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Study of the effect of intravenous magnesium sulphate on hemodynamic parameters in laparoscopic Cholecystectomy under general anesthesia: - A randomized, double blind, controlled interventional study at SMS hospital and attached group of hospitals, Jaipur.

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Abstract

Introduction: Laparoscopic cholecystectomy is one of the most common laparoscopic surgeries performed worldwide. The adverse cardiovascular effect during surgery is increased mean arterial pressure, systemic vascular resistance, and low cardiac output as a result of the release of both catecholamines and vasopressin. Magnesium is widely used to mitigate intubation-induced vasopressor response by blocking the release of catecholamines from both adrenal medullae and also mitigate vasopressin-induced vasoconstriction by causing vasodilation.

Aim: To study the effect of intravenous magnesium sulphate on hemodynamic parameters in laparoscopic cholecystectomy under general anesthesia with the following objectives among the case and control group. (Magnesium sulphate and Normal Saline group).

Methodology: Hospital based, randomized, double blind, controlled interventional study was conducted in the Department of Anesthesiology S.M.S Medical College and attached group of hospitals, Jaipur on 40 subjects in each of group.

Results: Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), did not have statistically significant differences at just before, just after and start time interval between the 2 groups. But after that at 5, 10, 15, 20-, 30-, 45- and 60-min time interval there were statistically significant differences in HR, SBP, DBP, and MAP between the 2 groups. (Lower in Magnesium group).

Conclusion: Administrating magnesium sulfate prior to induction of anesthesia attenuates pneumoperitoneum induced hypertension in patients undergoing laparoscopic cholecystectomy. Our results showed that magnesium sulfate, could induce significant hemodynamic stability during pneumoperitoneum in laparoscopic operations.

Keywords: Laparoscopic cholecystectomy, Magnesium, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP).

Introduction

Laparoscopic cholecystectomy is one of the most common laparoscopic surgeries performed worldwide.[1-3] During the procedure, Carbon dioxide (CO2) which is used for pneumoperitoneum may result in the adverse cardiovascular effects[4-6] such as increase of mean arterial pressure, systemic vascular resistance, and low cardiac output as a result of the release of both catecholamines and vasopressin.[7-9] Moreover the reverse Trendelenburg position used in the procedures may uher leads to decreased cardiac output.[10] Opioids, beta blockers, magnesium, and alpa-2 agonists have been used for the attenuation of these vasopressor responses.[11-13]

Magnesium is widely used to mitigate intubation-induced vasopressor response by blocking the release of catecholamines from both adrenal medullae [14] and also mitigate vasopressin-induced vasoconstriction by causing vasodilation.[10]

Therefore, there is imperative need of the appropriate method of anesthesia which prevents severe hemodynamic changes. For avoiding circulatory response to the pneumoperitoneum, the present drugs used includes alpha-adrenergic agonists, beta-blocker drugs, opioids and vasodilator drugs having their own merits and complications. [15]

The vasodilatory effect of magnesium sulfate (Mg) leads to reduction of blood pressure Mg acts as an antagonist of N-methyl D-Aspartate (NMDA) receptor and its related canals. [16] Mg has many other physiological activities and by acting as calcium channel blocking agents, decreases blood pressure also [17]. Besides it time to response to verbal commands was significantly higher in patients receiving Mg which may be attributed to central nervous system (CNS) depressant effects. . Various researches have shown that administration of Mg leads to a significant reduction in dose of intravenous anesthesia agents, including anesthetic, analgesic, and muscle relaxant agents in the perioperative period .[18]

Aims and objectives

To study the effect of intravenous magnesium sulphate on hemodynamic parameters in laparoscopic cholecystectomy under general anesthesia with the following objectives among the case and control group.

Material and methods

Hospital based, randomized, double blind, controlled interventional study was conducted in the Department of Anesthesiology S.M.S Medical College and attached group of hospitals, Jaipur on 40 subjects in each of group.

Sampling technique: Randomization was done by opaque sealed envelope method.

Blinding: The Magnesium sulfate was a clear transparent solution. Equal volume of normal saline would be given to control group. The Anesthetist who would prepare injections for both groups and label them A & B, He would be different from the anesthetist who could give anesthesia and record the data.

Study groups: The study was conducted in following two groups of patients [group A and group B]. Each group was consisting of 40 patients (n=40 per group).

- Group A (n=40)– In this, patients were given study drug in the form of magnesium sulphate 50 mg/kg 5 minutes after intubation over a period of 5 minutes diluted in normal saline to total volume 20ml @ 240 ml/hr through infusion pump.
- Group B (n=40): – In this, patients were given study drug in the form 20 ml of normal saline @ 240 ml/hr through infusion pump 5 minutes after intubation over a period of 5 minutes.

On the night prior to surgery all patients received tab pantoprazole 40 mg & Tab Alprazolam 0.5 mg orally as premedication and patients were kept nil by mouth 6 hrs. prior to surgery.

Inclusion criteria

- Patients willing to give written informed consent.
- ASA grade I & II
- Age groups 18-65 years
- Planned for elective laparoscopic cholecystectomy under general anesthesia.

Exclusion criteria

- H/O allergy to magnesium sulphate.
- Anticipated difficult intubation.
- History of consumption of antihypertensive drugs, sedatives, Hypnotics and antidepressants preoperatively.
- Pre-existing cardiovascular disease, significant respiratory, renal and hepatic disorder.
- Patients on treatment with calcium channel blockers or Magnesium.
- History of drugs or alcohol abuse.
- Pregnant women.
- Body weight >80kg.

Statistical analysis

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Descriptive statistics included computation of percentages, means and standard deviations. The unpaired t test (for quantitative data to compare two independent two groups) was used for quantitative data comparison of all clinical indicators. Chi-square test was used for qualitative data whenever two or more than two groups were used to compare. Level of significance was set at P≤0.05.

Table 1: HR wise distribution of the study

	Group 1		Group 2		P value
	Mean	Std. Deviation	Mean	Std. Deviation	
Just before	86.33	6.154	85.00	7.555	0.39
Just after	90.63	6.254	88.10	7.578	0.108
Start	92.88	6.123	92.13	6.977	0.61
5 min	94.88	5.979	97.68	6.403	0.04 (S)
10 min	96.43	6.771	101.28	6.496	0.002 (S)
15 min	97.63	5.438	103.25	6.246	0.001 (S)
20 min	98.93	5.166	103.53	7.626	0.002 (S)
30 min	101.58	5.103	108.13	7.637	0.001 (S)
45 min	103.42	5.071	109.17	6.952	0.03 (S)
60 min	102.00	4.619	115.00	9.000	0.03 (S)

HR did not have statistically significant differences at just before, just after and start time interval between the 2 groups. But after that at 5, 10, 15, 20-, 30-, 45- and 60-min time interval there were statistically significant differences in HR between the 2 groups. (Lower in Magnesium group).

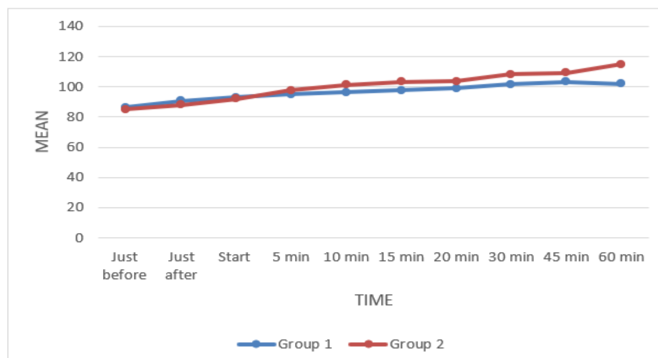


Table 2: SBP wise distribution of the study

	Group 1		Group 2		P value
	Mean	Std. Deviation	Mean	Std. Deviation	
Just before	126.45	7.742	128.35	8.833	0.39
Just after	130.28	7.723	132.45	8.820	0.24
Start	132.55	7.828	135.35	8.836	0.13
5 min	133.00	8.277	138.25	8.230	0.006 (S)
10 min	134.83	7.575	140.43	8.268	0.002 (S)
15 min	136.58	7.732	142.58	8.212	0.001 (S)
20 min	138.38	7.811	150.13	8.519	0.001 (S)
30 min	142.20	8.340	157.18	8.641	0.001 (S)
45 min	148.17	8.343	159.83	9.321	0.001 (S)
60 min	153.50	9.147	169.20	9.834	0.04 (S)

SBP did not have statistically significant differences at just before, just after and start time interval between the 2 groups. But after that at 5, 10, 15, 20-, 30-, 45- and 60-min time interval there were statistically significant differences in SBP between the 2 groups. (lower in Magnesium group)

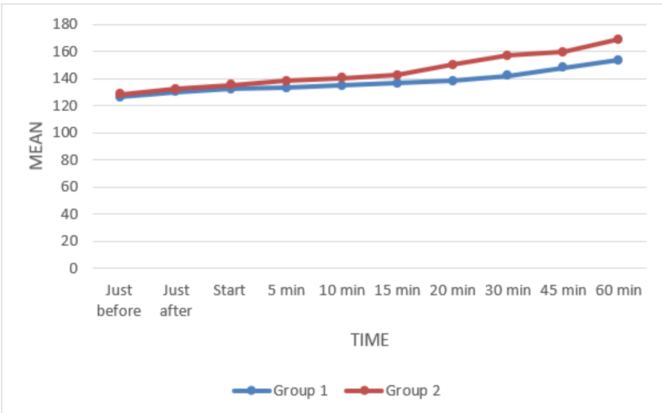


Table 3: DBP wise distribution of the study

	Group 1		Group 2		P value
	Mean	Std. Deviation	Mean	Std. Deviation	
Just before	80.53	6.872	80.85	5.517	0.81
Just after	83.63	6.909	85.00	5.791	0.33
Start	86.43	7.009	88.15	5.568	0.22
5 min	88.73	6.660	91.53	5.411	0.04 (S)
10 min	87.50	6.645	91.40	5.817	0.007 (S)
15 min	89.00	7.009	94.10	5.472	0.001 (S)
20 min	92.08	6.596	98.35	5.211	0.001 (S)
30 min	94.45	6.453	103.08	5.441	0.001 (S)
45 min	97.08	6.612	103.92	6.007	0.001 (S)
60 min	100.50	5.260	108.80	4.604	0.03 (S)

DBP did not have statistically significant differences at just before, just after and start time interval between the 2 groups. But after that at 5, 10, 15, 20, 30, 45 and 60 min time interval there were statistically significant differences in DBP between the 2 groups. (lower in Magnesium group).

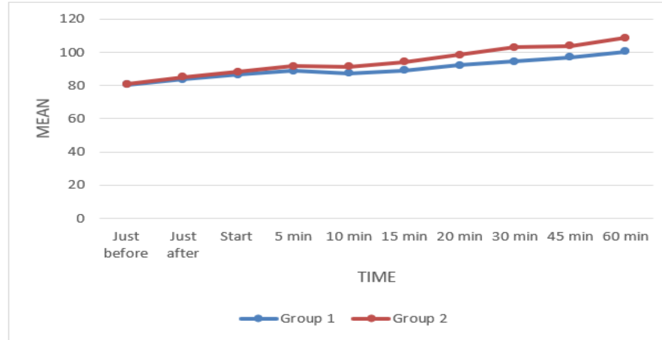


Table 4: MAP wise distribution of the study

	Group 1		Group 2		P value
	Mean	Std. Deviation	Mean	Std. Deviation	
Just before	95.83	6.710	96.68	6.061	0.55
Just after	99.20	6.634	100.80	6.039	0.26
Start	101.75	6.632	103.85	5.860	0.13
5 min	103.55	6.324	107.18	5.325	0.007 (S)
10 min	103.25	6.507	107.80	5.743	0.001 (S)
15 min	104.80	6.760	110.30	5.384	0.001 (S)
20 min	107.58	6.425	115.70	5.297	0.001 (S)
30 min	110.40	6.586	121.15	5.414	0.001 (S)
45 min	114.08	6.921	122.67	6.050	0.004 (S)
60 min	118.00	5.944	128.80	5.762	0.02 (S)

MAP did not have statistically significant differences at just before, just after and start time interval between the 2 groups. But after that at 5, 10, 15, 20-, 30-, 45- and 60-min time interval there were statistically significant differences in MAP between the 2 groups. (Lower in Magnesium group)

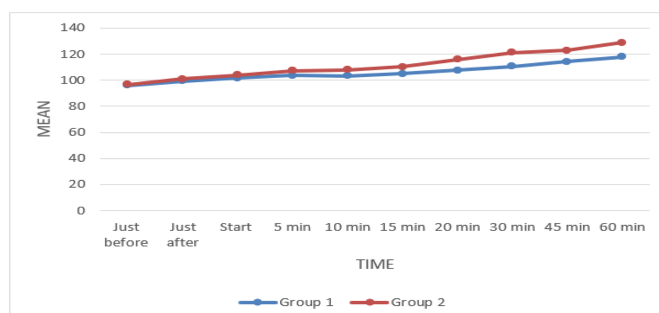
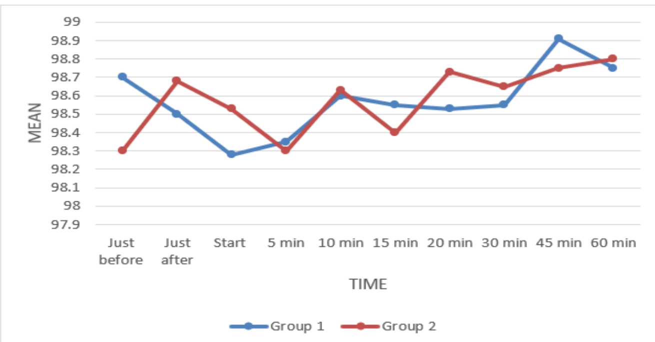


Table 5: SPO2 wise distribution of the study

	Group 1		Group 2		P value
	Mean	Std. Deviation	Mean	Std. Deviation	
Just before	98.70	1.043	98.30	1.265	0.12
Just after	98.50	1.062	98.68	.917	0.43

Start	98.28	1.198	98.53	1.037	0.32
5 min	98.35	1.075	98.30	1.137	0.84
10 min	98.60	.841	98.63	.807	0.89
15 min	98.55	.986	98.40	1.105	0.52
20 min	98.53	.784	98.73	.784	0.25
30 min	98.55	1.061	98.65	.949	0.65
45 min	98.91	.539	98.75	.622	0.52
60 min	98.75	.500	98.80	.447	0.87

SPO2 did not have statistically significant differences at any time interval between the 2 groups.



Discussion

The present study was conducted to evaluate the effect of IV MgSO4 on hemodynamic response to Pneumoperitoneum during laparoscopic cholecystectomy. Pneumoperitoneum results in rapid and immediate increase in plasma catecholamine which leads to activation of renin-angiotensin-aldosterone system, probably due to an increase in intraperitoneal pressure and stimulation of peritoneum by Carbon dioxide.[19-21]

In the present study, when comparing group magnesium sulphate with the group control there was no significant difference in the HR, SBP, DBP and MAP in both the groups immediately before intubation and after intubation among both groups. MgSO4 group was showed statistically significant effect by lowering hemodynamic parameter (HR, SBP, DBP and MAP) as compared to saline group after 5, 10, 15, 20, 30, 45 and 60 minutes. Kamble SP (2017) et al[10], found that systolic blood pressure, diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) were all significantly higher in the normal saline group compared to magnesium. DBP, MAP, and HR were significantly lower in the magnesium group. Mean extubation time and time to response to verbal commands were significantly more in the magnesium group.

First, CO2 insufflation in the first 10 minutes and extubation caused an apparent increase in HR and MAP, second, the range of variations of HR and MAP in magnesium group was significantly lower than control group, third, HR at the end fell in magnesium group compared to the base; however, it had increased in control group and MAP at the end showed no significant changes than the base in magnesium group while it had increased in control group.

Elsharnouby (2006) et al.[22] used magnesium 40mg/kg IV before induction and 15mg/kg/hr by continuous infusion intraoperatively. They noticed more episode of hypotension using this dose of magnesium. Ray M (2010) et al.[23] decreased the dosage of Mg, to 30 mg/kg, prior to induction followed by 10 mg/kg/hr infusion while during operation and the selected dose caused a gradual and sustained reduction in MAP and HR of the patients with no episodes of serious hypotension and no serious bradycardia. But Shariat Moharari (2016) et al.[24]. used the dosage of 40 mg/kg/hr, prior to induction and infusion of 10 mg/kg/hr while during operation, and no episodes of serious hypotension or bradycardia were reported. In the study of Jee D (2015) et al.[14] only one bolus dose of Mg (50 mg/kg) was prescribed prior to pneumoperitoneum and the amount of plasma rennin activity showed no differences in the magnesium group with control group, showing absence of serious hemodynamic fall in patients.

Similar to Schulz-Stübner et al.[25] study, in the the present study the infusion dose of Mg was omitted and only the bolus dose of Mg, was prescribed in 50 mg/kg, prior to anesthesia induction. In none of the subjects of magnesium group, serious hypotension or bradycardia occured during the anesthesia time. In addition, there was no significant increase in the anesthesia length compared with control group.

Magnesium sulphate blocks the release of catecholamines from adrenergic nerve terminals and adrenal glands associated with tracheal intubation moreover magnesium sulphate produce vasodilatation by acting directly on blood vessels and attenuates vasopressin stimulated vasoconstriction which ultimately modulate hypertension and tachycardia and neurohumoral response in patients during CO2 pneumoperitoneum. α2a receptors mediate sedation, analgesia and sympatholytic, are founded densely in the pontine locus coeruleus which is an important source of sympathetic nervous system innervation of the forebrain and a vital modulator of vigilance. The sedative effects of clonidine most likely reflect inhibition of this nucleus.[25]

Magnesium has a depressant effect at synapses by relative competition between calcium and magnesium, mainly inhibiting presynaptic release of acetylcholine at neuromuscular junction. It has an antagonist effect at N-methyl D-Aspartate (NMDA) receptors thus decreasing stimulus for excitatory postsynaptic potentials (EPSP) which indicate intrinsic analgesic properties. NMDA receptors play an important role in neuronal plasticity and processes leading to central sensitization to pain. Thus magnesium has been shown to be useful in the reduction of acute postoperative pain, analgesic consumption, or both. It has been reported that Mg improves general anesthesia, and Mg increases the effects of local anesthetics also. The depressant effects of Mg on CNS have been reported in animals too which caused a dose dependent neuroprotective effect in spinal cord injury.

Acting as an antagonist of NMDA receivers, Mg has the potential of pain relief. This pain relief effect of Mg was documented for intra and postoperative periods. In a recent meta-analysis in 2013, perioperative administration of Mg and post operative pain was evaluated in 25 trial studies and reported lesser cumulative postoperative morphine consumption by 24.4% reduction and lesser pain score in the first 24 hours after surgery.[25]

Seyhan (2006) et al.[26] studied the effects of different dosages of Mg, on reducing the amount of propofol demand, hemodynamic and relieving pain after gynecology surgeries. In their study, 80 women were divided into four equal groups. The control group received normal saline and in other groups, one received bolus dosage 40mg/kg, bolus dose plus infusion 10 mg/kg/h and 20mg/kg/h in 4 hours, respectively.

Most studies which were performed on laparoscopic surgery focus on hemodynamic changes during pneumoperitoneum. In laparoscopic surgery in which, the cardiovascular changes are among the prevalent side effects, and usually shows itself as hypertension, drugs that affect hemodynamic, causing hypotension might prove useful in such operations. As mentioned, the pneumoperitoneum by CO2, causes rapid increase in plasma catecholamines which is due to increase in internal peritoneum pressure and peritoneum stimulation via CO2 gas (sympathoadrenal stimulation).It is shown that bolus dose of Mg (50 mg/kg) increases the serum concentration of Mg, in this range and this serum level of Mg, blunts the increase of catecholamines level of the plasma, during pneumoperitoneum, and effectively, prevents the sympathoadrenal hemodynamic stress responses emerging form pneumoperitoneum. Moreover, the vasopressin hormone is one of the effective and basic factors in the pneumoperitoneum-caused hemodynamic variations.[25]

Conclusion

Administrating magnesium sulfate prior to induction of anesthesia attenuates pneumoperitoneum induced hypertension in patients undergoing laparoscopic cholecystectomy. ur results showed that magnesium sulfate, could induce significant hemodynamic stability during pneumoperitoneum in laparoscopic operations. No adverse effects were seen with administration of magnesium sulphate; hence it can be used as an alternative drug to attenuate hemodynamic response to pneumoperitoneum in laparoscopic cholecystectomy.

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