

Comparative Evaluation of Bilateral Erector Spinae Plane Block using Bupivacaine Combined with Magnesium Sulphate or Clonidine as an Adjuvant for Postoperative Analgesia in Laparoscopic Cholecystectomy – A Prospective Randomized Controlled Trial.

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ABSTRACT

Background: Laparoscopic cholecystectomy (LC) is a minimally invasive but often painful procedure, despite multimodal analgesia, which can increase mortality and morbidity. The ultrasound-guided Erector Spinae Plane (ESP) block is a novel technique providing analgesia in the thoracic and abdominal areas. This study investigates the effects of adding magnesium sulphate (MgSO₄) or clonidine to 0.25% bupivacaine in bilateral erector spinae blocks for postoperative pain relief in LC patients.

Results: Patients in Groups M and C were mainly aged 51-60, while Group L had more 20-30-year-olds. Mean age was comparable across all groups, with mostly male patients. Baseline measurements showed that Group L had the highest heart rate, and Group C had the highest MAP. Postoperatively, Group L had the highest heart rate at 1, 6, and 12 hours, and Group M at 24 hours. MAP was higher in Group M (at 1 and 12 hours) and Group C (at 6 and 24 hours). PONV rates were similar, and significant differences were observed in pain and rescue analgesia requirements among the groups at different time intervals.

Conclusions: In this study, MgSO₄ as an adjuvant to bupivacaine proved more effective than clonidine for postoperative pain relief in LC patients.

Key Words: American society of anaesthesiologists (ASA), erector spinae Plane (ESP), laparoscopic cholecystectomy (LC), magnesium sulphate (MgSO₄), numerical rating scale (NRS).

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BACKGROUND

Laparoscopic cholecystectomy (LC) is a commonly performed minimally invasive procedure for benign biliary diseases, offering numerous benefits, including reduced postoperative pain, shorter recovery times, and a quicker return to normal activities. However, postoperative pain remains a significant concern, potentially leading to increased morbidity and extended hospitalization. Patients often experience discomfort in the back, shoulder, and incision areas, with the most intense pain occurring shortly after surgery and gradually diminishing over several days^[1]. There is also a growing concern that severe acute pain following LC may serve as a predictor of the development of chronic pain^[2].

This study aims to investigate the potential of using magnesium sulphate (MgSO₄) and clonidine as adjuncts to 0.25% bupivacaine in bilateral erector spinae block to manage postoperative pain in LC patients. Previous research has suggested that MgSO₄ may enhance nerve

blockade by modulating nerve bundle hyperpolarization, making it difficult for nerve fibers to reach the threshold for conduction^[3]. Clonidine, on the other hand, acts as a centrally acting α_2 adrenergic agonist, reducing pain by inhibiting voltage-gated sodium channels, suppressing action potential generation in dorsal horn neurons, and stimulating postsynaptic α_2 adrenergic receptors in the spinal cord's dorsal horn^[4,5].

As no previous studies have explored the effects of MgSO₄ and clonidine in conjunction with 0.25% bupivacaine in bilateral erector spinae block for postoperative pain relief in LC patients, this research endeavours to assess its impact on postoperative pain scores (primary outcome), opioid consumption, and the occurrence of post-operative nausea and vomiting (PONV) (secondary outcomes) in LC patients.

METHODS

Study Setting and Duration: This prospective randomized controlled trial was conducted at a tertiary

care hospital from September 2019 to July 2021 Patient Selection: A total of 60 patients aged 18 to 65 and categorized as ASA grade I and II, were included in the study after obtaining institutional ethical clearance (IEC/2019/1780) and informed consent. Exclusion criteria encompassed patients under 18 or over 65 years, those classified as ASA grade III and IV, individuals with known local anaesthetic allergies, bleeding diathesis, and individuals on anticoagulant medications.

Group Allocation: The 60 patients were distributed into three groups, each comprising 20 individuals (Figure 1).

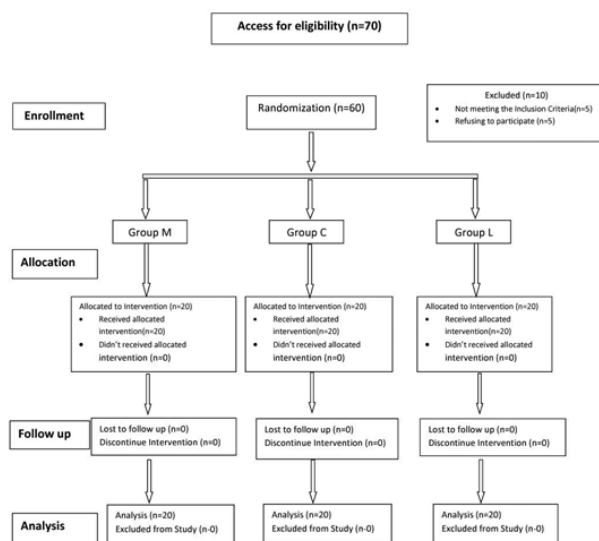


Fig. 1: Showing access to eligibility, group allocation, follow-up and analysis).

Group M (MgSO₄): This group received an Ultrasound-guided Bilateral Erector Spinae block 30 minutes preoperatively. The block consisted of 30 ml (15 ml per side) of 0.25% Bupivacaine combined with 500 mg of MgSO₄.

Group C (Clonidine): Patients in this group underwent the same block as Group M but with the addition of 1.5 mcg/kg of Clonidine.

Group L (Control group): Patients in this group received an Ultrasound-guided Bilateral Erector Spinae block with only 30 ml (15 ml per side) of 0.25% Bupivacaine.

Surgical Procedure

Surgical procedures commence 30 minutes after the block.

Data Collection

Hemodynamic parameters (heart rate and mean arterial pressure) were recorded at specific time points throughout surgery. Postoperatively, patients were monitored for pain relief, rescue analgesic requirements and postoperative nausea and vomiting (PONV). Pain levels were assessed

using the Numerical Rating Scale (NRS) at various intervals.

Data Analysis

Data on PONV, rescue analgesics, mean arterial pressure, and heart rate were collected and analyzed at specific time intervals (immediately post-surgery, 1, 6, 12, and 24 hours postoperatively).

Statistical analysis

Data obtained underwent rigorous analysis using SPSS version 20.0, with a significance level set at $p=0.05$. Continuous variables were expressed as Mean \pm standard deviation, while categorical data were presented in terms of frequency. Chi-square tests were used for categorical data analysis, enabling meaningful comparisons. For continuous data, both the Student's t-test and ANOVA were employed to examine differences and relationships, ensuring a comprehensive evaluation of study outcomes.

RESULTS

In our study, both Groups M and C had a maximum of 25% of participants aged 51-60, while Group L had a maximum of 30% in the 20-30 age range. The mean ages were (40.95 \pm 15.60), (40.90 \pm 15.17), and (38.70 \pm 15.35) in Groups M, C, and L, respectively. Male patients constituted the majority in all groups: Group M (60%), Group C (70%), and Group L (70%) (Table 1).

Baseline hemodynamic parameters were recorded, revealing that the mean heart rate was highest in Group L (84.85 \pm 5.94), followed by Group M (84.30 \pm 6.44) and Group C (83.35 \pm 7.31). Conversely, the mean arterial pressure (MAP) was highest in Group C, followed by Group M and L, with significant differences between all three groups. Intraoperative heart rate and MAP did not display significant differences between groups. (Table 2)

Postoperative hemodynamic parameters were assessed at various intervals. At 1 hour, Group L had the highest mean heart rate, while Group M and Group C followed. In contrast, MAP was highest in Group M, followed by Group L and C, with statistically significant differences in heart rate and MAP among groups. At 6 hours, Group L had the highest mean heart rate, and MAP was highest in Group C, both displaying significant differences. At 12 hours, Group L had the highest heart rate, while MAP was highest in Group M, both with significant differences. At 24 hours, Group M had the highest heart rate, and MAP was highest in Group C, again with significant differences for both parameters. The incidence of postoperative nausea and vomiting (PONV) was consistent across all groups at (1.1 \pm 0.30) during all follow-up intervals.

Significant differences were observed in pain scores in the three groups at 6, 12, and 24-hour intervals. Intergroup comparisons revealed significant differences

between Group M and C, and Group M and L, while differences between Group C and L were insignificant (Table 3; Figure 2).

Similarly, the time to rescue analgesia showed significant differences between all three groups at 6, 12, and 24-hour intervals. Intergroup comparisons indicated statistically significant differences between Group M and C, and Group M and L, whereas differences between Group C and L were insignificant (Table 4; Figure 3).

DISCUSSION

The findings of our study demonstrate that the addition of magnesium sulphate (MgSO₄), acting as a competitive NMDA antagonist, to bupivacaine in bilateral ESPB significantly prolongs postoperative analgesia compared to the addition of clonidine, a centrally acting α_2 agonist, or bupivacaine alone. This effect was more pronounced and statistically significant. These results are of notable clinical importance in the management of postoperative pain in patients undergoing Laparoscopic Cholecystectomy (LC).

Table 1: Demographic parameters of enrolled patients (n=60) showing frequency and percentage in each group (Group M=MgSO₄ with Bupivacaine, Group C= Clonidine with Bupivacaine and Group L= Plane Bupivacaine). *P*-value of <0.05 is considered significant and is mentioned in *mark

	Age group (Years)	GROUP M	GROUP C	GROUP L	<i>P</i> value
		Frequency (n)	Frequency (n)	Frequency (n)	
Age Group (Years)	<20	4	2	2	$\chi^2=2.001$ $p=0.074$
	20-30	2	4	6	
	31-40	4	4	4	
	41-50	3	4	3	
	51-60	5	5	4	
	>60	2	1	1	
	MEAN AGE	40.95	40.90	38.70	
Gender	FEMALE	8	6	6	$\chi^2=2.330$ $p=1.091$
	MALE	12	14	14	
	TOTAL	20	20	20	

Table 2: Hemodynamic parameters [(Heart Rate=beats per minute), (MAP=Mean Arterial Pressure=mmHg) and Postoperative Nausea and Vomiting (PONV) at different follow-ups. Group M=MgSO₄ with Bupivacaine, Group C= Clonidine with Bupivacaine and Group L= Bupivacaine). (**P*-value of <0.05= significant)

	Hemodynamic parameters	Group M		Group C		Group L		Anova Statistical Analysis	
		MEAN	SD	MEAN	SD	MEAN	SD	F-statistic	<i>p</i> -value
At 1 hour	HR(BPM)	83.35	7.31	82.25	6.47	84.40	6.95	11.771	0.021*
	MAP	76.00	6.22	75.35	6.59	75.95	4.66	10.542	0.051
	PONV	1.10	.30	1.10	.30	1.10	.30	-	-
At 6 hours	HR	82.25	6.47	81.90	6.40	83.35	6.44	12.001	0.032*
	MAP	75.35	6.59	75.65	6.46	74.70	4.61	11.661	0.043*
	PONV	1.10	.30	1.10	.30	1.10	.30	-	-
At 12 hours	HR	81.40	8.16	81.60	7.23	83.15	6.73	11.551	0.033*
	MAP	75.85	6.18	75.50	4.67	75.80	4.32	9.871	0.022*
	PONV	1.10	.30	1.10	.30	1.10	.30	-	-
At 24 hours	HR	82.25	7.69	82.20	6.99	81.60	9.04	11.590	0.036*
	MAP	75.75	6.16	75.95	6.07	74.00	4.86	10.320	0.043*
	PONV	1.10	.30	1.10	.30	1.10	.30	-	-

Table 3: NRS (Numerical Rating Scale) score at different intervals of enrolled patient groups Group M=MgSO4 with Bupivacaine, Group C= Clonidine with Bupivacaine and Group L= Bupivacaine). *P-value* of <0.05 is considered significant and is mentioned in *mark

NRS SCORE	GROUP M		GROUP C		GROUP L		STATISTICAL ANALYSIS	
	ZERO	≥4	ZERO	≥4	ZERO	≥4	CHI SQUARE	<i>p-value</i>
AT 1Hr	20	0	20	0	20	0		-
AT 6Hr	20	0	15	5	15	5	2.671	0.013*
AT 12Hr	15	5	10	10	12	8	2.781	0.032*
AT 24Hr	15	5	0	20	0	20	1.668	0.054

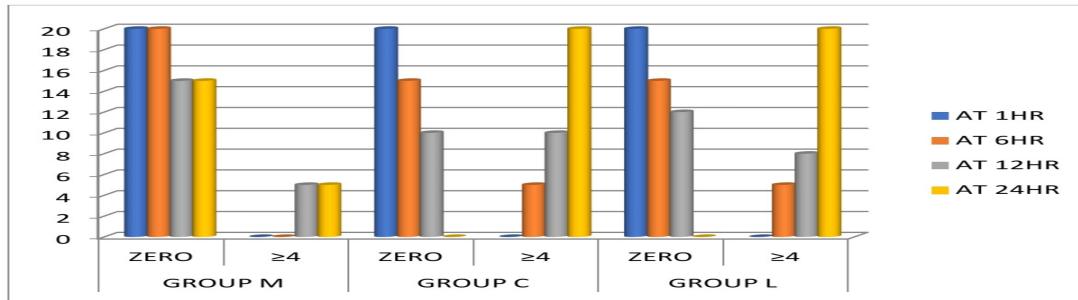


Fig. 2: NRS (Numerical Rating Scale) score at different intervals of enrolled patients

Table 4: Time to rescue analgesia at different intervals of enrolled patients. Group M=MgSO4 with Bupivacaine, Group C= Clonidine with Bupivacaine and Group L= Bupivacaine). *P-value* of <0.05 is considered significant and is mentioned in *mark

RESCUE ANALGESIA	GROUP M		GROUP C		GROUP L		STATISTICAL ANALYSIS	
	NO	Inj pcm 1g	NO	Inj pcm 1g	NO	Inj pcm 1g	CHI SQUARE	<i>p-value</i>
AT 1HR	20	0	20	0	20	0	-	-
AT 6HR	20	0	15	5	15	5	2.671	0.013*
AT 12HR	15	5	10	10	12	8	2.781	0.032*
AT 24HR	15	5	0	20	0	20	1.668	0.054

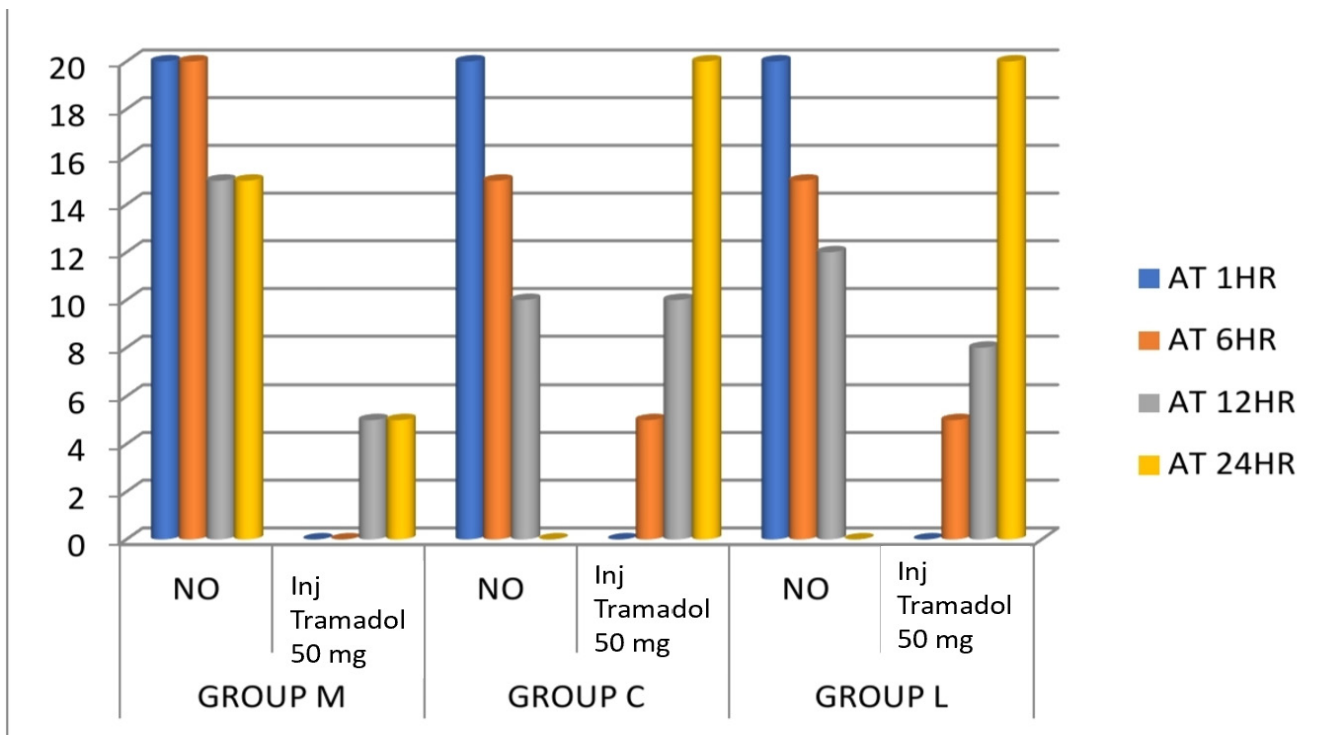


Fig.3: Time to rescue analgesia at different intervals of enrolled patients

The ESPB technique employed in our study is a promising truncal interfascial regional method, providing analgesia in the thoracic and abdominal regions. The injection site is either at the level of the T5 transverse process, resulting in a spread between the C7 and T8 segmental levels, or at the level of the T7-T9 transverse processes, resulting in a spread between the T6 and T12 segmental levels^[6].

Local anaesthetic penetrates anteriorly, presumably through the costo-transverse foramina to the paravertebral space, and it can thus be described as an indirect paravertebral block. However, the ESP block is presumably the most promising due to its anatomically close proximity to the costotransverse foramina^[7].

Similar to our study, Ghatak T *et al.*^[8] conducted a randomised, double-blind study to establish the effect of the addition of magnesium or clonidine, as an adjuvant, on epidural bupivacaine in lower abdominal and lower limb surgeries. In the present study, a maximum of 25% in both groups M and C were aged 51- 60 years, whereas, in Group L, a maximum of 30% were aged 20-30 yrs. The mean age was 40.95±15.60, 40.90±15.17, and 38.70±15.35 in groups M, C and L, respectively, with an insignificant difference. Thus, patients undergoing LC were around 40 years of age. Similar to our study, Al-Refaei K *et al.*^[9] observed that the mean age was around 32 years in patients undergoing LC. We observed a male predilection to undergo LC.

Mean values of parameters like heart rate and MAP were assessed at baseline; HR, MAP and PONV were assessed at different post-operative time periods. Similar to our study, Ghatak T *et al.*^[8] also evaluated onset time, heart rate, blood pressure, duration of analgesia, pain assessment by visual analogue score (VAS) and adverse effects. At baseline, heart rate was found to be maximum in group L, followed by Group M and Group C. On the contrary, MAP was maximum in group C, followed by Group M and L, with a significant difference between all three groups for both HR and MAP. PONV was also evaluated for all three groups (1.1±0.30), but it was observed to be the same for all three groups at all post-operative time periods. Thus, we found that the heart rate was maximum in the control group, whereas in groups M and C it was maintained. MAP was maximum in the MgSO₄ group, followed by the clonidine group until 12 hrs post-operatively. But after 24 hrs, the heart rate increased in group M, with a decrease in MAP. In contrast to our study, Ghatak T *et al.*^[8] found that systolic and diastolic arterial blood pressures, heart rates and oxygen saturations remained stable, and there was no significant difference between the groups.

We assessed the analgesic effects of adjuncts using the NRS scoring method. An NRS typically consists of a series of numbers with verbal anchors representing the entire possible range of pain intensity. We found that at 1 hr, all patients in all three groups showed zero pain

scores. At 6 hrs, in groups C and L, 5 patients had scored more than 4. At 12 hrs, in group M, only 5 patients had more than 4 scores, but in groups C and L, 10 and 8 patients, respectively, had more than 4 scores. In groups C and L, all patients had more than 4 scores. A significant difference was observed between all three groups at 6, 12 and 24 hrs time periods. Intergroup comparisons between groups M and C; and Group M and L showed statistically significant differences; whereas the relation was insignificant between groups C and L. This revealed that pain score was minimal in cases where MgSO₄ was given, followed by clonidine and the control group. This shows that the analgesic effect was maximum with MgSO₄ after giving Bilateral Erector Spinae block in LC.

Similar to our study, Farouk S^[10] observed that analgesic consumption in the pre-magnesium group was significantly less (78.5ml) than the other two groups and the dose consumed in the post-magnesium group was significantly smaller (91.2ml) than the control group (104.6ml). There were no cases of postoperative hemodynamic or respiratory instability in their study. Similarly, in our study, epidural magnesium had effective postoperative analgesia (~4-5 hours) with better hemodynamic stability. De Kock *et al.*^[11] observed that after the operation, epidural clonidine infusion provided complete analgesia lasting 30±21 min in group 1 compared with 251±237 min in group 2 or 369±256 min in group 3. They concluded that the larger doses of epidural clonidine used in the study provided substantial intra and postoperative analgesia without any side effects. Huang YS *et al.*^[12] observed that the clonidine group experienced less postoperative pain. Andrew D. *et al.*^[13] observed that morphine consumption was significantly lower in the clonidine group. Munshi BA *et al.*^[14] suggested that co-administration of inj. Magnesium sulphate 50 mg. or Clonidine 3µg/kg (150µg maximum) to epidural bupivacaine produced a predictable, rapid onset of surgical anaesthesia without significant side effects. The study suggests magnesium sulphate can be a useful alternative as an adjuvant to epidural bupivacaine without any side effects. In accordance with our study, Altan A *et al.*^[15] The induction of anaesthesia with propofol was rapid in the presence of magnesium sulphate and clonidine. The safety of the perineural use of MgSO₄ has been an issue of debate in multiple human and animal studies and also in many reports of inadvertent use. Our study concluded that the use of magnesium sulphate as an adjuvant to bupivacaine has proved more successful than clonidine based on postoperative pain scores (primary outcome), opioid consumption, and postoperative nausea and vomiting (PONV) (secondary outcomes) in patients undergoing LC using Bilateral Erector Spinae block.

The findings of our study indicate that MgSO₄ as an adjuvant to bupivacaine in bilateral ESPB is a promising approach for postoperative pain management in LC patients. Addition of MgSO₄ to bupivacaine in ESPB significantly prolongs postoperative analgesia, reduction in opioid consumption and PONV compared to the addition of clonidine or bupivacaine alone. These results are of notable clinical importance, however more studies are required to refine its application in clinical practice.

CONCLUSIONS

Our study establishes magnesium sulphate (MgSO₄) as a superior adjuvant to bupivacaine in Bilateral Erector Spinae block for patients undergoing Laparoscopic Cholecystectomy (LC). This conclusion is based on primary outcomes, such as postoperative pain scores, as well as secondary outcomes, including rescue analgesic requirement and postoperative nausea and vomiting (PONV).

MgSO₄ exhibits notable advantages, promoting hemodynamic stability and delivering effective postoperative analgesia with extended duration and reduced analgesic needs. Furthermore, its use is associated with a lower incidence of PONV.

These promising results underscore MgSO₄'s potential for improving pain management and patient outcomes in LC procedures. However, further comprehensive investigations into optimal dosages and its role in diverse clinical scenarios are warranted to maximize its clinical utility.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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Q1 *MG SULPHATE VS CLONIDINE IN ESPB FOR LAP. CHOLECYSTECTOMY POSTOP. PAIN*

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