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ORIGINAL RESEARCH

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

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ABSTRACT

Background: Hemodynamic response is considerable after laparoscopic procedures. Both magnesium and clonidine are known to reduce the hemodynamic response to pneumoperitoneum and block catecholamine and vasopressin production. The goal of this randomised, placebo-controlled trial is to determine which medication reduces the hemodynamic stress response to pneumoperitoneum the most effectively.

Martial and Methods: Randomization was used to divide the 60 patients undergoing elective laparoscopic cholecystectomy into 3 groups of 20 each. Ten minutes before the development of pneumoperitoneum, the research medications were intravenously administered. Group M received 50mg/kg magnesium sulphate in 10 ml of normal saline, while group NS received 10 ml of normal saline. Group C received 1mcg/kg of clonidine in 10 ml of normal saline. Before induction (baseline value), after the study drug was administered, 5 minutes after the formation of the pneumoperitoneum, and then every 10 minutes after that.

Results: Following pneumoperitoneum, the control group experienced a statistically significant increase in the mean heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and rate pressure product (NS). Both the magnesium (M) and clonidine (C) groups significantly reduced the hemodynamic response to pneumoperitoneum. However, the magnesium sulphate group experienced significantly longer extubation times and times to respond to spoken orders. None of the groups experienced any additional negative effects.

Conclusion: With equivalent effectiveness, magnesium sulphate or clonidine administration reduces the hemodynamic response to pneumoperitoneum.

Keywords: Hemodynamic response; laparoscopic cholecystectomy; clonidine; magnesium sulphate.

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INTRODUCTION

Patients can reap significant benefits from laparoscopic methods, including a smaller incision size, reduced postoperative discomfort, early ambulation, and a lower risk of postoperative wound infections.[1] All of these characteristics contribute to a shorter length of stay in the hospital as well as reduced morbidity during the perioperative period.[2-4] Despite this, laparoscopic surgery is not without its inherent dangers. Anesthesia risks are raised due to

complications caused by the physiological changes that occur during the development of pneumoperitoneum, as well as complications that are unique to each distinct laparoscopic method.[5-7] As a consequence of this, anaesthetic procedures for laparoscopic surgery need to be perfected in order to account for the variations between open surgery and laparoscopic surgery.[8] The extent of the cardiovascular changes that occur as a result of creating pneumoperitoneum is dependent on the intra-abdominal pressure that is reached, the volume of CO2 that is absorbed, the patient's intravascular volume, the ventilator strategy, the surgical conditions, and the anaesthetic agents that are utilised. The effects on hemodynamics include a rise in mean arterial pressure, a decrease in cardiac output, and an increase in the resistance of the systemic vascular system.[9-11]

These adjustments are better tolerated in patients with an ASA grade of I or II, but they have the potential to be harmful in patients who are elderly or have an ASA grade of III. These alterations in hemodynamic state are caused by a combination of mechanical and neurohumoral causes.[12,13] Catecholamines, prostaglandins, renin, and vasopressin are some of the potential mediators that have been suggested.[14] It has been attempted to lessen the hemodynamic abnormalities that are found with pneumoperitoneum by changing the nature of the insufflating gas, using low intra-abdominal pressure, and using procedures that raise the abdominal wall; however, all of these approaches have practical limitations.[15,16] Epidural, segmental spinal, mixed epidural and general anaesthesia, and the use of various pharmacologic therapies such as nitroglycerine and esmolol have all been utilised, with variable degrees of success and the same or similar limits in terms of their practical application.[17] Clonidine is a selective alpha-2 adrenergic agonist, and as a result, it induces a decrease in both the heart rate and blood pressure, in addition to a reduction in the systemic vascular resistance and cardiac output. Both the adrenergic nerve terminals and the adrenal gland can have their production of catecholamines inhibited by magnesium.[18-21] Magnesium also causes vasodilation by acting directly on blood vessels, and at high dosages, it reduces the constriction caused by the hormone vasopressin. This study was conducted to assess the effects of intravenous administration of magnesium sulphate and clonidine on intraoperative hemodynamics during laparoscopic cholecystectomy. Laparoscopic cholecystectomy is a surgical procedure that removes the gallbladder.[22-25]

OBJECTIVES

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.

MATERIALS & METHODS

Between June 2021 and November 2022, researchers from SVS Medical College, Mahaboobnagar. Telangana, India, worked on a project with the working title "A comparative study of intravenously administered clonidine and magnesium sulphate on hemodynamic responses during laparoscopic cholecystectomy." After receiving approval from the relevant ethical committee and ensuring that every patient provided their informed consent, this study was carried out. The study comprised a total of sixty patients who were scheduled to undergo elective laparoscopic cholecystectomy and who belonged to ASA I or ASA II.

Inclusion Criteria

1) Age 18 – 60 years

2) American Society of Anesthesiologists (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 who required an open cholecystectomy because the laparoscopic procedure could not be performed successfully were not included in the study. Patients, who had an extreme hypertensive response during surgery, as measured by a systolic blood pressure that was greater than 180 mm Hg or a diastolic blood pressure that was greater than 110 mm Hg, were not included in the study. Patients were assigned to one of three groups in a random manner using sealed envelopes that were selected by the patients themselves, and the randomization took place right before the pneumoperitoneum procedure.

The three groups were

Group C- Clonidine group (n=20)-received injection clonidine 1mcg/kg diluted in 10mL normal saline over 10 minutes, prior to pneumoperitoneum.

Group M- Magnesium sulphate group(n=20)-received injection magnesium sulphate 50mg/kg diluted in 10mL normal saline over 10 minutes, prior to pneumoperitoneum.

Group NS – control group (n=20)- received 10mL normal saline intravenously over 10 minutes, prior to pneumoperitoneum.

Patients were given an oral tablet of ranitidine 150 mg and an oral tablet of ondansetron 8 mg at bedtime on the night before their surgery. On the day of their operation, they were also given an intramuscular injection of glycopyrrolate 0.2 mg half an hour before being moved to the operating room. As soon as the patient was brought into the operating room, monitors were hooked up (heart rate, NIBP, SpO2, ECG, temperature), and baseline measurements of key parameters such as HR, SBP, DBP, MAP, and SpO2 were taken. Following a preoxygenation period of three minutes, patients received intravenous fentanyl citrate at a dose of 1 mcg/kg. Injections of propofol at a dose of 2 mg/kg were used to induce them. Intubation through the endotracheal tube was made easier with the help of the muscle relaxant vecuronium bromide administered at 0.1 mg/kg. An epidural catheter was inserted at the L3−L4 intervertebral space.

Statistical Methods Employed

Sample size

20 people in each group were recruited, calculated using the nMaster software, based on the information provided in the article Effects of Magnesium sulphate and Clonidine on Propofol Consumption, Hemodynamics, and Postoperative Recovery.

Statistical Analysis

In the current study, descriptive and inferential statistical analysis was completed. Results for categorical measures are shown as Number (%) while results for continuous measurements are presented as Mean SD (Min-Max). The 5% level of significance is used to determine significance. The following data-related assumptions are made: Dependent variables must have a normal distribution. Samples selected at random from the population must have independent cases, and 3.

ANOVA has been used to determine the significance of study parameters comparing three or more patient groups, The significance of study parameters on a continuous scale within each group has been determined using the Post-hoc Tukey test and the Student t test (two tailed,

dependent). Fisher / Chi-square The significance of study parameters on a categorical scale between two or more groups has been determined using an exact test.

RESULTS

The age distribution of the patients in each of the three groups is depicted in [Figure 1]. The mean ages of those in group C were 42.83+13.87, those in group M were 41.20+13.30, and those in group NS were 40.93+12.89. There was not a discernible gap in age between the three groups of patients in any way, shape, or form. There was no significant difference in the age distribution across any of the groups ($p > 0.05$).

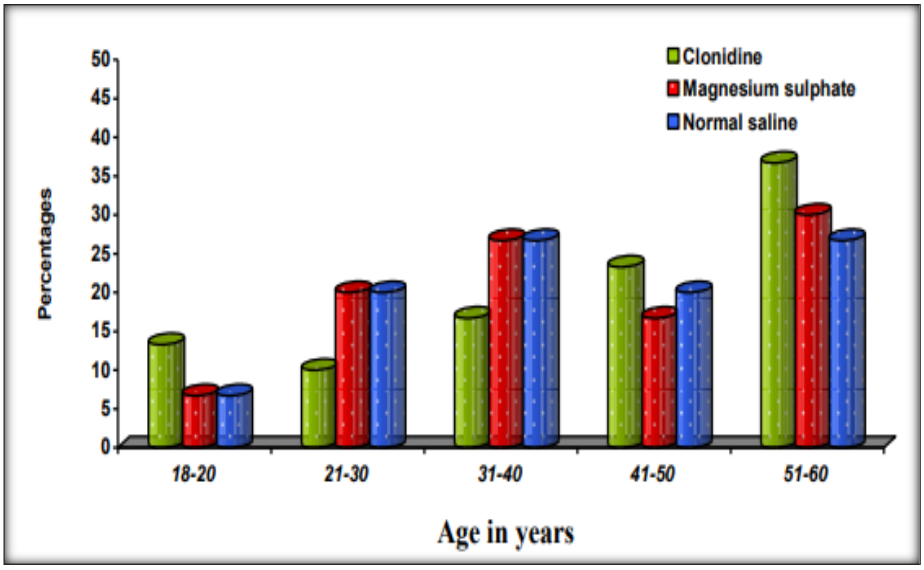

Figure 1: Bar diagram showing distribution of age in the three groups

Table 1:Gender distribution of patients studied

	Clonidine		Magnesium sulphate		Normal saline	
Gender	**No**	**%**	**No**	**%**	**No**	**%**
Male	9	46.7	12	60.0	11	53.3
Female	11	53.3	8	40.0	9	46.7
Total	20	100.0	20	100.0	20	100.0

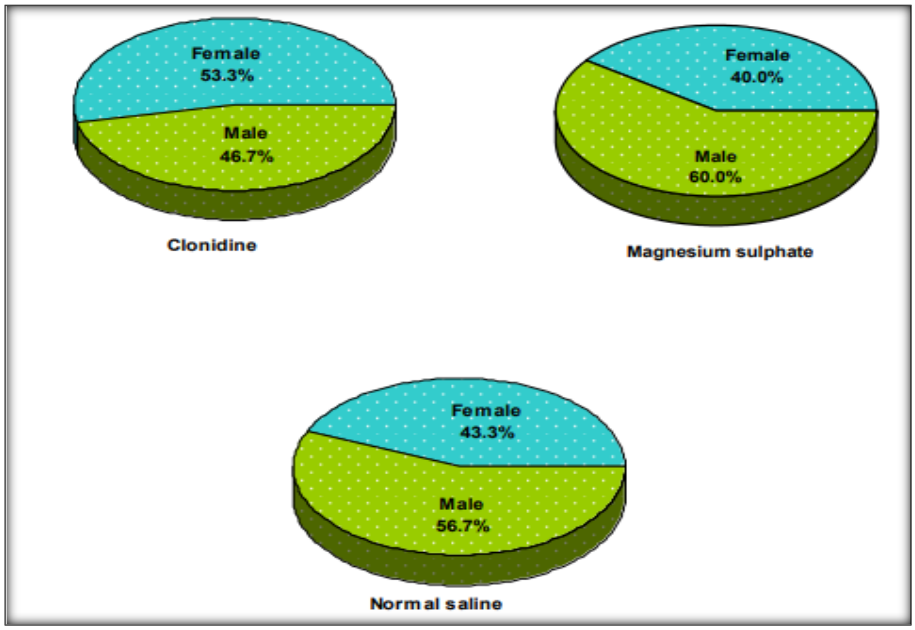

Figure 2: Pie diagram showing gender distribution in the three groups

Table 2: Comparison of Weight (kg) in three groups studied

Weight (kg)	Clonidine		Magnesium sulphate		Normal saline	
	No	%	No	%	No	%
41-50	03	13.3	2	13.3	1	3.3
51-60	07	46.7	4	16.7	7	40.0
61-70	07	30.0	7	36.7	6	33.3
71-80	03	10.0	6	30.0	5	20.0
>80	0	0.0	1	3.3	1	3.3
Total	20	100.0	20	100.0	20	100.0
Mean ±SD	60.33±8.38		66.00±10.66		64.27±9.86	

Samples are weight matched with P=0.100

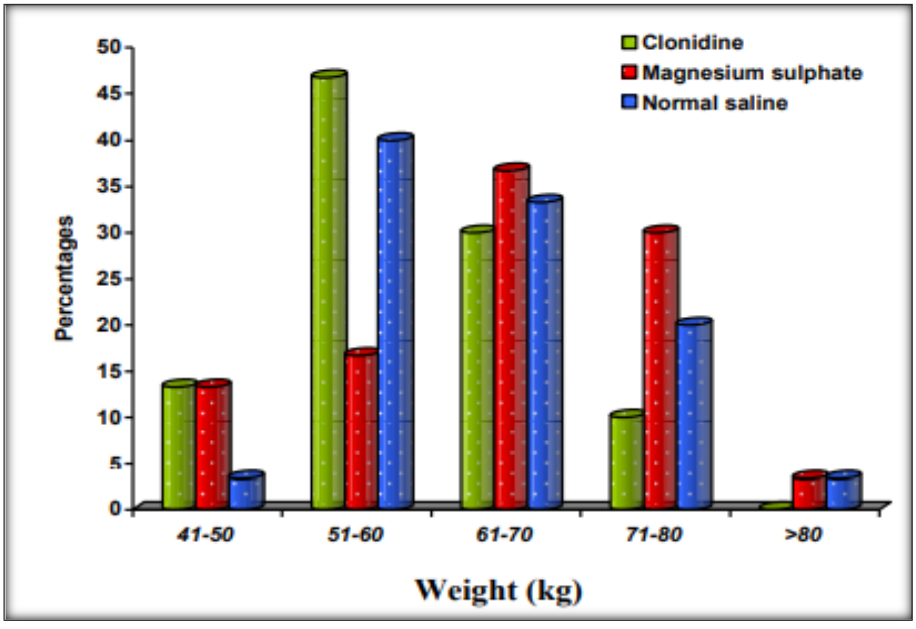

Figure 3: Bar diagram showing weight distribution in the three groups

[Table 2] shows the body weight distribution of the patients. The mean body weight in group C, M, NS, was 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 3: Comparison of ASA Grade in three groups studied

ASA Grade	Clonidine		Magnesium sulphate		Normal saline	
	No	%	No	%	No	%
Grade I	13	56.7	13	56.7	12	53.3
Grade II	07	43.3	07	43.3	08	46.7
Total	20	100.0	20	100.0	20	100.0

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

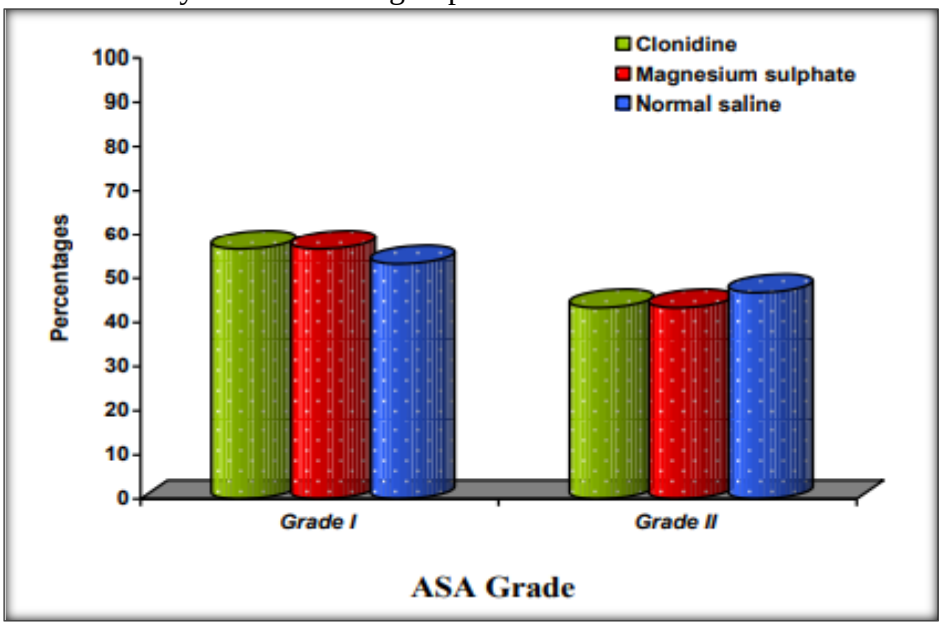

Figure 4: Bar diagram showing ASA status distribution in the three groups

[Table 3] 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 ($p>0.05$).

DISCUSSION

Pneumoperitoneum causes cardiovascular alterations that include an increase in MAP despite an absence of a significant change in heart rate. There have been previous investigations that have been carried out that have focused solely on the function of clonidine and magnesium sulphate in relation to laparoscopic procedures. The purpose of this randomised, placebo-controlled trial is to investigate the relative effectiveness of magnesium sulphate and clonidine in reducing the stress response induced by pneumoperitoneum. Magnesium sulphate is capable of inhibiting the release of catecholamines from adrenergic nerve terminals as well as the adrenal gland. The release of catecholamines that is linked with tracheal intubation can be inhibited by giving magnesium sulphate intravenously.[26-29] Magnesium also causes vasodilation by acting directly on blood vessels, and, at high doses, it reduces the constriction caused by vasopressin. Patients undergoing laparoscopic cholecystectomy were given magnesium sulphate at a dose of 50 milligrammes per kilogramme (mg/kg) over the course of two to three minutes before pneumoperitoneum. The researchers found that this effectively attenuated the effects of pneumoperitoneum without causing any episode of severe hypotension or bradycardia.[30-32]

Clonidine was administered intravenously at a rate of 3 micrograms per kg of the patient for duration of 15 minutes prior to induction, and then it was given intraoperatively at a rate of 2 micrograms per kilogramme per hour by a continuous infusion. During the course of their research, they came across numerous instances of bradycardia with hypotension. In the course of our research, we administered clonidine intravenously at a dose of 1 mcg/kg for a period of ten minutes.[33,34] There was no infusion that was delivered. There were no notable occurrences of bradycardia or hypotension that were observed. Because clonidine lowers blood pressure and boosts the effects of anaesthesia, it is often regarded as an excellent candidate for the role of an agent that can control the stress response induced by pneumoperitoneum. In their study, Shivinder Singh and colleagues came to the conclusion that oral clonidine was superior to the control group in terms of maintaining stable haemodynamics, having an isoflurane sparing effect, and having an extended time gap to the first request of analgesia postoperatively. In patients having laparoscopic cholecystectomy, the administration of oral clonidine 150 micrograms as a pre-medicant resulted in enhanced perioperative haemodynamic stability as well as a reduction in the requirements for intra-operative anaesthesia and post-operative analgesia.

In our study, when intravenous clonidine was administered at a dose of 1 mcg/kg ten minutes before pneumoperitoneum, the hemodynamic parameters such as MAP, SBP, and DBP were significantly lower than they were in the control group at all-time points following pneumoperitoneum. Additionally, there was no statistically significant increase in these parameters from the baseline value. These effects were on par with those seen in the magnesium sulphate group, which had been given 50 mg/kg of the medication prior to the pneumoperitoneum procedure. However, both HR and RPP were considerably greater in the group that received clonidine as opposed to the group that received magnesium sulphate. In their research, Kalra and colleagues compared two different dosages of clonidine (1 mcg/kg and 1.5 mcg/kg) against magnesium at a dosage of 50 mg/kg. It was discovered that there was no significant difference in SBP at any time interval between the effects of clonidine 1 mcg/kg and magnesium sulphate 50 mg/kg. However, the clonidine 1.5 mcg/kg group had a considerably reduced mean arterial pressure (SBP). They came to the conclusion that even while magnesium sulphate at a dose of 50 mg/kg causes hemodynamic stability that is equal to that produced by clonidine at a dose of 1 mcg/kg, clonidine at a dose of 1.5 mcg/kg suppressed the hemodynamic response more effectively.

It has been observed that magnesium sulphate can cause general anaesthesia as well as increase the effectiveness of local anaesthetic drugs. It has also been reported that magnesium sulphate has a depressant effect on the central nervous system (CNS) of animals. In the central nervous system, magnesium had the effect of blocking NMDA receptors. Magnesium could diminish peripheral nociceptor sensitization or the stress response after surgery through another method that involves the lowering of catecholamine release through sympathetic stimulation.[32-33]When compared to the control group, the findings of our study demonstrated a statistically significant reduction in the hemodynamic response following pneumoperitoneum in the presence of 50 mg/kg of magnesium sulphate. On the other hand, the efficacy was on par with that of clonidine at a dose of 1 mcg/kg. When compared to the baseline value, the magnesium sulphate group had a statistically significant reduction in HR, SBP, DBP, MAP, and RPP (P 0.001) in intragroup comparisons. HR and RPP were both considerably reduced in the magnesium sulphate group across all time periods, in comparison to the clonidine and normal saline groups.

CONCLUSION

It is possible to draw the following conclusion from the current research: intravenous clonidine and magnesium both have the ability to effectively reduce the hemodynamic

responses to pneumoperitoneum. In addition, it was discovered that magnesium sulphate prolonged the time it took to extubate the patient as well as the time it took for the patient to respond to spoken commands. We have come to the conclusion that both clonidine and magnesium sulphate can be recommended to reduce the hemodynamic response that occurs during the induction of pneumoperitoneum and its subsequent maintenance.

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