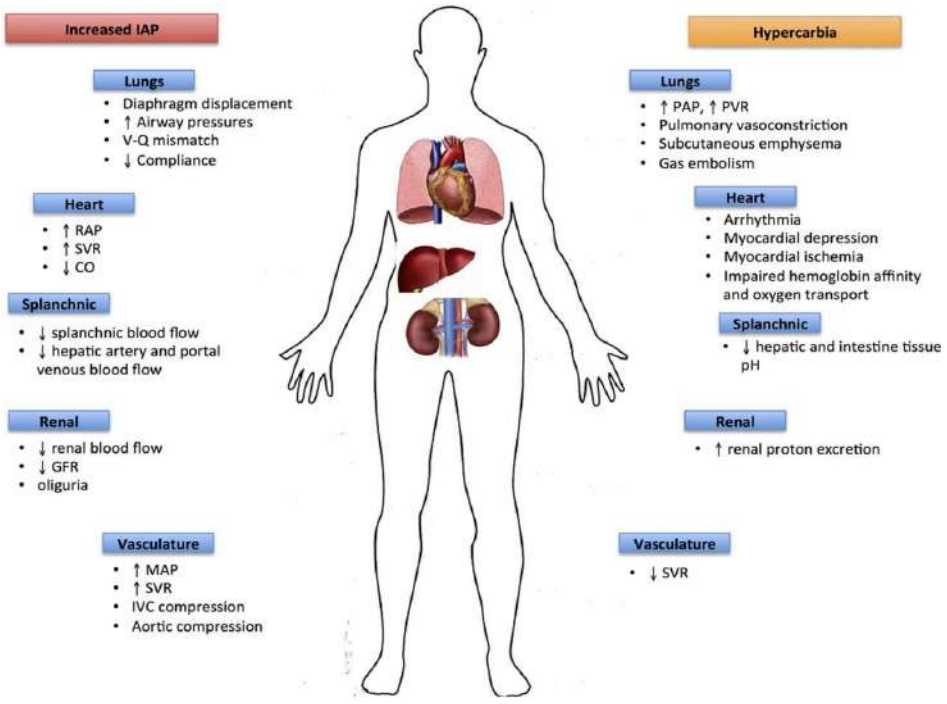

Figure 3: Two components of laparoscopic surgery [11,12]

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Pathophysiology of the Pneumoperitoneum

Methods

This study was conducted after the approval by the ethical committee of Satguru Partap Singh Hospitals, Ludhiana after signing of the informed consent by the patient. The datas were collected by the observer (myself) using the study proforma. It was collected and analysed from June 2019 to April 2021 at Satguru Partap Singh Hospital as per methodology.

Study population: 80 adult patients in two groups of 40 each, ASA I & II of either sex undergoing elective laparoscopic surgery under GA.

Study design: It was a Prospective, Randomized, Double Blind study.

Inclusion criteria:

Patients between the age of 18-65 years of either sex with ASA Grade I or II undergoing elective laparoscopic surgery under general anaesthesia.

Exclusion criteria:

Morbid obesity (BMI>40 kg/m2)**,** Intubation attempts more than two**,** Duration of pneumoperitoneum more than 120min, substance abuser, known allergy or hypersensitivity to study medicines, Pregnant and lactating mothers, Emergency surgeries**,** Patients who are on Calcium Channel Blockers as they interact with magnesium.

Eligible patients were explained regarding scope, nature of the study and about the study related risks in their own vernacular language. Informed and written consent were taken. They were given freedom of withdrawing at any stage from the study. Patients were divided into two groups. Randomization was done by a plan generator from www.randomization.com. The appropriate numbered envelope was opened and drug was prepared according to the card inside indicating patient group D and M.

Group D: Patients received Dexmedetomidine loading dose of 1µg/kg in 100ml NS over 10min followed by 0.2µg/kg/h in NS to make 50ml and given as infusion.

Group M: Patients received Magnesium Sulfate 30mg/kg in 100ml NS over 10 min as loading dose followed by 10mg/kg/h in NS to make 50ml and given as infusion.

A complete history of present and past illness was taken; general, physical examination and systemic examinations were conducted. Routine investigations were done along with ECG. Consents were obtained. All patients were premedicated with Tab. Zolpidem 10 mg orally at night before the surgery and Tab. Pantoprazole 40mg at 6:00 AM on the day of surgery.

Patients were kept fasting for 6 h for solids although clear fluids were allowed 2 h prior to the surgery. Preoperatively Patient's consent and PAC were checked. Pulse oximetry, non-invasive blood pressure and electrocardiography were started and baseline vital parameters like heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and arterial O_2 saturation (SpO_2) were recorded in all patients. In operating room iv cannulation done. Group M was given Magnesium Sulfate loading dose of 30mg/kg in 100 ml NS over 10 min followed by infusion at a rate of 10mg/kg/h in 50 ml NS. Group D was given Dexmedetomidine loading dose of 1µg/kg in 100ml NS over 10 min followed by infusion at a rate of 0.2µg/kg/h in 50 ml NS. Haemodynamic parameters were noted every 5 min starting from the time when patient was shifted to operating room to initial 30 min of pneumoperitoneum and thereafter every 10 min till the time of deflation.

Injection fentanyll 2 µg/kg iv was given, after preoxygenation with 100% O2 patient was induced with IV propofol (Dose was titrated by assessing the loss of eyelash reflex and verbal response). Tracheal intubation was done after giving rocuronium 0.8 mg/kg iv and confirmed by bilateral chest auscultation and $EtCo_2$ monitoring. Anaesthesia was maintained with sevoflurane (MAC-1), N_2O, O_2 (50:50). During CO_2 insufflation in to the peritoneum the intra-abdominal pressure was maintained between 12-14mmhg throughout laparoscopic procedure.

The patient was ventilated to keep end-tidal CO_2 between 35 and 45mmhg. Injection paracetamol 1gm was infused to all patients of both groups in the study. Vitals (HR, SBP, DBP, MAP) were recorded. Controlled ventilation with targeted $EtCO_2$ level 35-45 mmHg. Episodes of bradycardia (heart rate < 60/min) was treated with one dose of atropine 0.6 mg and for those who were not responding, the drug infusion was stopped and excluded the case from study. Hypotension (mean arterial pressure lower than 20% of baseline) incidents were treated with ephedrine 6 milligram incremental boluses. Hypertension (MAP>110) was managed by increasing sevoflurane up to a MAC value of 1.5 and for those who were not responding nitroglycerine infusion was started at a rate of 2.5-5 µg/min and excluded patient from study. The drug infusion in question was stopped as soon as pneumoperitoneum is deflated.

The time of inflation and deflation of pneumoperitoneum, total duration of surgery was noted. Ondansetron 4mg slow iv was given towards the end of surgery. Port sites were infiltrated with 0.2% ropivacaine 5ml at each site. Neostigmine and glycopyrrolate used to reverse neuromuscular blockade after surgery. Patients were then transferred to recovery room. All observations were made by anaesthetist unaware of the nature of drugs administered. After the procedure level of sedation was assessed in the recovery room by the observer (myself) every 30 min for two h using Ramsay Sedation Scale.

Results

All the relevant data was collected. Data were described in terms of range, mean ±standard deviation (±SD), median, frequencies (number of cases) as appropriate. Comparisons of quantitative variables between the study groups was done using student t-test and for independent samples for parametric and non - parametric data respectively. For comparing categorical data, chi-square test

(X2) test was performed and the exact test was used when the expected frequency is less than 5. A probability value (p-value) less than 0.05 was considered statistically significant. All statistical calculations were done using Statistical Package or Social Sciences (SPSS version 17) statistical programme for Microsoft window (Table 1).

A. Demographic Data

Table 1: Demographic Details off Both Group with Baseline Characteristics

		GROUP D		GROUP M		*p-value*
		MEAN	**SD**	**MEAN**	**SD**	
AGE(years)		39.58	12.41	41.58	9.37	*0.292*
WEIGHT(kg)		73.23	11.38	73.98	8.5	*0.768*
GENDER	MALE	12		8		*0.302*
	FEMALE	28		32		
ASA	1	25		29		*0.34*
	2	15		11		
DURATION OF SURGERY(min)		76.38	22.33	74.98	16.14	*0.743*
SPO2(%)		98.05	0.81	98.05	0.78	*0.992*
ETCO2(mmhg)		38.63	2.62	38.55	2.97	*0.779*

B. Haemodynamic Changes During Surgery

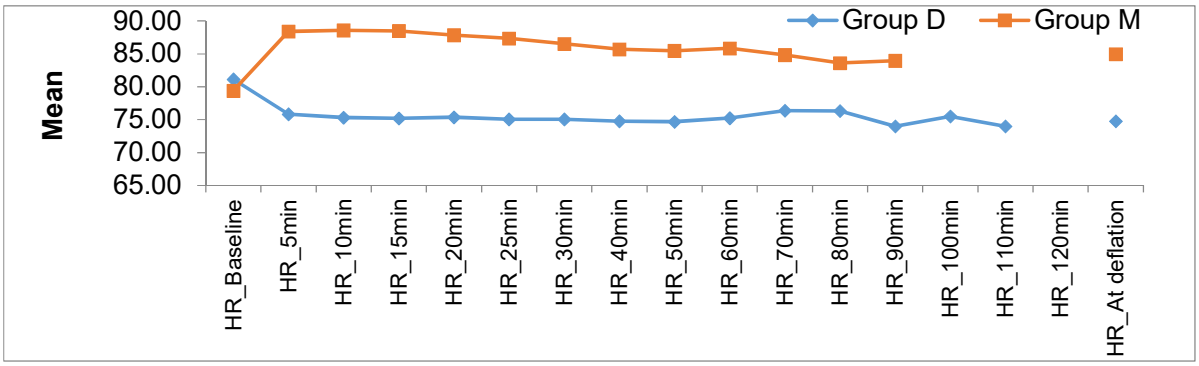

Figure 4: Distribution of Patients According to Heart Rate

Figure 4 shows the mean baseline HR and the mean HR at different time intervals from baseline. The mean baseline heart rate in group D was 81.15±7.91 bpm and the mean heart rate in group M was 79.43±6.66 bpm (*p = 0.605*). HR difference in group D and group M from 5 min to 70 min were found to be significant. There was better attenuation of HR in group D. At 80 min in group D was 76.36 ± 5.10 and the mean heart rate at 80 min interval in group M was 83.64±12.42 and the difference in heart rate were statistically analysed to be insignificant (*p = 0.122*). At 90 min in group D was 74.00±3.16 and the mean heart rate at 90 min interval in group M was 84.00±10.03 and the difference in heart rate were statistically analysed to be insignificant (*p= 0.110*).

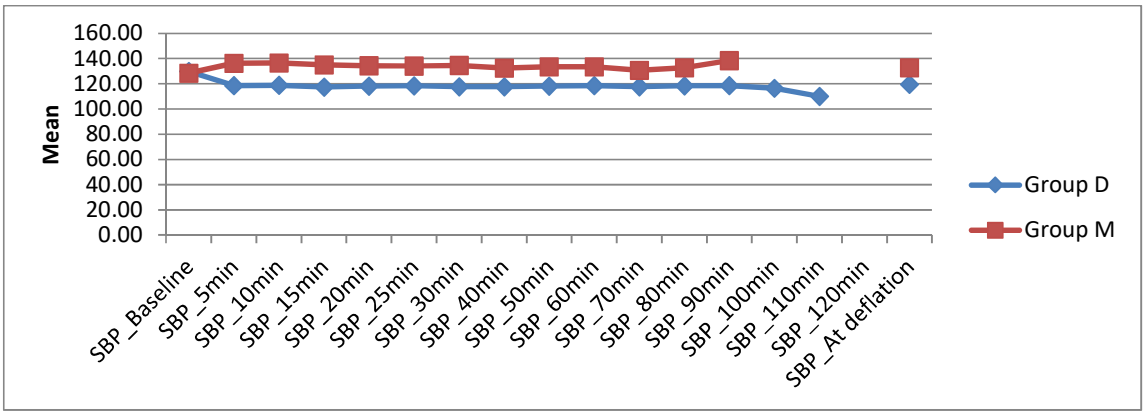

Figure 5: Distribution of Groups According to Systolic Blood Pressure (SBP)

Figure 5 describes the mean SBP at different time intervals from baseline. At baseline mean SBP in group D was 129.85±12.05 and the mean SBP in group M was 128.50±11.77. The mean SBP was compared among study groups and was insignificant (*p= 0.773*). From 5 min to 90 min interval, the difference of SBP in group D and group M were found to be significant. Better control of SBP was in group D.

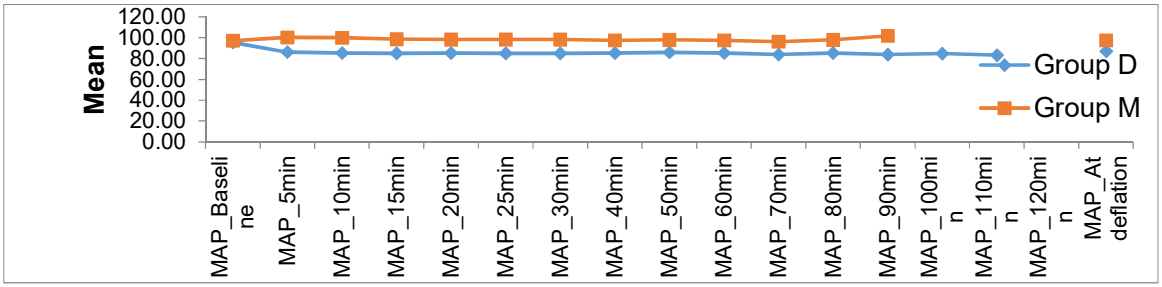

Figure 6: Distribution of Groups According to Mean Arterial Pressure

Figure 6 depicts the mean arterial blood pressure at different time intervals. The mean of mean arterial pressure in the group D was 95.42±8.31 and the mean of mean arterial pressure in group M was 97.12±6.88. The means were compared in the two groups and it was found to be statistically insignificant (*p = 0.437*). The means were compared in the two study groups and it was found to be statistically significant from 5 min to 90 min (*p= 0.014*).

Secondary Findings

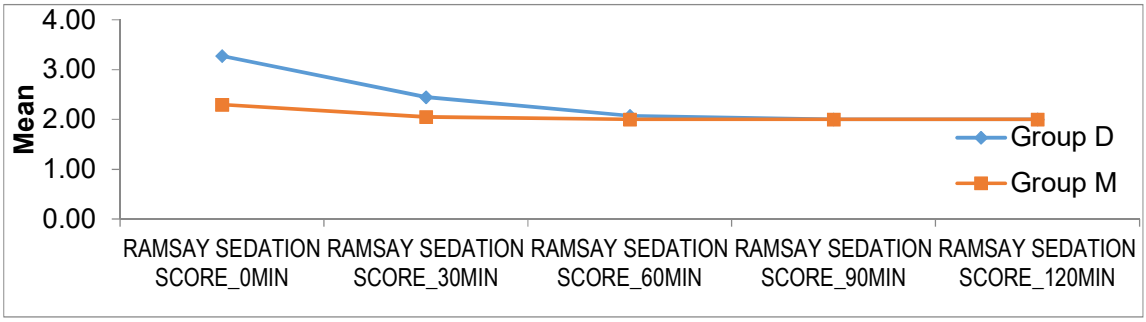

Figure 7: Distribution of Groups According to Ramsay Sedation Score

Figure 7 shows the mean Ramsay Sedation score at different intervals. The mean Ramsay Sedation score at immediate postoperative period in the group D was 3.28±0.60 and in group M was 2.30±0.52 difference was statistically significant (*p= 0.0001*). At 30 min, the mean of group D was 2.45±0.50 and in group M was 2.05±0.22. Statistical analysis was done to reveal that there was significant difference between two groups (*p = 0.0001*). From 60 min onwards differences were insignificant.

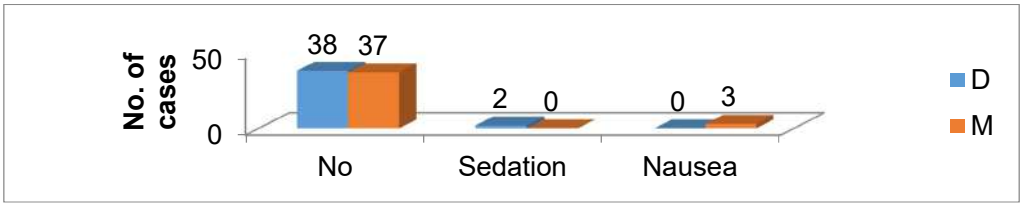

Figure 8: Distribution of Groups According to Side Effects Observed

Figure 8 shows the side effects observed postoperative period in the group D and group M. In group D, 2 (5 %) were having sedation and others having no side effects, while in group M 3 (7.5%) were having nausea and others having no side effects.

Discussion

Pneumoperitoneum creation by inflating CO_2 is the key element of all laparoscopic surgeries. The search for an ideal agent was started from 1970 to attenuate the haemodynamic responses during laparoscopic surgeries. The study was conducted as per the methodology described.

The baseline H.R was comparable in both groups. HR was found to be lower in Dexmedetomidine group than the other group (*p= 0.605*). This may be due to bolus dose of Dexmedetomidine before administrating maintenance dose as infusion. The difference at baseline and till 5 min was insignificant may be because of other agents used for induction. HR was significantly lower in Dexmedetomidine after 10, 20, 30, and up to 40 min of pneumoperitoneum than Magnesium Sulfate.

Zarif et al [13] in his study used Dexmedetomidine with a loading dose of 1µg/kg followed by infusion at 0.4µg/kg/h and Magnesium Sulfate at a loading dose of 2g followed by infusion at 15µg/kg/min, their results show that in Magnesium Sulfate group, both SBP and DBP increased abruptly after pneumoperitoneum and sustained high throughout procedure when compared to Dexmedetomidine group where it was better attenuated. These findings were comparable with our study even with infusion dose of Dexmedetomidine at 0.2µg/kg/h.

The comparison of baseline systolic blood pressure among two groups in our study revealed that there is no statistically significant difference (*p =0.773*). Then after starting and up to 60 min of pneumoperitoneum both SBP and DBP were significantly lower with Dexmedetomidine than with Magnesium Sulfate (*p = 0.0001*). Hence MAP was significantly lower with Dexmedetomidine than with Magnesium Sulfate. There was no significant difference among the groups at baseline mean blood pressure. These findings were comparable with Kalra et al. [14] study in which they compared clonidine and Magnesium Sulfate for attenuation of haemodynamic responses to pneumoperitoneum. They have found that Clonidine is better in blunting haemodynamic response than Magnesium Sulfate when used 15 min before pneumoperitoneum.

Dexmedetomidine acts by decreasing of sympathetic outflow from the locus ceruleus. As a result, norepinephrine levels will decrease and thereby decrease in MAP and HR.

Analgesic property is mediated mainly through the dorsal horn of spinal cord.

Jee et al. found that Magnesium Sulfate bolus of 50 mg/kg before pneumoperitoneum increased serum magnesium concentrations to 2-4 mmols/l, which is enough to inhibit catecholamine release in vitro [15]. Release of vasopressin can also cause change in haemodynamics during pneumoperitoneum. Vasodilatory effects of Magnesium Sulfate can counter effects of vasopressin which is released by compression abdominal capacitance vessels by pneumoperitoneum. Precise mechanism by which magnesium reduces vasopressin concentration need to be studied further. ***Jee et al.*** [14] in their study gave Magnesium Sulfate 50 mg/kg immediately before pneumoperitoneum for patients undergoing laparoscopic and observed that Magnesium Sulfate before pneumoperitoneum attenuates arterial pressure increases during laparoscopic cholecystectomy. This attenuation is apparently related to reductions in the release of catecholamine, vasopressin, or both.

Bryskin and Weldon [15] during laparoscopic resection of phaeochromocytoma used a combination of Dexmedetomidine and Magnesium Sulfate for haemodynamic control found to have haemodynamic stability, which favors the efficacy of both drugs. Ismail et al. [16] observed similar effects of when compared Magnesium Sulfate, Dexmedetomidine, and lignocaine on the haemodynamic responses in patients undergoing laparoscopic cholecystectomy. The HR and MAP changes were found to be greater in both the lignocaine and control groups than the Dexmedetomidine and Magnesium Sulfate groups after drug administration, after induction, after intubation, throughout pneumoperitoneum at 10 min intervals and in the postoperative period after 10 min with highly significant difference.

We also observed that in patient who received an infusion of Dexmedetomidine induction dose of propofol was less. However an objective criteria need to ascertain this. Reversible bradycardia and hypotension were recorded in the Dexmedetomidine group in our study. Very few of them required nitroglycerine infusion who developed hypertensive response. Among thirty patients two of them had sedation in Dexmedetomidine group while in Magnesium Sulfate group three of them showed only nausea as side effect. But none of the patient in our study had sedation score > 4, so none of the patient requires any type of airway or ventilator support. These findings are correlating with the study done by Kumar et al. [17] in 2014 on comparative study of effects of Dexmedetomidine and clonidine premedication in perioperative haemodynamic stability and postoperative analgesia in laparoscopic cholecystectomy. Clonidine group received 2 µg/kg of diluted in normal saline, given slow intravenous infusion over 10 min. Dexmedetomidine group received 1 µg/kg of diluted in normal saline, given slow intravenous infusion over 10 min. The studies with higher infusion rates had more incidences of adverse effects like hypotension and bradycardia.[33] In our study, we used Dexmedetomidine in an infusion rate of 0.2 µg/kg/h during laparoscopic surgeries and did not observe significant incidence of hypotension or bradycardia. Dexmedetomidine causes sedation but it does not cause delay in the recovery time as shown in the study.

In our study Dexmedetomidine group showed significant difference in sedation score for the first 30min when compared with Magnesium Sulfate group similar findings were noted by Hall et al. [18]. According to study done by Salman et al. [19]. Dexmedetomidine has comparable effects to remifentanil and may be an alternative to remifentanil in ambulatory anaesthesia.

Our study had some limitations. We had to exclude cases where duration of surgery more than 120 mins, IAP was restricted to 14 mmhg and since we chose different laparoscopic surgeries, positioning during surgeries, likely to alter the haemodynamics, which was not taken into account.

Conclusion

We did a prospective, randomized, double-blind study to compare the effect of

infusion of Dexmedetomidine and Magnesium Sulfate on haemodynamic changes in laparoscopic surgeries under general anaesthesia. The following conclusions were made, Dexmedetomidine infusion even at a dose of 0.2µg/kg/h provides a better attenuation of haemodynamic changes during pneumoperitoneum than Magnesium Sulfate in Laparoscopic surgeries. Dexmedetomidine also provides a better sedation score in terms of benefits versus side effects in patients undergoing laparoscopic surgeries.

Conflicts of interest

The authors declares that they do not have conflict of interest.

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