



# International Journal of Medical Anesthesiology

E-ISSN: 2664-3774  
P-ISSN: 2664-3766  
[www.anesthesiologypaper.com](http://www.anesthesiologypaper.com)  
IJMA 2020; 3(1): 177-183  
Received: 15-11-2019  
Accepted: 19-12-2019

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## Compare the efficacy of pre-anaesthetic single IV dose of magnesium sulphate versus clonidine for suppression of sympathetic response to pneumoperitoneum in patients undergoing elective laparoscopic cholecystectomy

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DOI: <https://doi.org/10.33545/26643766.2020.v3.i1c.87>

### Abstract

**Background:** Laparoscopic surgery is a routinely performed surgery and it is desirable to have stable intraoperative haemodynamic states by avoiding hypertension and tachycardia. The present study has been conducted to compare the beneficial effect of magnesium sulphate versus clonidine in maintaining the perioperative haemodynamic parameters during laparoscopic cholecystectomy.

**Aim & objective:** Hence the present study "A Randomised double-blind comparative study of efficacy of preanesthetic single dose Magnesium sulphate versus clonidine for suppression of sympathetic response to pneumoperitoneum in patients undergoing elective laparoscopic cholecystectomy",

**Methodology:** The Present study conducted in Yashoda Hospital, Malakpet during the period of 1st May 2016 to 1st June 2018, to compare the beneficial effects of Clonidine and magnesium sulphate. A total of 60 patients randomly allocated in two groups, to Magnesium sulphate (Group M) & Clonidine (Group C) of 30 each undergoing elective laparoscopic cholecystectomy, under GA were studied. Sex, age and weight were comparable in the two groups. There were no significant differences between the two groups with regard to demographic data such as sex, age and weight.

**Results:** Heart rates were on the lower side in Group M after induction, at 5 mins and 10 mins, 20 min after pneumoperitoneum and in the postoperative period as compared to Group C. Systolic blood pressure (SBP) is significantly lower in Group M patients after induction, 5 mins, 10 mins, 20 min after pneumoperitoneum and in the postoperative recovery period as compared to Group C. In Group M, Diastolic blood pressure (DBP) is significantly lower at 5 mins, 10 mins, 20 min after pneumoperitoneum and in the postoperative period as compared to Group C. Mean arterial pressure (MAP) is significantly lower in Group M patients at 5 mins, 10 mins, 20 min after pneumoperitoneum and in the postoperative recovery period as compared to Group C. In our study, two patients in group C developed bradycardia which was not statistically significant.

**Conclusion:** Both the drugs, Clonidine as well as magnesium sulphate, provided adequate analgesia and maintained cardiovascular stability throughout the intraoperative period during laparoscopic cholecystectomy and were found to be safe.

**Keywords:** Clonidine, magnesium sulphate, mean arterial pressure (MAP), pneumoperitoneum, laparoscopic cholecystectomy

### Introduction

Laparoscopy is a surgical procedure in which a fiber optic instrument inserted through the abdominal wall to view the organs in the abdomen or permits surgery. They are performed far from their location through small incision elsewhere in the body. Laparoscopic cholecystectomy is one of the most common laparoscopic surgeries performed worldwide. Pneumoperitoneum is commonly induced by carbon dioxide (CO<sub>2</sub>).

Pneumoperitoneum, as well as hypercapnia due to CO<sub>2</sub>, is responsible for the adverse cardiovascular effects. An abrupt elevation of mean arterial pressure (MAP), systemic vascular resistance, and decreased cardiac output are commonly noted [1, 2]. This vasopressor response is due to the release of both catecholamines [3, 4] and vasopressin [5].

The cardiac output will be further decreased by the reverse Trendelenburg position used in these surgeries. These events will be less tolerated, especially by patients with compromised cardiac function. Hence, attenuation of these vasopressor responses is of paramount

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importance to an anesthesiologist. Opioids [6] beta blockers [7], magnesium, and  $\alpha_2$  agonists [8] have been used for this purpose.

Magnesium has shown to block the release of catecholamines release from both adrenal medullae, as well as from nerve terminals [9]. It has been used to attenuate intubation-induced vasopressor response. Magnesium also acts directly on blood vessels causing vasodilation, thus attenuating vasopressin-induced vasoconstriction [10].

Clonidine, a selective  $\alpha_2$  agonist ( $\alpha_2: \alpha_1=220:1$ ) with elimination half-life of 6-10 hour. It has e. It is known to induce sedation, decrease anaesthetic drug requirement and improve perioperative haemodynamics by attenuating blood pressure and heart rate response to surgical stimulation and protecting against perioperative myocardial ischemia. Clonidine provides sympathoadrenal stability and suppresses renin angiotensin activity. It has been used for attenuating vasopressor responses [11]. We hypothesized that magnesium and clonidine can be used for attenuating the hemodynamic responses to pneumoperitoneum.

The purpose of this study was to compare the efficacy of pre-anaesthetic single IV dose of Magnesium sulphate versus Clonidine for suppression of sympathetic response to pneumoperitoneum in patients undergoing elective laparoscopic cholecystectomy.

### Aims & objectives

The aim of the present study was to compare the effects of a single IV dose of Magnesium sulphate and Clonidine, prior to pneumoperitoneum on haemodynamic parameters in patients undergoing elective laparoscopic cholecystectomy.

### Primary objective

To study the efficacy of pre-anaesthetic single dose Magnesium sulphate versus Clonidine for suppression of sympathetic response to pneumoperitoneum in patients undergoing elective laparoscopic cholecystectomy.

### Secondary objectives

1. To assess the incidence of associated adverse effects i.e. bradycardia and hypotension with the drug.
2. To assess the analgesic effects of the study drugs.

### Materials and Methods

The present study "Randomised double blind comparative study of efficacy of preanesthetic single dose magnesium sulphate versus clonidine for suppression of sympathetic response to pneumoperitoneum in patients undergoing laparoscopic cholecystectomy", was conducted in Yashoda Hospital, Malakpet, Hyderabad, during the period of 1st May 2016 to 1st June 2018.

### Study site

OT (Operation theatre) complex, Yashoda Hospital, Malakpet, Hyderabad.

### Study population

The study protocol was approved by the Institutional Ethical Committee and informed consent was taken from each of the patients. It was prospective, randomised and double blinded study. The study included total 60 patients belonging to ASA grade I and II of either sex with age between 20-55 years posted for laparoscopic cholecystectomy.

### Study design

A prospective, randomised, double blind comparative study consisting of 30 patients in group C (Clonidine) and 30 patients in group M (Magnesium sulphate) is undertaken to compare the haemodynamic parameters in patients undergoing elective laparoscopic cholecystectomy and adverse effects of drugs used.

A group consisting of 60 patients was randomly divided into 2 groups, as statistical analysis were performed using SPSS. The sample size was determined by power analysis.

### Inclusion criteria

1. Patients planned for Elective Laparoscopic Cholecystectomy surgery.
2. Age group of 20-55 years.
3. ASA I & II patients.

### Exclusion criteria

1. Patients unwilling for the study.
2. History of Hypertension and Diabetes.
3. Obese with BMI >30.
4. ASA III, IV & V patients.
5. Patients with cardiovascular, pulmonary, hepatic, neurological and endocrine abnormalities.
6. Pregnant patients.
7. Known case of Pre op hypotension.
8. Surgeries converted to Open Cholecystectomy.
9. Hypersensitivity to dexmedetomidine or clonidine.

### Study procedure

A Pre-anaesthetic evaluation comprising of history of previous medical and surgical illnesses, previous anaesthetic exposures, drug allergies and baseline investigations of blood, radiograph of the chest and airway examination will be done. Informed written consent will be taken from the patient. Patient will be kept nil by mouth for at least 6 hours prior to surgery. Preoperative vital parameters in the form of baseline pulse, blood pressure and oxygen saturation will be recorded.

Study is undertaken in patients planned for Elective Laparoscopic Cholecystectomy surgery. Patients are selected between 20 to 55 years of ASA I&II grades. They are divided into 2 groups of 30 each and allocated randomly. All patients are explained about the procedure and its complications and informed consent obtained.

There were no significant differences between the two groups with regard to demographic data such as age, sex and weight.

### Monitors used Philips multi parameter

NIBP, Pulse oximeter, EtCo<sub>2</sub>, ECG.

After baseline parameters were noted, patients were allocated randomly to the two groups using a computer-generated random numbers table. An anaesthesiologist who was not one of the study participants prepared syringes containing either magnesium sulphate or clonidine. Both syringes were labeled "study drug" and coded to maintain the double-blinded nature of the study. Immediately before induction, patients in the clonidine group (Group C) received clonidine 1 $\mu$ g/kg in normal saline and in the magnesium sulphate group (Group M) received Magnesium sulphate 50mg/kg in normal saline. Total volume of the study drug was adjusted to 50ml and administered over a period of 10 min before induction.

All patients were pre-medicated with intravenous Fentanyl 2 µg/kg, Glycopyrrolate 4µg/kg, Ondansetron 15µg/kg. All patients were Preoxygenation with 100% O2 for 3 minutes and were induced with Propofol 2mg/kg IV. Intubation was facilitated by using Vecuronium bromide 0.1mg/kg. The lungs were ventilated with 100% oxygen for 3 minutes.

**The parameters recorded were**

1. Heart Rate.
2. Systolic Blood Pressure.
3. Diastolic Blood Pressure.
4. Mean Arterial Pressure.
5. SPO2.
6. EtCO2.

The recordings were noted at various intervals as detailed below, from the study conducted.

1. Pre-operatively i.e. before premedication (basal line value)
2. After Induction
3. After Intubation

4. 5 min, 10 min, 20min, 30 min,45 min,60 min,75 min,90 min after pneumoperitoneum.
5. Extubation
6. Post op first hour.

At the end of surgery, neuromuscular blockade was reversed with neostigmine 50 µg/kg and glycopyrrolate 10µg/kg IV. After satisfying the extubation criteria, patient was extubated and transferred to post-anaesthesia care unit (PACU).

**Stastical analysis**

The data was expressed as mean and standard deviation. The homogeneity in two groups of mean and standard deviation was analysed using SPSS version. Comparison between two groups at a time (inter-group comparison) was done using student’s unpaired t- test. *P* <0.05 was considered statistically significant, value <0.01 was considered highly significant, >0.05 was considered insignificant.

**Table 1:** Demographic profile (MEAN±SD)

Variable	Mean of clonidine group	SD	Mean of magnesium sulphate group	SD	P value	Significance
AGE_YEARS_	37.0667	8.578	36.4	8.6924	0.7660	NS
ASA_Grade	1.4	0.4983	1.3	0.4661	0.4254	NS
WEIGHT_KG_	65.4667	7.1859	64.2333	8.7284	0.5525	NS

**Table 2:** Comparison of gender distribution in between two groups

Group	Male	Female
Clonidine	14	16
Magnesium Sulphate	14	16

**Table 3:** Comparison of heart rate between two groups

Variable	Mean of clonidine group	SD	Mean of Magnesium sulphate group	SD	P value	Significance
HR_Pre_op	80.6667	7.3077	77.4	7.968	0.1033	NS
HR_Induction	80.1	6.7382	72.2	9.679	0.0005	HS
HR_Intubation	75.6667	5.2215	72.4667	5.4755	0.0241	S
HR_05_min after PNP	86.3103	6.0244	77.8333	5.14	<0.0001	HS
HR_10_min after PNP	84.8621	6.0221	75.5667	5.144	<0.0001	HS
HR_20_min after PNP	83.0667	6.164	74.4667	5.0016	<0.0001	HS
HR_30_min after PNP	83.5667	9.1263	74.9333	8.2585	0.0003	HS
HR_45_min after PNP	74.9667	8.7316	70.9667	8.688	0.0805	NS
HR_60_min after PNP	76.3333	5.7102	72.45	5.501	0.0662	NS
HR_75_min after PNP	74.4286	6.5283	70.8571	1.5736	0.1848	NS
HR_90_min after PNP	73	4.1633	68.6667	1.1547	0.1468	NS
HR_Extubation	72.2333	7.7845	72.6	6.5369	0.8441	NS
HR_Postop	78.7667	7.5689	76	3.7046	0.0773	NS

In this study heart rate after 5 min of pneumoperitoneum in group C was 86.310 6.02 and in group M was 77.833 5.14(p<0.0001), after 10 min in group C was 84.862 6.02 and in group M was 75.566 (p<0.0001), after 20 min in group C was 83.066 and in group M was 74.466 (p<0.0001).

The difference of heart rate in both groups was statistically significant rates were on the lower side in Group M (Magnesium sulphate) after induction, 5min, 10min, 15min after pneumoperitoneum when compared to clonidine, which is statistically significant.

**Table 4:** Comparison of SBP between two groups

Variable	Mean of clonidine group	SD	Mean of Magnesium sulphate group	SD	P value	Significance
SBP_Pre op	124.1	7.3172	120.8667	5.8648	0.0640	NS
SBP_Induction	122.8667	10.0163	117.6333	6.478	0.0195	S
SBP_Intubation	124.0667	5.343	120.0667	7.7635	0.0236	S
SBP_05_min after PNP	132.3667	4.1646	124.6333	5.5615	<0.0001	HS
SBP_10_min after PNP	131.1667	4.602	122.6	5.703	<0.0001	HS
SBP_20_min after PNP	131.0667	7.3105	121.3333	9.6609	<0.0001	HS
SBP_30_min after PNP	125.5	10.5135	113.0333	12.7779	0.0001	HS

SBP_ 45_min after PNP	116.2	13.7324	114.3	9.4837	0.5354	NS
SBP_ 60_min after PNP	117.5385	8.7237	112.1	9.0082	0.0963	NS
SBP_ 75_min after PNP	113.1429	5.1455	113.1429	6.9625	1.0000	NS
SBP_ 90_min after PNP	116	2.8284	110	7	0.1726	NS
SBP_ Extubation	113.6333	8.471	117.9333	11.1291	0.0976	NS
SBP_ Post op	123.1667	4.4573	120.1667	11.8061	0.1980	NS

SBP after 5 of pneumoperitoneum in group C was 132.366 and in group M was 124.633 5.56 (p<0.0001), after 10 min in group C was 131.166 4.60 and in group M was 122.60 5.70(<0.0001), after 20 in group C was 131.066 and in

group M was 121.333 SBP was lower in Group M (Magnesium sulphate) after 5min, 10min, 15min, 30min after pneumoperitoneum compared to Clonidine which is statistically significant.

**Table 5:** Comparison of DBP between two groups

Variable	Mean of clonidine group	SD	Mean of Magnesium sulphate group	SD	P value	Significance
DBP_ Pre_op	76.3333	6.6037	75.9333	6.8175	0.8183	NS
DBP_ Induction	76.8	5.933	73.6	5.0213	0.0279	S
DBP_ Intubation	75.4	6.3713	71.8667	4.1334	0.0135	S
DBP_ 05_min after PNP	85.2667	5.0986	78.9333	5.705	<0.0001	HS
DBP_ 10_min after PNP	84.1	5.2677	77.4	4.4691	<0.0001	HS
DBP_ 20_min after PNP	80.8	6.1611	75.9333	5.9302	0.0028	HS
DBP_ 30_min after PNP	78.5667	10.0505	69.0333	7.2086	0.0001	HS
DBP_ 45_min after PNP	71.7667	6.6524	73.4667	8.7877	0.4017	NS
DBP_ 60_min after PNP	76.3077	7.4765	75	10.6029	0.7023	NS
DBP_ 75_min after PNP	75.4286	5.6231	79.5714	10.5017	0.3756	NS
DBP_ 90_min after PNP	77.5	1.9149	75	5.5678	0.4308	NS
DBP_ Extubation	72.4667	9.0239	73.6667	10.3635	0.6342	NS
DBP_ Post_op	77.5	7.2955	76	6.5548	0.4056	NS

DBP after 5min of pneumoperitoneum in group C was 85.266 5.09min and in group M was 78.93 5.70min (<0.0001), after 10min in group C was 84.1 5.26min and in group M was 77.4 4.46min (<0.0001), after 20min in group C was 80.8 6.16min and in group M was 75.93 min

(0.0028), after 30min in group C was 78.56 10.05min and in group M was 69.03 7.20min (0.0001). DBP were on the lower side in Group M (Magnesium sulphate) after 5min, 10min of pneumoperitoneum when compared to Group C which is statistically significant

**Table 6:** Comparing map between two groups

Variable	Mean of clonidine group	SD	Mean of Magnesium sulphate group	SD	P value	Significance
MAP_ Pre_op	92.2556	5.8772	90.9111	5.0666	0.3466	NS
MAP_ Induction	92.1556	5.9208	88.2778	4.4516	0.0058	HS
MAP_ Intubation	91.6222	5.3238	87.9333	4.2104	0.0042	HS
MAP_ 05_min after PNP	100.9667	3.9395	94.1667	4.5945	<0.0001	HS
MAP_ 10_min after PNP	99.7889	4.4338	92.4667	4.083	<0.0001	HS
MAP_ 20_min after PNP	97.5556	5.3257	91.0667	6.3935	0.0001	HS
MAP_ 30_min after PNP	94.2111	8.8428	83.7	7.9353	<0.0001	HS
MAP_ 45_min after PNP	86.5778	7.7003	87.0778	7.4898	0.7997	NS
MAP_ 60_min after PNP	90.0513	7.406	87.3667	9.7182	0.4034	NS
MAP_ 75_min after PNP	88	5.1208	90.7619	9.1928	0.5006	NS
MAP_ 90_min after PNP	90.3333	2.0728	86.6667	3.6056	0.1458	NS
MAP_ Extubation	86.1889	7.9083	88.4222	9.3053	0.3207	NS
MAP_ Post_op	92.7222	4.8598	90.7222	7.2878	0.2161	NS

MAP after 5min of intubation in group C was 100.96 3.93 and in group M was 94.16 4.59(<0.0001), after 10min in group C was 99.78 4.43 and in group M was 92.46 (<0.0001), after 20min in group C was 97.55 5.32 and in group M was 91.06 6.39(0.0001), after 30 min in group C was 94.21 8.84 and in group M was 83.7 7.93(0.0001)

MAP was on the lower side in Group M (Magnesium sulphate) after 5 min, 10min, and 15min after pneumoperitoneum when compared to Group C (Clonidine) which is statistically significant

**Table 7:** Comparison of adverse effects between two groups

Adverse effects	Group M (n=30)	Group C (n=30)
1.Bradycardia	0(0%)	2(6.6%)
2.Hypotension	0(0%)	0(0%)

**Discussion**

In our study, we didn't encounter episodes of hypotension in any case of both the study groups. But we have seen two cases of bradycardia in our Clonidine group (GROUP C), which required atropine which is statistically insignificant. In the present study, "Randomised double blind comparative study of efficacy of preanesthetic single dose magnesium sulphate versus clonidine for suppression of sympathetic response to pneumoperitoneum in patients undergoing laparoscopic cholecystectomy", we compared the effects of magnesium sulphate and clonidine administered before induction on haemodynamic parameters in patients undergoing elective laparoscopic cholecystectomy. Pneumoperitoneum-induced cardiovascular changes include elevated arterial pressures with little or no change in HRs [1].

<sup>21</sup>. The role of magnesium and clonidine in attenuating hemodynamic responses to pneumoperitoneum have been studied earlier

In laparoscopic surgery, CO<sub>2</sub> is routinely used to create pneumoperitoneum. Elevated intra-abdominal pressure induced by pneumoperitoneum and CO<sub>2</sub> itself produce some adverse effects on the cardiovascular system.

Immediately after pneumoperitoneum, plasma level of norepinephrine, epinephrine and plasma renin activity is increased. Increased catecholamine level activates the renin-angiotensin-aldosterone-system (RAAS) leading to some characteristic haemodynamic alterations, which include:

1. Decreased cardiac output (25-35%).
2. Elevated mean arterial pressure.
3. Increased systemic/pulmonary vascular resistance.

Laparoscopic cholecystectomy is performed in reverse Trendelenburg position. This particular position causes diminished venous return which ultimately leads to further decrease in cardiac output. Normal heart can cope with the increase in afterload under physiologic conditions. But patients with compromised cardiac function may not be able to tolerate the changes in afterload produced by pneumoperitoneum and it may have deleterious effects on their haemodynamics. Pneumoperitoneum used for laparoscopic procedures is a complex patho-physiologic phase with significant haemodynamic variation.

CO<sub>2</sub> is most commonly used as it is colorless, non-combustible, highly soluble and permeable in tissues thus reducing the risk of gas embolism. The haemodynamic changes associated with pneumoperitoneum are the result of both increased intra-abdominal pressure and hypercarbia.

To attenuate this haemodynamic response, a wide variety of agents are being used both during premedication and induction. Research fellows have tried beta blockers,  $\alpha_2$  agonists, magnesium sulfate, opioids, vasodilators and gasless approach to negate the haemodynamic variations.

This study was carried out on 60 ASA grade I and II patients posted for laparoscopic cholecystectomy. Then they were randomly divided into two study groups consisting of 30 patients each;

1. **Group 'C':** Received Clonidine 1mcg/kg by slow i.v over 10min prior to induction
2. **Group 'M':** Received Magnesium sulphate 50mg/kg by slow i.v over 10min prior to induction

In my study we compared HR, SBP, DBP, and MAP in both group

Magnesium sulfate has shown to reduce the plasma catecholamines and vasopressin levels, thus contributing to its blunting effect on sympathoadrenal hemodynamic stress response<sup>[9]</sup>. These effects of magnesium are noted at serum concentrations of 2-4 mmol/L<sup>[12, 13]</sup>.

However, in our study, the serum magnesium levels were not measured. In an earlier study, a dose of 50 mg/kg has been shown to achieve these levels<sup>[9]</sup>. Magnesium has also been shown to have a vasodilator action, thus contributing to the reduction of blood pressure<sup>[10]</sup>. Vasopressin concentrations raise in pneumoperitoneum due to increased compression of abdominal capacitance vessels with a consequent reduction in venous return to the heart<sup>[14, 15]</sup>. Magnesium due to its vasodilator action might reduce vasopressin release. In our study, we noted that magnesium reduced arterial pressures more significantly as compared to

both clonidine and the control group

Yatish Bevinaguddaiah *et al.* in 2017<sup>[16]</sup> conducted a study in Ninety American Society of Anesthesiologists health status Classes I and II patients. Group C received injection clonidine 1 $\mu$ g/kg. Group M received injection magnesium sulfate 50mg/kg. Group NS received 10ml normal saline intravenously. On comparing MAP in Groups M and C, it was significantly lower in M Group at P5 ( $P = 0.035$ ), P10 ( $P = 0.048$ ), P30 ( $P = 0.027$ ), and P40 ( $P = 0.05$ ). On comparing HR of patients in Group NS with Groups M and C, Group NS had significantly higher HR at P5 to P40 ( $P < 0.001$ ). Moreover, HR was significantly lower in M Group as compared to C Group at all-time points ( $P < 0.001$ ). They concluded both magnesium and clonidine attenuated the hemodynamic response to pneumoperitoneum.

In present study we have taken magnesium sulphate 50mg/kg based on Showket Ahmad Dar *et al.*<sup>[17]</sup> and Yatish Bevinaguddaiah *et al.*<sup>[16]</sup> in which they observed that magnesium sulphate 50mg/kg significantly decreased sympathetic response in laparoscopic cholecystectomy

In present study we have taken clonidine 1mcg/kg which was based on Kalra *et al.*<sup>[8]</sup> (1mcg/kg, 1.5mcg/kg), and Yatish Bevinaguddaiah *et al.*<sup>[16]</sup> (1mcg/kg). In above studies clonidine 1mcg/kg significantly decreased sympathetic response in laparoscopic cholecystectomy But lower dose of clonidine i.e. 1mcg/kg is hemodynamically stable with less side effects like bradycardia.

A higher dose of IV clonidine (3 $\mu$ g/kg) used by Altan *et al.*<sup>[18]</sup> had a significant incidence of bradycardia and hypotension. We used a much lower dose of clonidine (1  $\mu$ g/kg) and did not have any incidence of hypotension or bradycardia.

### Demographic data

In this study the mean age group in group C was 37.06 8.57 years and in group M was 36.40 8.69 years ( $p=0.766$ ) which were statistically comparable and not significant. Mean weight in group C was 65.46 years and in group M was 64.23 8.72 years ( $p=0.552$ ) which were statistically comparable and not significant.

The age, weight, sex, of the patients in both groups were comparable which shows that the patients of equal age, weight, sex were enrolled in the study and seems that it has no influence on outcome of the study which were similar to studies Yatish Bevinaguddaiah *et al.*<sup>[16]</sup>; Kalra *et al.*<sup>[8]</sup>

### Haemodynamic parameters

#### Heart rate

#### Pre-operative heart rates were comparable in both groups

In this study heart rate after 5 min of pneumoperitoneum in group C was 86.310 6.02 and in group M was 77.833 5.14 ( $p < 0.0001$ ), after 10 min in group C was 84.862 6.02 and in group M was 75.566 ( $p < 0.0001$ ), after 20min in group C was 83.066 and in group M was 74.466 ( $p < 0.0001$ ). The difference of heart rate in both groups was statistically significant. In our study, patients receiving magnesium sulfate had significantly lower HRs as compared to clonidine. This is in contrast to earlier study karla *et al.*<sup>[8]</sup> where there was no significant difference in HRs between magnesium sulfate (50mg/kg) and clonidine (1  $\mu$ g/kg). But similar to the Yatish Bevinaguddaiah *et al.*<sup>[16]</sup> study.

**Systolic blood pressure [SBP]****Pre-operative SBP were comparable in both groups**

SBP after 5 min of pneumoperitoneum in group C was 132.366 and in group M was 124.633 5.56 ( $p < 0.0001$ ), after 10 min in group C was 131.166 4.60 and in group M was 122.60 5.70 ( $< 0.0001$ ), after 20 in group C was 131.066 and in group M was 121.333 Yatish Bevinaguddaiah *et al.* [16] in 2017 in their study they observed SBP in both groups (clonidine & magnesium sulphate) is statistically significant At 5min after pneumoperitoneum in clonidine group 126.17 10.59 and in magnesium sulphate group 111.76 15.43 ( $< 0.019$ ) they got significant. After that no significant difference in both groups. Jee *et al.* [9] administered magnesium sulfate 50 mg/kg over 2-3 min, before pneumoperitoneum in patients undergoing laparoscopic cholecystectomy and found that systolic and diastolic arterial pressures were significantly higher in the control group ( $P < 0.05$ ) than in the magnesium group at 10 [144 12)/103 16) vs 130 9)/89 13) mm Hg], 20 [140 7.0)/96 9) vs 126 10)/87 10) mm Hg], and 30 min [135 13)/94 9) vs 123 10)/84 7) mm Hg] post-pneumoperitoneum In our study we observed SBP was lower in magnesium sulphate group after 5min, 10min, 20min of pneumoperitoneum similar to jee *et al.* [9] and Yatish Bevinaguddaiah *et al.* [16]

**Diastolic blood pressure [DBP]**

In our study DBP after 5min of pneumoperitoneum in group C was 85.266 5.09min and in group M was 78.93 5.70min ( $< 0.0001$ ), after 10min in group C was 84.1 5.26min and in group M was 77.4 4.46min ( $< 0.0001$ ), after 20min in group C was 80.8 6.16min and in group M was 75.93 min (0.0028), after 30min in group C was 78.56 10.05min and in group M was 69.03 7.20min (0.0001).

Showket Ahmad Dar *et al.* [17] in 2015 conducted a randomized, double-blind, prospective study on 62 patients, randomly divided in to two groups, group I and group II. Magnesium group (group I) received magnesium sulphate 50 mg/kg diluted in normal saline to total volume of 20ml at 240ml/hour over 5 minutes. Diastolic blood pressure 10 minutes after pneumoperitoneum in group I ( $65.94 \pm 13.05$  mm Hg versus  $74.29 \pm 14.27$  mm Hg with  $p = 0.019$ ), 15 minutes after pneumoperitoneum ( $68.03 \pm 9.84$  mm Hg versus  $76.71 \pm 11.56$  mm Hg with  $p = 0.002$ ).

In our study we observed DBP was lower in group M when compared to group C after 5min, 10min, and 20min of pneumoperitoneum similar lo Yatish Bevinaguddaiah *et al.* [16] and Showket Ahmad Dar *et al.* [17]

**Mean arterial pressure [MAP]**

In our study MAP after 5min of intubation in group C was 100.96 3.93 and in group M was 94.16 4.59 ( $< 0.0001$ ), after 10min in group C was 99.78 4.43 and in group M was 92.46 ( $< 0.0001$ ), after 20min in group C was 97.55 5.32 and in group M was 91.06 6.39 (0.0001), after 30 min in group C was 94.21 8.84 and in group M was 83.7 7.93 (0.0001)

Yatish Bevinagud daiah *et al.* [16] in 2017 in their study they observed MAP at 5 min in clonidine group 95.23 10.20 in magnesium sulphate group 88.60 12.30 (0.035) at 10 min in clonidine group 95.77 9.49 in magnesium sulphate group 88.57 14.69 (0.048) at 20 min in clonidine group 93.80 9.23 in magnesium sulphate group 89.03 11.12 (0.205) at 30 min in clonidine group 91.97 8.93 in magnesium sulphate group 85.27 11.22 (0.027) In our study MAP was lower in group M compared to group C after 5min, 10min. 20min, 30min of

pneumoperitoneum similar to Yatish Bevinaguddaiah *et al.* [16]

In our study we observed MAP was lower in group M when compared to group C after 5min, 10min, 20min after pneumoperitoneum similar to Yatish Bevinaguddaiah *et al.* [16]

Two of our patients in group C developed bradycardia which is statistically not significant.

Thus in the present study we found that, Magnesium sulphate (50mg/kg) given in IV infusion over 10 minutes is more effective than clonidine (1 $\mu$ g/kg) given IV, in attenuating the haemodynamic response to pneumoperitoneum and in reduction of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure, this could be attributed to attenuation of catecholamine release from the adrenal medulla and calcium antagonistic effects on vascular smooth muscle cells and competitive antagonism on hippocampal presynaptic calcium channels that regulate neurotransmitter release in the central nervous system by Magnesium sulphate [9]

**Conclusion**

In conclusion, our results show that a close relationship exists between increases in plasma levels of catecholamines and vasopressin and arterial pressure during pneumoperitoneum. Furthermore, the administration of magnesium sulphate before pneumoperitoneum effectively attenuated arterial pressure increases in subjects undergoing laparoscopic cholecystectomy. We suggest that this attenuation results from reductions in the release of catecholamines and vasopressin caused by magnesium sulphate. Moreover, the possibility remains that vasodilatory effects of magnesium sulphate could provide haemodynamic stability during pneumoperitoneum. Magnesium sulphate can be recommended to avoid pressor response during the induction and maintenance of pneumoperitoneum attenuating the haemodynamic response to pneumoperitoneum and in reduction of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure during and after pneumoperitoneum. So we can say that magnesium sulphate 50mg/kg is better premedication drug for laparoscopic cholecystectomy.

**Acknowledgment**

The author thankful to Department of Anaesthesiology for providing all the facilities to carry out this work.

**Conflict of interest**

None

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