

A Comparative Study of Intravenously Administered Clonidine and Magnesium Sulphate on Hemodynamic Responses During Laparoscopic Cholecystectomy

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Abstract

Background & Objectives: Laparoscopic surgeries are associated with significant hemodynamic response. Magnesium and clonidine both are known to inhibit catecholamine and vasopressin release and attenuate hemodynamic response to pneumoperitoneum. This randomized, placebo controlled study has been designed to assess which agent attenuates hemodynamic stress response to pneumoperitoneum better. **Methods:** Ninety patients undergoing elective laparoscopic cholecystectomy were randomized into 3 groups of 30 each. The study drugs were given intravenously over 10 min prior to creation of pneumoperitoneum. Group C received 1mcg/kg of clonidine in 10 ml normal saline, group M received 50mg/kg magnesium sulphate in 10 ml normal saline and group NS received 10 ml normal saline. Blood pressure and heart rate were recorded before induction (baseline value), after the study drug administration, 5 minutes after creation of pneumoperitoneum and then for every 10 minutes. **Results:** Statistically significant rise in the mean heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product occurred, post pneumoperitoneum, in the control group (NS). Hemodynamic response to pneumoperitoneum was significantly attenuated in both the clonidine(C) and magnesium (M) groups. However, extubation time and time to response to verbal commands was significantly prolonged in the magnesium sulphate group. No other adverse effects were noted in any of the groups. **Interpretation & Conclusion:** Administration of magnesium sulphate or clonidine attenuates hemodynamic response to pneumoperitoneum with comparable efficacy.

Keywords: Laparoscopic cholecystectomy; clonidine; magnesium sulphate; pneumoperitoneum; hemodynamic response.

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Introduction

Laparoscopic techniques offer major benefits to the patient such as small incision size, reduced postoperative discomfort, early ambulation, and a lower incidence of postoperative wound infections. All these factors contribute to the shorter in-patient stay and reduced perioperative morbidity. Nonetheless, laparoscopic surgery is not risk free. Complications due to the physiological changes associated with the creation of pneumoperitoneum, as well as the complications specific to the individual laparoscopic techniques pose increased anesthetic risks. As a result, anaesthetic techniques for laparoscopic surgery must be refined to anticipate these differences from open surgery. [1]

Major physiological changes seen in laparoscopic cholecystectomy are due to the following causes: 1) initial trendelenberg position 2) pneumoperitoneum, 3) systemic absorption of CO₂ reverse trendelenberg position. The extent of cardiovascular changes associated with creating of pneumoperitoneum depends on intra abdominal pressure attained, volume of CO₂ absorbed, patient's intravascular volume, ventilator strategy, surgical conditions and the anesthetic agents used. The hemodynamic effects include increase in mean arterial pressure, decreased cardiac output and increased systemic vascular resistance. [2]

These changes are better tolerated in ASA grade I and II patients, but can be detrimental in elderly and ASA grade III patients. Both

mechanical and neurohumoral factors contribute to these hemodynamic changes. Several mediators have been proposed: catecholamines, prostaglandins, renin and vasopressin. Change in nature of insufflating gas, use of low intra-abdominal pressure, use of abdominal wall lift methods, have been tried to decrease the hemodynamic alterations seen with pneumoperitoneum, but all with practical limitations. Epidural, segmental spinal, combined epidural and general anaesthesia, use of various pharmacologic interventions like nitroglycerine, esmolol have been used with varying success and practical limitations. [3]

Clonidine, a selective α_2 adrenergic agonist, causes a fall in the heart rate and blood pressure along with decreased systemic vascular resistance and cardiac output.⁴ Magnesium blocks release of catecholamines from both adrenergic nerve terminals and adrenal gland. Magnesium also produces vasodilation by acting directly on blood vessels and in high doses, attenuates vasopressin-mediated vasoconstriction. [4]

This study was designed to compare the effects of intravenously administered magnesium sulphate and clonidine on intraoperative hemodynamics during laparoscopic cholecystectomy. Objectives

Primary Objective

- To compare the effect of intravenous clonidine and magnesium sulphate on intraoperative hemodynamics during laparoscopic cholecystectomy.

Secondary Objective

- To compare the effects of clonidine and magnesium sulphate on post operative recovery, like time for extubation, and time to response to verbal commands.

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Materials and Methods

A study entitled "A comparative study of intravenously administered clonidine and magnesium sulphate on hemodynamic responses during laparoscopic cholecystectomy" was undertaken in Govt Medical College, Suryapet during the period of October 2020 to November 2021.

This study was undertaken after obtaining ethical committee clearance as well as informed consent from all patients.

Ninety patients scheduled for elective laparoscopic cholecystectomy belonging to ASA I and II were included in the study.

Inclusion Criteria

- 1) Age 18 – 60 years
- 2) American Society of Anaesthesiologists (ASA) grade I-II
- 3) Patients undergoing elective laparoscopic cholecystectomy under general anesthesia.

Exclusion criteria:

- 1) Severe Hypertension
- 2) Drug or alcohol abuse
- 3) Severe Hepatic dysfunction
- 4) Severe Endocrine dysfunction
- 5) Severe Renal dysfunction
- 6) Severe Cardiac dysfunction

Patients in whom surgery could not be completed laparoscopically and open cholecystectomy done were excluded from the study. Patients who showed exaggerated hypertensive response (taken as systolic BP>180mmHg or Diastolic BP>110mmHg) during surgery and administered antihypertensive drugs were excluded from the study.

Patients were randomly divided into three groups using sealed envelopes chosen by the patients and the randomization was done immediately before pneumoperitoneum.

The three groups were

Group C- Clonidine group (n=30)-received injection clonidine 1mcg/kg diluted in 10mL normal saline over 10 minutes, prior to pneumoperitoneum.

Group M- Magnesium sulphate group(n=30)-received injection magnesium sulphate 50mg/kg diluted in 10mL normal saline over 10 minutes, prior to pneumoperitoneum.

Group NS – control group (n=30)- received 10mL normal saline intravenously over 10 minutes, prior to pneumoperitoneum

Patients were premedicated with Tab ranitidine 150mg and Tab ondansetron 8mg orally at bed time the previous night before surgery and on the day of surgery, Injection glycopyrrolate 0.2 mg IM half an hour before shifting to OT. On arrival in the operation theatre, monitors were attached (heart rate, NIBP, SpO₂, ECG, temperature) and baseline vital parameters like HR, SBP, DBP, MAP, SpO₂ were recorded.

After preoxygenation for 3 minutes, patients received 1mcg/kg of fentanyl citrate intravenously. They were induced by injection propofol, 2mg/kg. Endotracheal intubation was facilitated by muscle relaxant vecuronium bromide 0.1mg/kg.

The patients were categorized randomly into three groups, the group NS received 10mL normal saline over 10 mins before creating pneumoperitoneum. The group C received 1mcg/kg Clonidine diluted to 10mL with normal saline over 10 mins before pneumoperitoneum. Group M received 50mg/kg Magnesium sulphate diluted to 10mL with normal saline over 10 mins before creating pneumoperitoneum. SBP, DBP, Mean arterial pressure, and heart rate were recorded before induction (baseline values), at the end of Magnesium sulphate/Clonidine/saline administration and before pneumoperitoneum (P0), 5min (P5), 10 min (P10), 20 min (P20), 30 min (P30) and 40 min(P40) after pneumoperitoneum. CO₂ pneumoperitoneum was maintained to a pressure of 14mmHg by an automatic insufflations unit throughout the surgery. The surgical technique used was identical in the 3 groups. During surgery, Ringer's lactate/ normal saline was administered in accordance with fasting volumes, maintenance volumes and blood losses. Anaesthesia was maintained by nitrous oxide and oxygen (50% +50%). Dose adjustment of fentanyl was based on standard clinical signs and haemodynamic measurements. Signs of inadequate analgesia, defined as an increase of heart rate and MAP of more than 20% of baseline, were managed by a bolus dose of fentanyl 0.5 mcg/kg. Muscle relaxation was achieved by intermittent bolus doses of vecuronium bromide 0.02mg/kg. The patients were mechanically ventilated to keep EtCO₂ between 35 and 40 mm Hg. Normothermia was maintained during the surgery. All patients were operated in a head up tilt of 15°. At the end of the surgical procedure, residual neuromuscular block was reversed by an appropriate dose of neostigmine and glycopyrrolate. Tracheal extubation was performed and the following times were noted down: (i) time to tracheal extubation, (ii) time to response to verbal commands Heart rate, MAP, SpO₂, EtCO₂ were also recorded throughout the surgical procedure at an interval of 10 minutes. The patients were observed for any adverse events or side effects during the postoperative period.

Statistical Methods Employed

Statistical Analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented as Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

Results

Table 1: Age distribution of patients studied

Age in years	Clonidine (group C)		Magnesium Sulphate (Group M)		Normal saline (Group NS)	
	No	%	No	%	No	%
18-20	4	13.3	2	6.7	2	6.7
21-30	3	10.0	6	20.0	6	20.0
31-40	5	16.7	8	26.7	8	26.7
41-50	7	23.3	5	16.7	6	20.0
51-60	11	36.7	9	30.0	8	26.7
Total	30	100.0	30	100.0	30	100.0
Mean ± SD	42.83±13.87		41.20±13.30		40.93±12.89	

Samples are age matched with P=0.837

Table 1 shows age distribution of the patients in the three groups. The mean age in group C, M, & NS were 42.83±13.87, 41.20±13.30 &

40.93±12.89 respectively. There was no significant difference in the age of patients between the three groups. All groups were similar with

respect to age distribution (p>0.05).

Table 2: Gender distribution of patients studied

Gender	Clonidine		Magnesium sulphate		Normal saline	
	No	%	No	%	No	%
Male	14	46.7	18	60.0	17	56.7
Female	16	53.3	12	40.0	13	43.3
Total	30	100.0	30	100.0	30	100.0

Table 3: Comparison of Weight (kg) in three groups studied

Weight (kg)	Clonidine		Magnesium sulphate		Normal saline	
	No	%	No	%	No	%
41-50	4	13.3	4	13.3	1	3.3
51-60	14	46.7	5	16.7	12	40.0
61-70	9	30.0	11	36.7	10	33.3
71-80	3	10.0	9	30.0	6	20.0
>80	0	0.0	1	3.3	1	3.3
Total	30	100.0	30	100.0	30	100.0
Mean ±SD	60.33±8.38		66.00±10.66		64.27±9.86	

Samples are weight matched with P=0.100

Table 3 shows the body weight distribution of the patients. The mean body weight in group C, M, NS, were 60.33±8.38, 66.0±10.66 and 64.27±9.86 respectively. There was no significant difference in the body weight of patients between the group C, M and NS (p>0.05).

Table 4: Comparison of ASA Grade in three groups studied

ASA Grade	Clonidine		Magnesium sulphate		Normal saline	
	No	%	No	%	No	%
Grade I	17	56.7	17	56.7	16	53.3
Grade II	13	43.3	13	43.3	14	46.7
Total	30	100.0	30	100.0	30	100.0

ASA grade is statistically similar in two groups with P=0.908

Table 4 shows ASA grade distribution of patients. There was no significant difference in the ASA status of patients between the group C, M, and NS group(p>0.05)

Table 5: Comparison of duration of surgery in three groups studied

Duration of surgery	Clonidine		Magnesium sulphate		Normal saline	
	No	%	No	%	No	%
<1	0	0.0	1	3.3	1	3.3
1-2	28	93.3	26	86.7	27	90.0
>2	2	6.7	3	10.0	2	6.7
Total	30	100.0	30	100.0	30	100.0
Mean ± SD	1.43±0.39		1.48±0.45		1.40±0.41	

Duration of surgery is statistically similar in three groups with P=0.752

Table 5 shows the duration of surgery in hours in each group. There was no significant difference in the duration of surgery between the group C, M and NS. (p>0.05).

Table 6: Comparison of Extubation time in three groups studied

Extubation of time	Clonidine		Magnesium sulphate		Normal saline	
	No	%	No	%	No	%
<5	3	10.0	0	0.0	3	10.0
5-10	27	90.0	26	86.7	27	90.0
>10	0	0.0	4	13.3	0	0.0
Total	30	100.0	30	100.0	30	100.0
Mean ± SD	5.87±0.95		8.12±1.59		5.78±0.99	

P=<0.001**

Clonidine – Magnesium Sulphate P:<0.001

Clonidine- Normal saline P=0.956 Magnesium sulphate – Normal Saline: P<0.001

In clonidine group the mean extubation time is 5.87±0.95 minutes, Magnesium sulphate group 8.12±1.59 minutes and

Normal saline group 5.78±0.99 minutes. Statistical evaluation between the groups showed statistically significant

longer extubation times in magnesium sulphate group compared to clonidine or normal saline group. There was no significant

difference in extubation times between clonidine and normal saline group.

Table 7: Comparison of Time to response to verbal commands in three groups studied

Time to respond	Clonidine		Magnesium sulphate		Normal saline	
	No	%	No	%	No	%
<5	0	0.0	0	0.0	0	0.0
5-10	30	100.0	24	80.0	30	100.0
>10	0	0.0	6	20.0	0	0.0
Total	30	100.0	30	100.0	30	100.0
Mean ± SD	7.15±1.05		8.97±1.69		7.07±1.00	

P=<0.001**

Clonidine – Magnesium Sulphate P:<0.001

Clonidine- Normal saline P=0.968 Magnesium sulphate – Normal Saline: P<0.001

In clonidine group the mean Time to respond to verbal commands is 5.87±0.95 minutes, Magnesium sulphate group 8.12±1.59 minutes and Normal saline group 5.78±0.99 minutes. Statistical evaluation between the groups showed statistically

significant longer times in magnesium sulphate group compared to clonidine or normal saline group. There was no significant difference in time to respond between clonidine and normal saline group.

Table 8: Inter group comparison of Heart rate (bpm) in three groups studied

Heart rate (bpm)	Clonidine	Magnesium sulphate	Normal saline	Pair wise Significance		
				Clonidine - MgSo4	Clonidine- NS	MgSo4 - Normal saline
Baseline	87.23±14.75	76.13±9.98	82.7±11.24	0.002*	0.323	0.098+
After admin	86.23±16.12	67.80±8.32	86.43±11.91	<0.001*	0.998	<0.001*
Before Pneumo	83.33±14.07	67.83±8.24	88.23±13.34	<0.001*	0.269	<0.001*
5 min	87.10±15.36	68.67±10.42	108.13±21.62	<0.001*	<0.001*	<0.001*
10 min	91.40±17.23	69.50±9.93	112.43±23.29	<0.001*	<0.001*	<0.001*
20 min	87.23±15.02	68.33±7.99	104.63±19.64	<0.001*	<0.001*	<0.001*
30 min	84.80±12.02	67.73±7.53	100.63±16.67	<0.001*	<0.001*	<0.001*
40 min	83.27±11.93	68.67±7.79	92.47±12.47	<0.001*	0.005	<0.001*

Baseline heart rates were similar in all groups. However Heart rates were significantly higher in the control group than magnesium sulphate group at all time points. Between Clonidine and control group, heart rates were significantly higher in control group except at

P40, post pneumoperitoneum. Between magnesium sulphate and clonidine group heart rates were significantly lower in Magnesium sulphate group at all time points.

Table 9: Within group Comparison of Heart rate in three groups studied

Heart rate	Clonidine		Magnesium sulphate		Normal saline	
	Difference	P value	Difference	P value	Difference	P value
Baseline	-	-	-	-	-	-
After administration	1.00	0.551	8.33	<0.001**	-3.73	0.015*
Before Pneumo	3.90	0.005**	8.30	<0.001**	-5.53	0.008**
5 min	0.13	0.936	7.47	0.001**	-25.43	<0.001**
10 min	-4.17	0.094+	6.63	0.001**	-29.73	<0.001**
20 min	0.00	1.000	7.80	<0.001**	-21.93	<0.001**
30 min	2.43	0.115	8.40	<0.001**	-17.93	<0.001**
40 min	3.97	0.030*	7.47	<0.001**	-9.77	0.002**

There was no statistically significant increase in heart rate in clonidine group from the baseline value. In magnesium sulphate group there was significant fall in heart rate compared to

baseline at all time points. In Control group there was statistically significant increase in heart rates at all time points from the baseline value.

Table 10: Comparison of SBP (mm Hg) in three groups studied

SBP (mm Hg)	Clonidine	Magnesium sulphate	Normal saline	Pair wise Significance		
				Clonidine -MgSo4	Clonidine - NS	MgSo4 – NS
Baseline	131.27±17.05	141.83±20.58	130.40±13.31	0.051+	0.979	0.032*
After admin	123.00±16.35	116.77±19.55	128.97±14.10	0.327	0.359	0.017*
Before Pneumo	120.53±10.31	117.10±15.97	125.80±10.64	0.543	0.242	0.024*

5 min	126.17±10.59	117.60±15.43	142.60±8.94	0.019*	<0.001*	<0.001*
10 min	129.17±13.00	120.47±19.82	151.43±13.62	0.089	<0.001*	<0.001*
20 min	124.60±12.56	121.93±14.77	143.37±14.60	0.742	<0.001*	<0.001*
30 min	122.90±11.40	117.03±13.89	137.03±11.28	0.158	<0.001*	<0.001*
40 min	120.47±10.53	116.60±11.83	130.57±13.56	0.431	0.005*	<0.001*

There is no significant difference between the baseline SBP between all three groups. Among clonidine and control group, SBP showed significant higher values in control group at all time points post pneumo peritoneum. No significant difference between clonidine and

magnesium sulphate at any time point. Between magnesium sulphate and control group SBP was significantly higher in control group at all time points post pneumo peritoneum.

Table 11: Within group Comparison of SBP (mm Hg) in three groups studied

SBP (mm Hg)	Clonidine		Magnesium sulphate		Normal saline	
	Difference	P value	Difference	P value	Difference	P value
Baseline	-	-	-	-	-	-
After administration	8.27	0.002**	25.07	0.000**	1.43	0.479
Before Pneumo	10.73	0.002**	24.73	0.000**	4.60	0.026*
5 min	5.10	0.147	24.23	0.000**	-12.20	0.000**
10 min	2.10	0.585	21.37	0.000**	-21.03	0.000**
20 min	6.67	0.087+	19.90	0.000**	-12.97	0.000**
30 min	8.37	0.024*	24.80	0.000**	-6.63	0.008**
40 min	10.80	0.004**	25.23	0.000**	-0.17	0.948

There was no statistically significant decrease in SBP in clonidine group from the baseline value except at P30 & P40. In magnesium sulphate group there was significant fall in SBP compared to baseline

at all time points. In Control group there was statistically significant increase in SBP at all time points from the baseline value except at P40.

Table 12: Comparison of DBP (mm Hg) in three groups studied

DBP (mmHg)	Clonidine	Magnesium sulphate	Normal saline	Pair wise Significance		
				clonidine-MgSo4	clonidine- NS	MgSo4 -NS
Baseline	81.23±12.88	83.37±14.32	79.90±10.73	0.793	0.913	0.545
After admin	77.30±13.52	69.27±13.81	80.90±10.85	0.045*	0.523	0.002*
Before Pneumo	74.60±10.29	71.10±11.95	78.40±10.07	0.425	0.365	0.028*
5 min	80.63±11.22	73.97±11.91	93.70±6.59	0.034*	<0.001*	<0.001*
10 min	80.80±8.56	73.57±13.12	97.13±8.44	0.021*	<0.001*	<0.001*
20 min	80.00±7.97	73.57±12.09	90.53±11.19	0.053+	0.001*	<0.001*
30 min	77.90±9.01	69.33±11.31	85.03±9.26	0.003*	0.018*	<0.001*
40 min	76.63±8.21	69.23±11.10	81.53±7.12	0.005*	0.093+	<0.001*

There is no significant difference between the baseline DBP between all three groups. Among clonidine and control group, DBP showed significant higher values in control group at all time points except P30 & P40 post pneumo peritoneum. No significant difference between

clonidine and magnesium sulphate at any time point. Between magnesium sulphate and control group DBP were significantly higher in control group at all time points post pneumo peritoneum.

Table 13: Within group Comparison of DBP (mm Hg) in three groups studied

DBP (mm Hg)	Clonidine		Magnesium sulphate		Normal saline	
	Difference	P value	Difference	P value	Difference	P value
Baseline	-	-	-	-	-	-
After administration	3.93	0.055+	14.10	0.000**	-1.00	0.523
Before Pneumo	6.63	0.006**	12.27	0.000**	1.50	0.406
5 min	0.60	0.827	9.40	0.001**	-13.80	0.000**
10 min	0.43	0.884	9.80	0.004**	-17.23	0.000**
20 min	1.23	0.649	9.80	0.001**	-10.63	0.000**
30 min	3.33	0.204	14.03	0.000**	-5.13	0.014*
40 min	4.60	0.052+	14.13	0.000**	-1.63	0.356

There was no statistically significant decrease in DBP in clonidine group from the baseline value. In magnesium sulphate group there was significant fall in DBP compared to baseline at all time points. In

Control group there was statistically significant increase in DBP at all time points from the baseline value except at P30 & P40 post pneumo peritoneum.

Table 14: Comparison of MAP (mm Hg) in three groups studied

MAP (mm Hg)	Clonidine	Magnesium sulphate	Normal saline	Pair wise Significance		
				Clonidine - MgSo4	Clonidine - NS	MgSo4 - NS
Baseline	96.00±14.75	102.23±18.05	95.90±11.41	0.246	1.000	0.236
After admin	91.53±13.71	84.20±15.56	96.03±11.92	0.105	0.420	0.004*
Before Pneumo	89.00±9.73	85.53±13.06	93.13±9.59	0.439	0.312	0.023*
5 min	95.23±10.20	88.60±12.30	109.33±7.38	0.035*	<0.001*	<0.001*
10 min	95.77±9.49	88.57±14.69	114.47±9.98	0.048*	<0.001*	<0.001*
20 min	93.80±9.23	89.03±11.12	106.93±11.75	0.205	<0.001*	<0.001*
30 min	91.97±8.93	85.27±11.22	101.60±9.27	0.027*	0.001*	<0.001*
40 min	90.17±8.30	84.27±9.65	97.77±11.25	0.057+	0.010*	<0.001*

There is no significant difference between the baseline MAP between all three groups. Among clonidine and control group MAP showed significant higher values in control group at all time points. No significant difference between clonidine and magnesium sulphate at

any time point. Between magnesium sulphate and control group MAP were significantly higher in control group at all time points post pneumo peritoneum.

Table 15: Within group Comparison of MAP (mm Hg) in three groups studied

MAP (mm Hg)	Clonidine		Magnesium sulphate		Normal saline	
	Difference	P value	Difference	P value	Difference	P value
Baseline	-	-	-	-	-	-
After admin	4.47	0.087+	18.03	0.000*	-0.13	0.938
Before Pneumo	7.00	0.018*	16.70	0.000*	2.77	0.113
5 min	0.77	0.817	13.63	0.000*	-13.43	0.000*
10 min	0.23	0.946	13.67	0.001*	-18.57	0.000*
20 min	2.20	0.495	13.20	0.000*	-11.03	0.000*
30 min	4.03	0.179	16.97	0.000*	-5.70	0.007*
40 min	5.83	0.061+	17.97	0.000*	-1.87	0.360

There was no statistically significant decrease in MAP in clonidine group from the baseline value. In magnesium sulphate group there was significant fall in MAP compared to baseline at all time points. In

Control group there was statistically significant increase in MAP at all time points from the baseline value except at P40 post pneumoperitoneum.

Table 16: Comparison of RPP in three groups studied

RPP	Clonidine	Magnesium sulphate	Normal saline	Pair wise Significance		
				Clonidine - MgSo4	Clonidine - NS	MgSo4 -NS
Baseline	15228.13±20623	10646.50±1885	10874.30±2280	0.308	0.344	0.997
After admin	10712.80±2855	7897.43±1522	11195.00±2390	<0.001*	0.702	<0.001*
Before Pneumo	10075.60±2025	7961.20±1564	11098.30±1932	<0.001*	0.088+	<0.001*
5 min	11070.70±2531	8140.33±1869	15476.07±3427	<0.001*	<0.001*	<0.001*
10 min	11936.07±3054	8388.10±1907	17219.03±4469	<0.001*	<0.001*	<0.001*
20 min	10928.87±2434	8241.60±1505	15149.63±3726	0.001*	<0.001*	<0.001*
30 min	10470.90±2048	7964.70±1505	13813.30±2708	<0.001*	<0.001*	<0.001*
40 min	10167.53±1855	8015.57±1519	12093.20±2173	<0.001*	<0.001*	<0.001*

There is no significant difference between the baseline RPP between all three groups. Among clonidine and control group RPP showed significant higher values in control group at all time points. Between magnesium sulphate and control group RPP were significantly higher

in control group at all time points post pneumo peritoneum. Among clonidine & magnesium sulphate group RPP were significantly lower in magnesium sulphate group.

Table 17: Within group Comparison of RPP in three groups studied

RPP	Clonidine		Magnesium sulphate		Normal saline	
	Difference	P value	Difference	P value	Difference	P value
Baseline	-	-	-	-	-	-
After admin	4515.33	0.228	2749.07	0.000**	-320.70	0.296
Before Pneumo	5152.53	0.167	2685.30	0.000**	-224.00	0.538
5 min	4157.43	0.267	2506.17	0.000**	-4601.77	0.000**

10 min	3292.07	0.374	2258.40	0.000**	-6344.73	0.000**
20 min	4299.27	0.249	2404.90	0.000**	-4275.33	0.000**
30 min	4757.23	0.209	2681.80	0.000**	-2939.00	0.000**
40 min	5060.60	0.184	2630.93	0.000**	-1218.90	0.035*

There was no statistically significant decrease in RPP in clonidine group from the baseline value. In magnesium sulphate group there was significant fall in RPP compared to baseline at all time points. In Control group there was statistically significant increase in RPP at all time points from the baseline value post pneumoperitoneum.

Discussion

Cardiovascular changes in pneumoperitoneum include increase in MAP with no significant change in heart rate. Studies to investigate the role of magnesium sulphate and clonidine in laparoscopic surgeries individually have been conducted earlier. This randomized, placebo controlled study is done to compare the role of magnesium sulphate and clonidine in attenuating stress response to pneumoperitoneum.

Magnesium sulphate blocks release of catecholamines from both adrenergic nerve terminals and adrenal gland. Intravenous magnesium sulphate inhibits catecholamine release associated with tracheal intubation. Magnesium also produces vasodilation by acting directly on blood vessels and in high doses, attenuates vasopressin mediated vasoconstriction. [4]

Clonidine, a selective alpha-2 adrenergic agonist, causes a fall in the heart rate and blood pressure along with decreased SVR and cardiac output. [4]

Jee et al [5], administered magnesium sulphate 50mg/kg over 2-3 min, before pneumoperitoneum in patients undergoing laparoscopic cholecystectomy and found that it effectively attenuated the effects of pneumoperitoneum without any episode of severe hypotension or bradycardia. Same dose of magnesium sulphate was used in this study to compare it with clonidine.

Altan and Turgut et al, [6] used clonidine 3 µg/kg intravenously over a period of 15 minutes before induction and 2 µg/kg/hour by continuous infusion intraoperatively. They observed significant incidences of bradycardia and hypotension in their study. In our study we used clonidine in the dose of 1mcg/kg intravenously over 10 minutes. No infusion was given. No episodes of significant bradycardia or hypotension were noted.

Clonidine has anti-hypertensive properties and augments the effects of anaesthesia, hence it is considered to be an ideal agent to contain the stress response to pneumoperitoneum. Shivinder singh et al,³⁰ in their study concluded that oral clonidine was better in terms of maintaining stable haemodynamics, having an isoflurane sparing effect and having a prolonged time interval to the first request of analgesia postoperatively compared to the control group. Administration of oral clonidine 150 µg as a pre-medicant in patients undergoing laparoscopic cholecystectomy resulted in improved perioperative haemodynamic stability and a reduction in the intra-operative anaesthetic and post-operative analgesic requirements.

In our study, with intravenous clonidine in the dose of 1mcg/kg administered 10 minutes before pneumoperitoneum, hemodynamic parameters like SBP, DBP, MAP were significantly lower than the control group at all time points post pneumoperitoneum and there was no statistically significant increase in these parameters from the baseline value. These effects were comparable with the magnesium sulphate group which received 50mg/kg of the drug before pneumoperitoneum. However HR and RPP was significantly higher in the clonidine group compared to the magnesium sulphate group. Kalra et al [4] in their study compared two doses of clonidine (1mcg/kg and 1.5 mcg/kg) with magnesium 50 mg/kg. No significant

difference in SBP at any time interval between clonidine 1 mcg/kg and magnesium sulphate 50 mg/kg was observed. However SBP was significantly lower in clonidine 1.5 mcg/kg group. Hence they concluded that although magnesium sulphate 50 mg/kg produces hemodynamic stability comparable to clonidine 1 mcg/kg and clonidine in doses of 1.5 mcg/kg blunted hemodynamic response more effectively.

MgSO₄ has been reported to produce general anaesthesia and enhance the activity of local anaesthetic agents. Depressant effects of MgSO₄ on the central nervous system (CNS) of animals has been reported too. Magnesium antagonised NMDA receptors in the CNS. Another mechanism could involve the reduction of catecholamine release through sympathetic stimulation, by which magnesium might decrease peripheral nociceptor sensitisation or stress response to surgery [7,8].

Our study revealed statistically significant attenuation of hemodynamic response post pneumoperitoneum with 50mg/kg of magnesium sulphate when compared to the control group. However the efficacy was comparable to that of clonidine 1 mcg/kg. Intragroup comparison showed a significant decrease in HR, SBP, DBP, MAP, and RPP (P< 0.001) from the baseline value in magnesium sulphate group. HR and RPP was significantly lower in magnesium sulphate group as compared to the clonidine and normal saline at all time points. However the extubation time and time to response for verbal commands were significantly higher in the magnesium sulphate group when compared to both clonidine and control group (p<0.001). Studies conducted by Altun et al [6] also showed delayed recovery with magnesium sulphate. Similar effects of magnesium were observed in the study conducted by Nanda kishore kalra et al [4] and Manjushree ray et al. [9]

D. H.Lee et al [10] in their study investigated the effect of i.v. magnesium sulphate on anaesthetic depth and analgesic efficacy during caesarean section under general anaesthesia. Magnesium sulphate in the dose of 30 mg/kg bolus & 10 mg/kg/hr continuous infusion or 45 mg/kg bolus & 15 mg/kg/hr continuous infusion was administered after induction. Bispectral index (BIS) value, mean arterial pressure (MAP), and midazolam, fentanyl, and atracurium consumptions were recorded. They concluded that preoperative i.v. magnesium sulphate attenuated BIS and arterial pressure increases during the pre-delivery period and hence can be recommended as an adjuvant during general anaesthesia.

Altun A et al [28] in their study assessed the effects of magnesium sulphate and clonidine on preoperative hemodynamics, propofol consumption and post operative recovery in sixty ASA I-II patients undergoing spinal surgery. Group M received magnesium sulphate 30 mg/kg as a bolus before induction and 10 mg/kg/hr by infusion. Group CL received clonidine 3 mcg/kg as a bolus before induction and 2 mcg/kg/hr by infusion during the surgery. Control group received similar volume of normal saline. They observed no statistical difference in heart rate and blood pressure between the groups but propofol requirements for induction and maintenance of anaesthesia were significantly lower with magnesium and clonidine (P<0.001). They concluded that clonidine and magnesium sulphate can be used as adjuvant agents.

To conclude, administration of magnesium sulphate or clonidine before commencement of pneumoperitoneum effectively attenuates hemodynamic response to pneumoperitoneum, although the effects are comparable. Besides magnesium caused a delay in recovery

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Conclusion

From the present study it can be concluded that, intravenous clonidine and magnesium both effectively attenuates hemodynamic responses to pneumoperitoneum. In addition, magnesium sulphate was found to prolong the extubation time and time to response to verbal commands. We conclude that, clonidine and magnesium sulphate both can be recommended to decrease the hemodynamic response during induction and maintenance of pneumoperitoneum.

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