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Original Research Article

Intraperitoneal Instillation of Levobupivacaine with Adjuvants (Magnesium Sulphate & Dexmedetomidine) for Post Operative Analgesia in Laparoscopic Cholecystectomy: A Randomized Double Blinded Controlled Study

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Abstract

Background and Aims: Intraperitoneal instillation of local anaesthetics with adjuvants is emerging treatment modality for postoperative pain relief following laparoscopic surgeries. This study was conducted to compare the postoperative analgesia and other recovery variables on intrapaeritoneal instillation of $MgSO_4$ and dexemedetomidine added to levobupivacaine for laproscopic chlolecystectomy.

Methods: Total 90 patients were enrolled for the study and randomized into three groups (Group L, Group LM, and Group LD) of 30 patients each. Primary outcomes were comparison of post-operative analgesia in terms of; pain assessment using Visual Analogue Scale [VAS] and time to request for first rescue analgesia [TFA] along with total number and dose of rescue analgesics in 24 hours. Secondary objectives were to measure; Haemodynamic variables, Ramsay Sedation Score, recovery variables, adverse effects of study drugs and satisfaction score of patient and surgeon.

Results: Group LD showed lower VAS at all time intervals than other two groups. The time (minutes) to first rescue analgesic requirement was prolonged in group LD (269.09±54.76 min) as compared to group LM (170±57.28 min) and group L (63.10±28.08 min) which was found to be highly significant ($p<0.001$).Total number and dose of rescue analgesic required in 24 hours was lowest in group LD as compared to group LM and group L which was statistically highly significant ($p<0.001$). Patients and surgeons satisfaction scores were high in group LD; however

haemodynamic variables, Ramsay Sedation Score, recovery variables and adverse effects were comparable among all groups.

Conclusion: Dexmedetomidine and magnesium sulphate both are safe as an adjuvant with 0.25% levobupivacaine for postoperative pain relief however dexmedetomidine provides longer duration of post-operative analgesia with minimal side effects as compared to magnesium sulphate.

Keywords: Laparoscopic cholecystectomy, dexmedetomidine, magnesium sulphate, post-operative analgesia

Introduction

Cholecystectomy is the most commonly performed surgery on biliary tract in present era. Laparoscopic surgery is often preferred over open surgery as it can be performed as day care procedure because of various advantages like; lesser post-operative pain, decreased risk of haemorrhage, small size of incision providing better cosmetic results, less expenditure faster recovery and hence shorter duration of hospital stay. [1,2] Pain after cholecystectomy is multifactorial with visceral, parietal and referred components and is still a challenge after laparoscopic cholecystectomy. It can be best managed by multimodal technique of analgesia. Recently intraperitoneal instillation of local anaesthetics (LA) has been included in multimodal analgesic techniques to provide adequate pain relief after laparoscopic surgery. Levobupivacaine is the S [-] isomer of bupivacaine and has a safer pharmacological profile than bupivacaine with less cardiac and neurotoxic adverse effects. Magnesium sulphate ($MgSO_4$) acts as a NMDA receptor antagonist and inhibits central sensitization from peripheral painful stimuli whereas dexmedetomidine is selective alpha-2-adrenergic agonist with sympatholytic, sedative, amnestic, anxiolytic, neuroprotective and analgesic properties. Previous studies reported excellent analgesia and is associated with prolongation of local anaesthetic effect after laparoscopic cholecystectomy on intraperitoneal instillation of magnesium sulphate and dexmedetomidine with levobupivacaine. [3-7] Present study was done to compare the postoperative analgesia and other recovery variables with these two adjuvants on intrapaeritoneal instillation of $MgSO_4$ and dexemedetomidine added to levobupivacaine.

Materials and Methods

After obtaining approval from institutional research ethical board (HREC APPROVAL NO: - GU/HREC/EC/2019/785) and clinical trial registration (CTRI/2021/01/030532), this prospective randomized controlled double blinded study was performed in accordance with the Declaration of Helsinki at a tertiary care hospital, over a period of one and a half year, from January 2019 to June 2020.A total of 90 patients of American Society of Anaesthesiologists (ASA) grade I or II, between the age group of 18 to 60 years posted for elective laparoscopic cholecystectomy under general anaesthesia were included in this study after obtaining written informed consent. Patients having allergy to study drugs, known hypomagnesemia or hypermagnesemia, chronic alcoholism, pre-existing cardiac diseases, uncontrolled hypertension, severe asthma, severe chronic obstructive pulmonary diseases, hepatic and renal dysfunction, chronic pain syndromes, pregnant or lactating women and those with peritoneal drain after surgery were excluded from the study.

Based on previous study [8] significant reduction in VAS score between control and adjuvant group, with a power of 80% (α error 5%, β error 20% i.e; 95% confidence

level) a sample size of 28 patients in each group was calculated using the formula for difference in mean and standard deviation. Considering 10% dropouts from the study and to reject the null hypothesis, total of 30 patients were included in each group.

Patients were randomly assigned to one of the three groups using computer generated random number tables. Group assignment was sealed within the opaque envelopes. The envelope was opened by the principle investigator just before the administration of the study drug. Anaesthesiologist who was not involved in study and data collection prepared the drug according to randomization group. The anaesthesiologist who monitored and recorded the data, nurses, surgeon, research assistant and patients were blinded to the randomization. Study drug was prepared for each group as per protocol. Group L: levobupivacaine [0.25%] 40 ml added to 10 ml normal saline to make a total volume of 50 ml; Group LD: levobupivacaine [0.25%] 40 ml + dexmedetomidine 0.5 mcg/kg added to normal saline to make a total volume of 50ml; Group LM: levobupivacaine [0.25%] 40 ml + magnesium sulphate 50 mg/kg added with normal saline to make a total volume of 50 ml.

All patients were subjected to thorough pre anaesthetic evaluation and were explained about the procedure and visual analogue scale [VAS] pain score of 0-10. [0-3: no pain, 4-7: discomfort, 8-10: severe pain]. All the patients were given tablet alprazolam0.25 mg orally a night before surgery and tablet ranitidine150 mg orally a night before and on the morning of surgery. Patients were kept nil orally 6 hours prior to surgery. An 18 gauge cannula was inserted and an infusion of crystalloid was started at 6-8ml/kg.

On arrival in operation theatre, standard monitoring including pulse oximetry (SpO_2), non-invasive blood pressure (NIBP), End tidal CO2 (ETCO2) and three lead electrocardiography (ECG) was done. After routine premedication with inj. ondansetron 0.1mg/kg, inj. glycopyrrolate 0.005mg/kg, general anaesthesia was administered and maintained according to standard technique. During surgery pneumoperitoneum was created by insufflation of carbon dioxide at the rate of 2litre/minute to a maximum pressure of 10-12 mmHg. The intra-abdominal pressure was maintained at 10-12mmHg throughout the laparoscopic procedure. Intraperitoneal instillation of study drugs was done at the conclusion of the surgery, before deflation of pneumoperitoneum through laparoscopic ports under vision of laparoscope. Extubation was performed only when extubation criteria were met. Patients were transferred to post-anaesthesia care unit for further monitoring.

Demographic data recorded were age, sex, weight, ASA grade, duration of surgery (from skin incision to last suture), duration of anaesthesia (from start of induction till extubation) and duration of pneumoperitoneum (from inflation of carbon dioxide to deflation). Haemodynamic parameters like: Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure(MAP) and oxygen saturation (SpO2)were recorded at the time of drug instillation (baseline), at the time of extubation, 5 minutes after extubation and then after at various time intervals (15,30,45,60,90minutes and 2,4,8,12,24 hours) postoperatively.

Pain assessment by VAS score was noted at 0 minutes and 30 minutes post operatively and then after 1, 2, 4, 8, 12 and at 24 hours.

Patients received a rescue dose of analgesic (inj Paracetamol (PCM) 1g; i.v. slowly) on demand or if the VAS>4. Subsequent dose of PCM was repeated for pain only after 6 hours. If patient complained of pain before this period, inj diclofenac sodium 75mg i.v. was given. The time to first rescue analgesic (PCM), total number and doses of PCM in 24 hours were recorded. Total no of patients requiring Inj diclofenac and total dose of diclofenac used were also recorded. Incidence of adverse effects like drowsiness, anxiety, nausea and vomiting, loss of tendon

reflexes, hypotension, hypertension, tachycardia, bradycardia, shivering, delayed extubation, shoulder pain, shallow breathing, delayed extubation, tingling and numbness were recorded. Patients with sedation scale of ≥3 were considered as sedated. Inj ondansetron 4mg i.v. was given for nausea and vomiting.

Recovery variables (Time to start unassisted ambulation, time of oral intake and time of return of bowel function) were recorded at 6,8,12 and 24 hours preoperatively. Time of return of bowel function was defined as presence of intestinal sound or first passage of flatus. At the time of discharge, satisfaction scores were recorded for patients and surgeons as excellent (4), good (3), satisfactory (2) and not satisfactory (1).

This study was aimed to compare the effects of intraperitoneal instillation of dexmedetomidine versus magnesium sulphate with levobupivacaine after laparoscopic cholecystectomy. Primary outcomes were comparison of post-operative analgesia in terms of; pain assessment using Visual Analogue Scale [VAS] and time to request for first rescue analgesia [TFA] along with total number and dose of rescue analgesics in 24 hours. Secondary objectives were to measure; Haemodynamic variables, Ramsay Sedation Score, recovery variables, adverse effects of study drugs and satisfaction score of patient and surgeon.

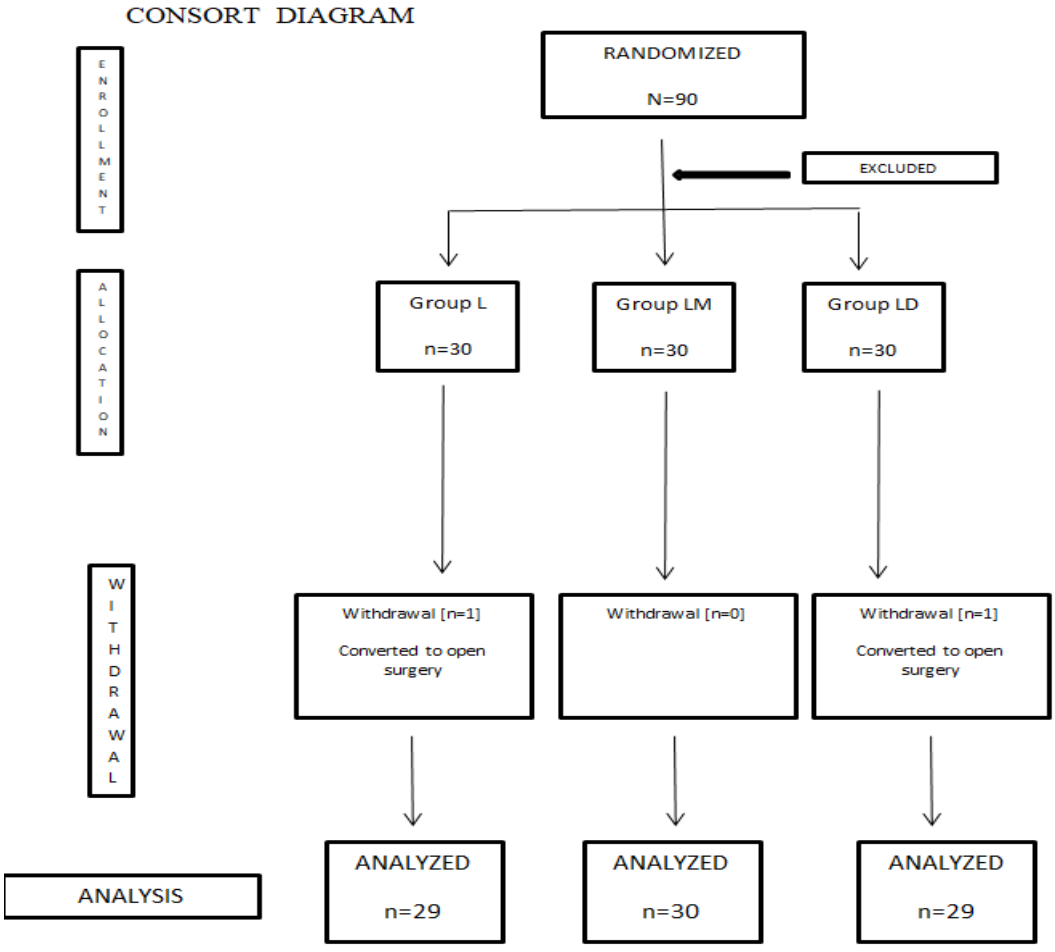

Figure 1: Consort flow diagram showing allocation of patients at different stages of the study

Results

Total 90 patients were enrolled for the study and randomized into three groups (Group L, Group LM, and Group LD) of 30 patients each. One patient out of 30 patients in group L and 1 patient from group LD was

excluded from the study so total of 29, 30 and 29 patients were analysed in group L, LM and LD respectively. (Figure 1)

In this study, all three groups were comparable regarding age, weight, height ,ASA grade, duration of surgery, anaesthesia and pneumoperitoneum (p>0.05) (Table 1)

VAS score for abdominal pain was assessed at rest, on movement as well as for shoulder pain at various time intervals till 24 hours. It was found that Group LD showed lower VAS at all time intervals than other two groups except at 4 hours (p<0.001). The increased VAS score in LD group at 4 hours as compared to other groups showed time to request for first rescue analgesic in LD group while other groups received rescue analgesics earlier than 4 hours. (Table 2)

The time (minutes) to first rescue analgesic requirement was prolonged in group LD (269.09±54.76 min) as compared to group LM (170±57.28 min) and group L (63.10±28.08 min) which was found to be highly significant (p<0.001).Total number and dose of rescue analgesic required in 24 hours was lowest in group LD as compared to group LM and group L which was statistically highly significant (p<0.001). Similarly number of patients' required additional analgesia with inj diclofenac sodium 75mg was found to be highest in group L, followed by group LM and least in group LD (P). (Table 3)

Intraoperative changes in HR, SBP, DBP and MAP were statistically insignificant among three groups (p>0.05). (Figure 2, 3)

In current study RSS≥ 4 was considered sedated. RSS was found to be significantly high in group LD for initial 60 minutes post-operatively (p<0.001) and then after no significant difference was observed in sedation score till 24 hours in three groups (p>0.05)

Post-operative recovery variables like time to start oral intake, unassisted ambulation, return of bowel function and total hours of hospital stay were comparable.(p>0.05)

Incidence of various adverse effects were comparable among three groups (p>0.05). Number of cases of drowsiness(13.79%)and hypotension (6.89%) were observed only in group LD while group LM and L showed no such incidences however it was found to be statistically insignificant(p>0.05). Number of cases of nausea, and vomiting were higher in group L (13.79%) than group LM (6.67%) and LD (6.89%). Delayed extubation was observed only in 2(6.67%) patients of group LM. Four patients (13.79%) in group L complained of postoperative shoulder pain while it was not noted in other two groups (p>0.05).

In present study 51.72% surgeons experienced excellent satisfaction regarding postoperative analgesia in group LD patients while it was 30% in group LM and 0% in group L (p<0.001),. All surgeons were satisfied in group LD. Only 1 surgeon was not satisfied in group LM that may be due to delayed extubation in this group while 3(10.34%)surgeons were not satisfied in group L(p=0.125).

It was found that most of the patients experienced excellent satisfaction in group LD (48.28%) whereas it was 30% in group LM while 0% in group L(p<0.001). However all patients were satisfied in group LD and LM except 5 (17.24%) patients in group L which was found to be statistically significant (p<0.001).

Table 1: Comparison of demographic data and baseline parameters in three groups

Data	Group L (n=29)	Group LM (n=30)	Group LD (n=29)	p value
	Mean±SD	Mean±SD	Mean±SD	
Age (yrs)	44.87±14.05	44.93±9.91	46.50±11.72	>0.05
Sex (M/F)	12/18	8/22	7/23	>0.05
Height (cm)	158.07±7.19	159.57±8.65	158.69±9.45	>0.05
Weight (kg)	62.53±8.62	57.96±6.36	60.67±6.56	>0.05

ASA grade (1/2)	20/10	24/6	20/10	>0.05
Duration of surgery(min)	84.00±26.70	83.43±26.00	84.67±20.84	>0.05
Duration of anaesthesia(min)	102.27±27.69	103.50±27.66	103.33±22.57	>0.05
Duration of pneumoperitoneum (min)	70.47±23.80	72.54±21.26	70.83±18.90	>0.05

Data are mean ± SD, p>0.05 = Non significant(NS)

Table 2: Comparison of Visual Analogue Scale in three groups

Time	Abdominal pain at rest, on movement andShoulder pain	Group L (n=29) Mean ±SD	Group LM (n=30) Mean ±SD	Group LD (n=29) Mean ±SD	p value
0 (Baseline)	At rest	2.76±0.44	2.47±0.51	2.38±0.56	<0.01(S)
	On movement	3.00±0.00	2.90±0.31	2.83±0.38	<0.05(S)
	Shoulder pain	2.79±0.41	2.53±0.57	2.52±0.57	<0.05(S)
30 min	At rest	3.07±0.46	2.40±0.50	2.31±0.47	<0.001(HS)
	On movement	3.14±0.74	3.00±0.00	2.69±0.47	<0.001(HS)
	Shoulder pain	2.97±0.42	2.33±0.48	2.07±0.26	<0.001(HS)
60 min	At rest	3.21±0.62	2.60±0.56	2.48±0.51	<0.001(HS)
	On movement	3.62±0.78	3.13±0.43	2.86±0.35	<0.001(HS)
	Shoulder pain	2.69±0.54	2.17±0.53	1.93±0.37	<0.001(HS)
2 hr	At rest	3.00±0.65	3.07±0.58	2.79±0.49	>0.05(NS)
	On movement	3.34±0.90	3.40±0.67	3.03±0.33	>0.05(NS)
	Shoulder pain	2.45±0.57	2.03±0.49	1.97±0.33	<0.001(HS)
4 hr	At rest	2.66±0.86	3.30±0.79	2.97±0.78	>0.05(NS)
	On movement	3.21±0.98	3.83±0.70	3.90±0.90	<0.001(HS)
	Shoulder pain	2.45±0.63	1.90±0.66	1.83±0.60	<0.001(HS)
8 hr	At rest	2.83±0.66	2.50±0.86	2.28±0.70	>0.05(NS)
	On movement	3.62±0.73	3.23±0.73	2.90±0.67	<0.001(HS)
	Shoulder pain	2.14±0.64	1.47±0.68	1.38±0.56	<0.001(HS)
12 hr	At rest	2.55±0.51	2.37±0.81	1.93±0.65	>0.05(NS)
	On movement	2.76±0.64	2.87±0.68	2.52±0.69	>0.05(NS)
	Shoulder pain	1.93±0.53	1.13±0.35	1.10±0.31	<0.001(HS)
24 hr	At rest	1.86±0.52	1.53±0.63	1.03±0.42	<0.05(S)
	On movement	1.86±0.52	1.83±0.59	1.28±0.45	<0.001(HS)
	Shoulder pain	1.59±0.63	1.0±0.26	0.69±0.47	<0.001(HS)

Data = Mean ± SD; p>0.05 = Non significant (NS) p<0.05 = significant (S), p<0.001=highly significant (HS)

Table 3: Comparison rescue analgesia in three groups

Rescue analgesic Injparacetamol	GROUP L (n=29) Mean ±SD	GROUP LM (n=30)\ Mean ±SD	GROUP LD (n=29) Mean ±SD	P value
Time to request for 1st rescue analgesia	63.10±28.08	170±57.28	269.09±54.76	<0.001

(PCM) (min)				
Total no. of rescue analgesic (PCM) doses in 24 hr (n)	1.90±0.49	1.40±0.50	0.83±0.54	<0.001
Total dose of rescue analgesic (PCM) doses in 24 hrs (mg)	1896.55±488.79	1400.00±498.27	827.59±539.11	<0.001
No. of patients who required inj Diclofenac sodium	14 (48.27%)	10 (33.33%)	4 (13.79%)	<0.05
Total dose of Diclofenac used (mg)	36.21±38.14	25.00±35.96	10.34±26.32	<0.05

Data = Mean ± SD; p<0.001=highly significant (HS)

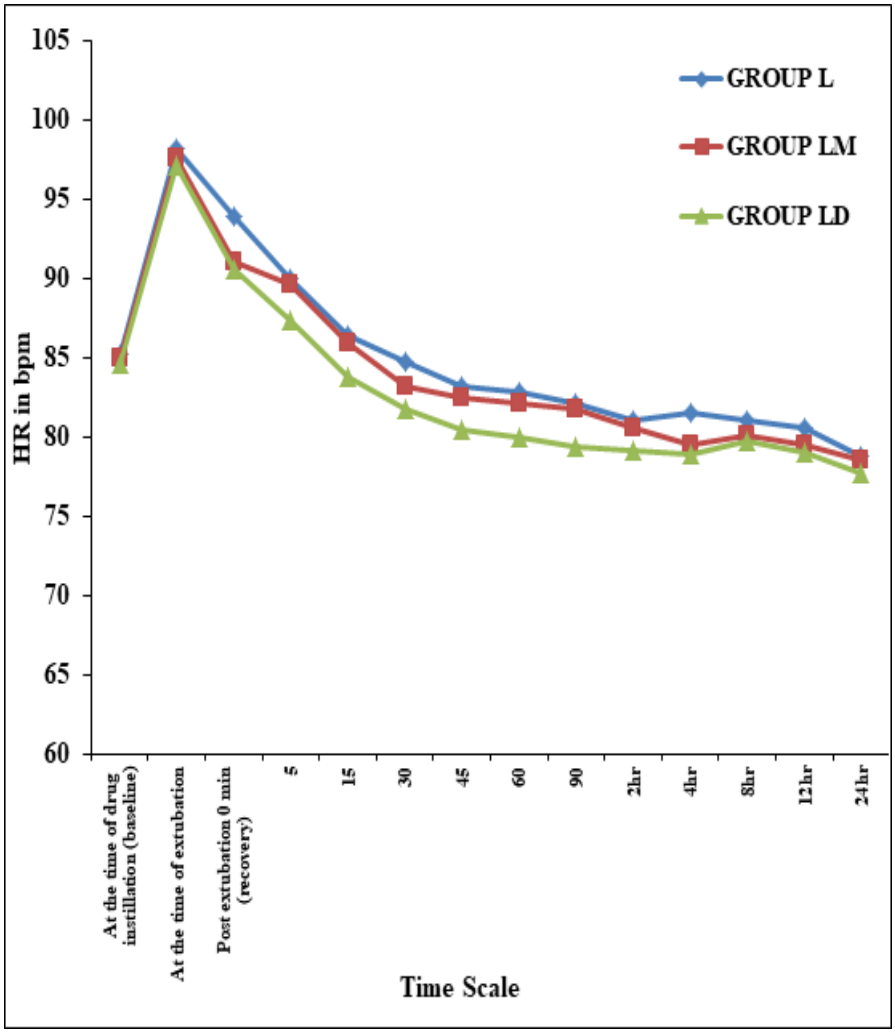

Figure 2: Comparison of Heart Rate (HR) between three groups

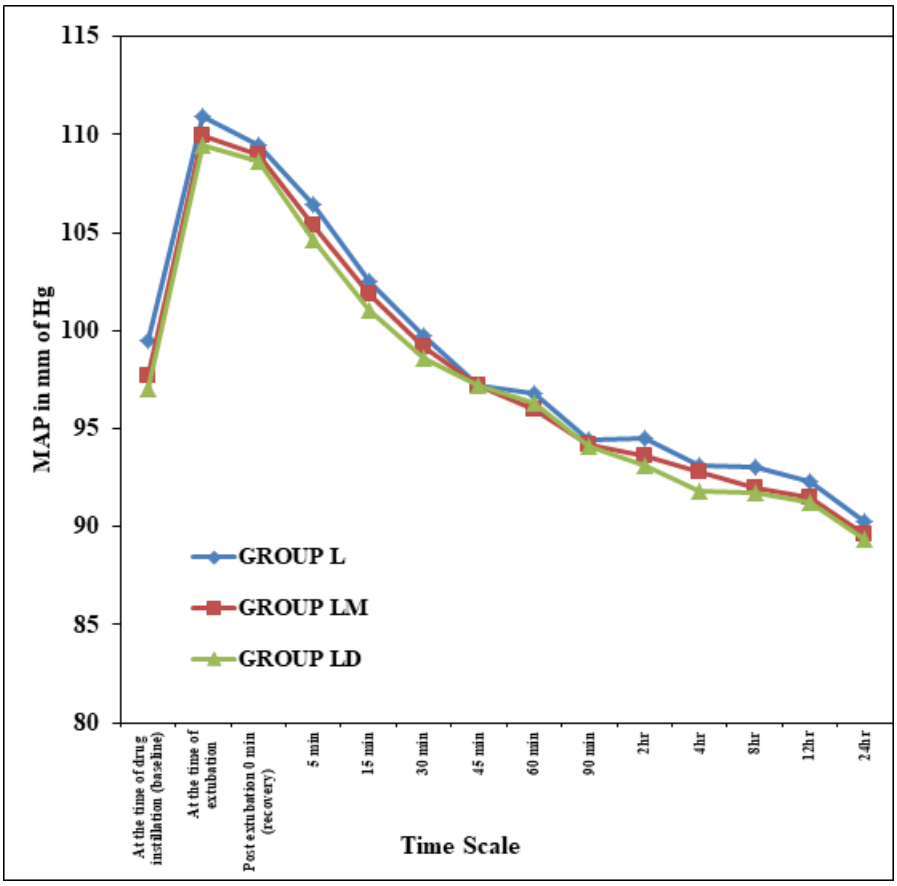

Figure 3: Comparison of Mean Arterial Pressure (MAP) between three groups

Discussion

Laparoscopic cholecystectomy is a preferred surgical technique cholelithiasis due to many advantages over open surgery. Despite all the benefits post-operative pain remains a major challenge and requires multimodal technique likewound infiltration with local anaesthetic, Transversus abdominis plane block (TAP Block), neuraxial blocks, opioids, acetaminophen, non-steroidal anti-inflammatory drugs, and cyclooxygenase-2-specific inhibitors. Analgesic adjuncts such as steroids, ketamine, α-2 agonists, and anticonvulsants to alleviate postoperative pain is always helpful to enhance the quality of analgesia, recovery and reduce the requirement of opioids and side effects. [9]

Intraperitoneal instillation of local anaesthetics (LA) is one of the technique which blocks the visceral nociception. [10] Various adjuvants have been added to LA to improve their anti-nociceptive efficacy.

In present study age, sex, height, weight, ASA grade, duration of surgery, anaesthesia and pneumoperitoneum were comparable among three groups ($p>0.05$) which was similar to other studies. [11-13]

Magnesium sulphate and dexmedetomidine both are known for their effects in attenuating catecholamine response to various painful stimuli like laryngoscopy, surgical pain and other procedural pain. Magnesium sulphate blocks the release of catecholamines from both adrenergic nerve terminals and the adrenal glands. Magnesium reduces the calcium influx to the cell and also antagonizes NMDA receptors which decrease both somatic and visceral pain.

Dexmedetomidine is an alpha-2-adrenergic agonist. Presynaptic activation of the $\alpha_2$adrenoceptor inhibits the release of norepinephrine, terminating the propagation of pain signals. Postsynaptic activation of α_2 adrenoceptors in the central nervous system (CNS) inhibits sympathetic activity

and decreases the blood pressure and heart rate. [14]. It does not affect the ventilator response to carbon dioxide and hence provides respiratory stability and does not lead to respiratory depression. [15] Levobupivacaine is a pure S (-) enantiomer of racemic bupivacaine. It exerts its pharmacological actions through reversible blockade of neuronal sodium channels. It has a lower risk of cardiovascular and central nervous system toxicity. [16]

Analgesic efficacy of dexmedetomidine and magnesium sulphate in combination with different local anaesthetics has been proved to present with various results. [11,13,17-19]

In this study patient in group L experienced more pain with higher VAS score at various time intervals (from the time of extubation till 24 hours) as compared to the other two groups. At certain time intervals the patients in group LD and LM showed more VAS as compared to group L which may be due to difference in their time to request for rescue analgesics. In accordance Pati BK et al [17] and Chiruvellaet al [18] also observed that VAS scores significantly decreased in patients who received dexmedetomidine with LA for intraperitoneal instillation in laparoscopic cholecystectomy. Yadava et al [19] and Badawy et al [20] reported lesser VAS with magnesium sulphate added to LA for Intraperitoneal instillation in laparoscopic cholecystectomy.

Previous studies [12-14, 18-20] showed that addition of adjuvant to the local anaesthetic increases the duration of analgesia, as well as decrease the requirement of analgesics postoperatively. Pati BK et al [17] and Chiruvella S et al [18] observed delay in TFA (Time to first recue analgesic) with dexmedetomidine and Maharajan et al [21] and Sadaqa W et al [8] reported that magnesium sulphate delays the TFA when used as an adjuvant to bupivacaine. In contrast Badawy AM et al [20] reported delay in TFA (6±1.4hr) in patients who received magnesium sulphate which is almost double of the time observed in our study. This difference could be due to the fact that they used higher volume of drugs (bupivacaine0.5%; 40ml with magnesium sulphate; 40mladded to 40 ml of normal saline to make a total volume of 120ml).

In present study total number of rescue analgesic doses (inj paracetamol or inj diclofenace) required in 24 hours were highest with bupivacaine plain (Group L) as compared to adjuvant groups (Group LD and LM; $p<0.001$) which shows the synergistic property of adjuvants to levobupivacaine for analgesia. These findings are supported by the studies done by Pati BK et al [17], Chiruvella S et al [18] , Yomna M et al [22] and Shukla U et al [23] in which requirement of analgesics were least in patients who received dexmedetomidine as an adjuvant to LA. Similar to our study BK Pati [17] also observed that total dose of rescue analgesic (inj paracetamol 1g) required in 24 hours was lower in dexmedetomidine group than control group (1.2± 0.8 g vs 3.6±0.4 g). Shukla U et al [23] and Chiruvella S et al [18] also found that total dose of analgesic required in 24 hours was significantly less in dexmedetomidine group as compared to plain LA group. Yadava et al [19] and Maharajan et al [21] studied the analgesic effects of bupivacaine alone and with magnesium sulphate and found that total dose of tramadol required was significantly higher in bupivacaine group as compared to magnesium sulphate group.

In current study no significant change in HR and BP was observed after giving study drugs in three groups at various time intervals ($p>0.05$). This is supported by Yadava et al [19] where intraperitoneal instillation of drug did not result in significant changes in heart rate and MAP from baseline. However Zarrif P et al [24] observed significant drop in HR and MAP with dexmedetomidine and magnesium sulphate group as compared to control (normal saline) group in their study. This different result can be attributed to different route of drug administration (intravenous) in higher concentration in their study as compared to present study (intraperitoneal). The findings of these studies strengthen the

technique of Intraperitoneal drug administration for post-operative analgesia with minimal hemodynamic variations.

Dexmedetomidine acts at α_2-receptors both peripherally and centrally. Activation of receptors centrally at the level of locus ceruleus attenuates excitatory response of central nervous system and produces sedation and anxiolysis.We observed significantly higher RSS in patients who received dexmedetomidine as compared to other two groups for initial 60 minutes ($p<0.001$).On subsequent time intervals sedation scores were comparable among three groups. ($p>0.05$) Abdelnaim HE et al [25] and Abd El Hamid AM et al [26] also observed significantly higher RSS when dexmedetomidine (70 mcg) was added to bupivacaine (0.25%) than magnesium sulphate (1gm) added to bupivacaine till initial 120 minutes postoperatively although they used study drugs for wound infiltration before skin incision in hernia repair surgeries. Some studies reported that when these adjuvants (dexmedetomidine and magnesium sulphate) were used epidurally with LA, the patients in dexmedetomidine showed higher sedation scores. [27, 28]

In current study incidence of nausea, vomiting was comparable in three groups, although number of patients who had these symptoms was higher in group L. Similarly, most of the studies reported nausea and vomiting as a common adverse effect after laparoscopic cholecystectomy. [18,19,24] In accordance to this study Chiruvella S et al [18] also observed nausea and vomiting in 10(16.66%) patients of plain ropivacaine group (R)while it was 4 (6.67%) in dexmedetomidine group (RD). Lower incidence of nausea and vomiting in magnesium sulphate group may be attributed to inhibitory action of $MgSO_4$ on NMDA receptors found in emetic pathways and structures related with the final common pathway for vomiting. [19]

Shoulder pain is a common outcome after laparoscopic cholecystectomy due to phrenic nerve neuroprexia because of pneumoperitoneum with CO_2. In this study shoulder pain was noted only in group L (n=4, 13.79%). Studies done by Shukla U et al [23], Chiruvella S et al [18] also showed a decrease in incidence of shoulder pain when adjuvants were added to local anaesthetics for intraperitoneal instillation. Similarly Acharya R et al [29] also noticed shoulder pain in 2 patients in ropivacaine group while it was not observed in dexmedetomidine group.

Incidence of drowsiness was observed only in group LD (n=4, 13.79%) while it was not noticed in any patients of other two groups. ($p>0.05$).

Delayed extubation was observed in 2 patients of magnesium sulphate group (6.67%) in present study which could be due to the potentiating effect of $MgSO_4$ on neuromuscular blockade. Ali RM et al [30] also reported delayed time of extubation when MgSO4 was given intraperitoneally as compared to control group (saline).

In current study we monitored various recovery variables like time to start oral intake, unassisted ambulation, return of bowel function and total hours of hospital stay. These variables were not found to be significantly different among three groups ($p>0.05$). These findings are in consistence with the studies done by Sarvestani AS et al [31] and Tapno N et al [14] where they also found that the groups were comparable with regards to recovery variables ($p>0.05$).

In present study 51.72% surgeons experienced excellent satisfaction regarding postoperative analgesia in group LD patients while it was 30% in group LM and 0% in group L ($p<0.001$),. All surgeons were satisfied in group LD. Only 1 surgeon was not satisfied in group LM that may be due to delayed extubation in this group while 3(10.34%)surgeons were not satisfied in group L($p=0.125$) which may be due to inadequate analgesia in those patients. Donadi PK et al [32] found no significant difference in satisfaction score when they used bupivacaine alone and with magnesium sulphate for local infiltration after lumbar laminectomy. Parikh DA et al [33] reported

significantly better surgeon satisfaction score after local infiltration of dexmedetomidine as compared to fentanyl and midazolam for tympanoplasty surgery.

It was found that most of the patients experienced excellent satisfaction in group LD (48.28%) whereas it was 30% in group LM while 0% in group L($p<0.001$). However all patients were satisfied in group LD and LM except 5 (17.24%) patients in group L were not satisfied, as the VAS scores were increased within one hour postoperatively and required additional doses of analgesics ($p<0.01$). These findings are supported by Donadi PK et al [32] and Parikh DA et al [33].

Regarding satisfaction score, the results of above mentioned studies show that dexmedetomidine is better adjuvant to local anaesthetics than magnesium sulphate for postoperative analgesia. [34]

In present study, the blood magnesium sulphate levels were not estimated in post-operative ward. This could be done to adjust the dosage of magnesium sulphate according to its safe levels for intraperitoneal instillation. Further studies can be done with different drugs, varying concentrations of local anaesthetics and different doses of dexmedetomidine and magnesium sulphate according to individualized pain perception. This modality could be combined with other pain relieving techniques to enhance the efficacy of pain management. This study was done on patients of ASA grade I and II. Larger studies can be done to see the efficacy of these treatment modalities in elderly patients and patients with comorbidities to determine the safety and efficacy of dexmedetomidine and magnesium sulphate.

Conclusion

In conclusion, intraperitoneal instillation of local anaesthetic drugs is a safe and effective method for post-operative analgesia after laparoscopic cholecystectomy. When two adjuvants (dexmedetomidine and magnesium sulphate) were compared with 0.25% levobupivacaine, dexmedetomidine showed significantly longer duration of post-operative analgesia with minimal side effects and greater satisfaction as compared to magnesium sulphate.

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