*Original Research Article*

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# Study of Intraperitoneal Bupivacaine-Tramadol with Bupivacaine-Magnesium Sulphate for Pain Relief after Laparoscopic Cholecystectomy

**Samba Siva Rao Jupalli[1], K Ravi Nayak[2]**

[1]Associate Professor, [2]Assistant Professor, Department of Anesthesiology, Gandhi Medical College, Secunderabad, Telangana 500003, India.

**Abstract**

*Introduction:* Cholecystectomy is surgical removal of the gall bladder. Intraperitoneal administration of other drugs along with the local anesthetics will reduce the consumption of supplementary postoperative analgesic medication. *Aims:* To compare between $MgSO_4$ and Tramadol when used along with Intraperitoneal Local Anesthetics (IPLA) by instillation of drug for postoperative pain relief in terms of Visual Analog Scores. *Materials and Methods:* Prospective analytical study in Sixty adult patients of Class I and Class II as per American Society of Anesthesiology (ASA) of either sex were posted for elective laparoscopic cholecystectomy. These patients participated in prospective open randomized study for postoperative pain relief after laparoscopic cholecystectomy. *Results:* Bupivacaine along with Magnesium sulphate instillation significantly reduced VAS pain scores over 24 hrs. Prolonged duration of analgesia was noted with Magnesium sulphate. Total analgesic required over 24 hrs was less with Magnesium use. No signs of drug allergy and toxicity were observed. *Conclusions:* Bupivacaine and Magnesium sulphate are safe and efficacious in reducing postoperative pain following intraperitoneal instillation in laparoscopic surgeries. Thus, the intraperitoneal instillation of Bupivacaine-$MgSO_4$ combination provides good analgesia in first 24 hours after surgery, with longer duration of pain free period.

**Keywords:** Cholecystectomy; Intraperitoneal Bupivacaine; Tramadol.

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## Introduction

Cholecystectomy is surgical removal of the gallbladder. It took a significant amount of time before the risk of the procedure was low enough to justify its routine use. The benefits of a minimally invasive procedure were joined with a century long proven treatment of gallbladder disease. Laparoscopy involves insufflation of the abdomen by gas, so, that the endoscope (usually 6–10 mm in diameter) can view the intraabdominal contents without being in direct contact with the viscera or tissues. It is widely practiced now-a-days, because of its potential benefits as compared to conventional open cholecystectomy. Diminished surgical trauma, associated low morbidity, net low-cost of procedure has made laparoscopy, a standard technique for removal of the diseased gallbladder.

Postoperative pain is reduced in laparoscopic, as compared with open traditional cholecystectomy,

**Corresponding Author: K Ravi Nayak,** Assistant Professor, Department of Anesthesiology, Gandhi Medical College, Secunderabad, Telangana 500003, India.

**E-mail:** ravikaramchand@gmail.com

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but effective analgesic treatment after LC has remained a clinical challenge.[1] Patients complain more of a parietal pain after open cholecystectomy, whereas after Laparoscopy mostly visceral pain results. In 17–41% of the patients, pain is the main reason for staying overnight in the hospital on the day of surgery.[2] Postoperative pain associated with laparoscopic cholecystectomy, although less severe and of shorter duration than that after open cholecystectomy, is still a dominating complaint and the primary reason for prolonged convalescence after LC.[3] Characteristically, overall pain after LC carries a high interindividual variability in intensity and duration and is largely unpredictable.

Visceral pain accounts for most of the discomfort experienced in the early postoperative period. Its intensity quickly decreases after the first 24 hours postoperatively. Parietal pain is less intense than visceral pain, owing to the small abdominal incisions and the limited damage to the abdominal wall. Shoulder-tip pain, insignificant during the first postoperative hours, increases thereafter, to become the main complaint on the second day postoperatively. Optimal management of postoperative pain has a potential for shortening of hospital stay and for speeding up of recovery. There are varieties of anesthetic techniques available to control postoperative pain after LC. Administration of intraperitoneal local anesthetic (LA), either during or after surgery, is a common practice by many surgeons as a method of reducing postoperative pain. This technique was first evaluated in patients undergoing gynecological laparoscopic surgery.[4] Injection of LA subcutaneously into the incisional site, into the periportal fascia, and into the muscle and parietal peritoneum to provide pain relief after LC has been documented in the literature. LA can be injected into the peritoneum through the ports created either before the start of surgery or prior to closure. It may be injected over the visceral peritoneum through the trocar site or into the surgical bed after the excision of the organ or under the diaphragm. Injection of subdiaphragmatic LA is given to decrease the incidence of shoulder pain.

Intraperitoneal administration of other drugs along with the local anesthetics will reduce the consumption of supplementary postoperative analgesic medication. Administration of local anesthetic in combination with opioids, steroids dexmedetomidine, ketamine, NSAIDs, tramadol, $MgSO_4$ for the relief of postoperative pain, has already been reported after laparoscopic cholecystectomy.

Effectiveness of local anesthetics, instilled intraperitoneally, solely or mixed with other drugs, has been shown in a number of studies on laparoscopic cholecystectomy, but there is no agreement regarding the dose, concentration, site and manner of administration. Therefore, in our study an effort has been made to compare primarily the antinociceptive effects of $MgSO_4$ with bupivacaine to tramadol with bupivacaine.

## Materials and Methods

Prospective analytical studybetween March 2017 and August 2018 conducted in Osmania General Hospital. Sixty adult patients of Class I and Class II as per American Society of Anesthesiology (ASA) of either sex were posted for elective laparoscopic cholecystectomy. These patients participated in prospective open randomized study for postoperative pain relief after laparoscopic cholecystectomy. After the informed and written consent was obtained, these patients were randomly allocated using computer generated table to one of the Two Groups:

***Group BT*** (30 ml of 0.25% bupivacaine along with 100 mg tramadol) (30 patients)

***Group BM*** (30 ml of 0.25% bupivacaine along with 50 mg/kg of $MgSO_4$) (30 patients)

Dose of bupivacaine not exceeding 2.0 mg/kg BW.

### *Inclusion Criteria*

Age 18–65 years**,** Elective Casesand ASA-I & ASA-II patients.

### *Exclusion Criteria*

Patients with history of allergies to bupivacaine, $MgSO_4$ or tramadol, with acute cholecystitis, Emergency and urgency for surgery, Patient known for hypomagnesemia or $MgSO_4$, Chronic alcoholism, heart block, renal failure and cognitive impairment or mental retardation, progressive degenerative disorders of CNS, Patients with peritoneal drain after surgery.

A thorough examination of the patient was done which included a detailed history, general and systemic examination. The BMI of all the patients was noted. The baseline investigations were done and Other investigations were done as per individual patient assessment and requirement.

All the patients underwent thorough preanesthetic evaluation one day prior to surgery. Clinical assessment with detailed history was taken. All

systems were examined including the airway. The procedure to be carried out was explained and the patients were made familiar with Visual Analog Scale (0–10 cm; 0- no pain and 10- the worst possible pain) and its employment in pain assessment. All the patients were kept nil peroral as perthe fasting guidelines. All of the received Tab. Alprazolam 0.25 mg orally the night before surgery and Tab. Ranitidine 150 mg the night before and on the morning of surgery. A written informed consent was taken.

After confirming adequate starvation for 8 hours, written informed consent, verifying PAC, patient was attached for continuous electrocardiogram monitoring. Preoperative Heart Rate (HR), systolic and diastolic blood pressure and respiratory rate were recorded 5 min before induction (i.e., baseline parameters). An intravenous line was secured and Ringer lactate infusion started.

The patients were premedicated withInjection Glycopyrrolate 0.005 mg/kg IV, Injection Ranitidine 1mg/kg IV, Injection Ondansetron 0.1 mg/kg IV and Injection Midazolam 0.05 mg/kg IV.

Injection Fentanyl 2 mcg/kg IVwas administered for intraoperative analgesia. Anesthesia was induced with intravenous (IV) lignocaine 1.0 mg/kg, propofol 2.0 mg/kg. IV vecuronium 0.1 mg/kg was administered to facilitate endotracheal intubation. Intraoperative anesthesia was maintained with $O_2$: $N_2O$ (40:60), sevoflurane 1–2%, closed circuit with controlled ventilation. Intermittent doses of injection Vecuronium IV was administered for muscle relaxation. The patients were monitored intraoperatively for pulse, blood pressure, oxygen saturation, and end tidal $CO_2$, intraabdominal pressure, urine output and blood loss. All the patients received Ringer Lactate at 5 ml/kg/hr for intraoperative fluid requirements. Intraabdominal pressure was maintained between 12–14 mmHg and end tidal $CO_2$ was maintained between 30–40 mmHg during the period of surgery.

***Operating Technique***

*Position*

Patient with Supine with 15° head up and 15° tilt to left.

*Creating Pneumo-peritonium*

Small infraumbilical incision about 1cm is taken. Then, blunt tip veress needle with safety valve is introduced with the needle pointing towards the sacral promontory. Confirmation of intraperitoneal location of the needle tip is made by the saline drop test and $CO_2$ insufflations is started. Maximum pressure is set at around 12 mmHg and initial flow rate around 1:2 lit/min. Later the rate was increased to 4–6 lit/min. The machine has automatic shut off the gas, if the pressure rises above the maximum pressure set.

*Primary port placement*

It was introduced blindly by a 10 mm trocar with a finger guard, after lifting the abdominal wall. Through this a 10 mm telescope was introduced and a peritoneoscopy was done. The other ports were placed as shown below under vision.

*Dissection of the triangle of calot*

Dissection should be close to gall bladder and to the right of the hepatic duct. Adhesiolysis is done taking care of surrounding structures. Cystic duct and cystic artery are clearly dissected and then clipped. The cystic artery should be doubly clipped.

*Dissection of gall bladder from its bed*

During dissection, gentle traction is applied to the gall bladder, moving it from side to side so that loose areolar tissue can be demonstrated. With a hook or spatula, the dissection was carried down the under surface of the gall bladder. The fundic attachment should be preserved till the end as it helps in the elevation of the gall bladder and the fossa can be inspected for any ooze or blood or bile. Before final detachment of the gallbladder, the cystic artery and duct stumps are reexamined, and a through wash given. Then the gall bladder was detached and held over the liver.

*Extraction of gall bladder*

Through the epigastric port, gall bladder was held with an Ellis forceps at its neck. Care was taken to avoid spillage of stone or billiary sludge. If the gallbladder was tense, it was decompressed by suction and opened to remove the stone. The camera is withdrawn last under vision after final inspection. A drain if required is kept through one of the 5 mm ports. The ports are closed with vicryl and skin stitches. Light dressings are applied.

*Instillation of study drugs*

After the gall bladder was extracted, $15^0$ of head up and left tilt position was removed and $CO_2$ was stopped, $15^0$ of head low and right till position was given. A preaspirated syringe of 30 ml of study drug was instilled in the same position over the gall bladder fossa and right subdiaphragmatic space under direct vision by the operating surgeon. After the drug was instilled the head low and right till position was maintained for the next 10 minutes.

Pneumoperitoneum was completely evacuated by the surgeon before closing port sites by manual compression of the abdomen. At the end of surgery muscle relaxant was reversed with Inj. Neostigmine 0.06 mg/kg IV and Injection Glycopyrrolate 0.01 mg/kg IV. The total duration of surgery was recorded for all the patients. The patients in the both groups were instilled with 30ml of study drug by the same method described above.

In the postoperative period the patients continued to receive intravenous fluid and all the patients were monitored for the following:

*Hemodynamic monitoring:* The pulse rate and the systolic and diastolic blood pressure were recorded for all of the patients every 5 min for the first 20 min after the administration of study drugs and during postoperative period at intervals of 30 min,1 h, 2h,4h, 5h,6h, and 24 h after surgery.

*Respiratory rate monitoring:* The respiratory rate was recorded for all the patients at 0, 2, 4, 8, 12, 18 and 24 hrs after surgery.

*VAS pain score Assessment:* The patients were asked to indicate their pain scores on a 10 cm visual analog pain scale where "0" indicated no pain and "10" indicated worst possible pain. The VAS was recorded at 0, 1, 2, 4, 6, 8, 12 and 24 h after surgery, (Fig. 1).

*Rescue analgesia:* Rescue analgesic (Inj. Paracetamol 1g IV) was administered when the VAS was 3 or when the patient demanded an analgesic. The time taken to the first dose of rescue analgesia and the total dose of rescue analgesics received by each patient were recorded.

*Site of pain:* The site of pain was determined by asking the patient to indicate the site of discomfort. Also, the patient was asked whether he was experiencing shoulder tip pain.

*Associated side effects:* The patients were monitored for side effects such as Nausea and Vomiting (NV), loss of tendon reflex, hypotension (defined as more than 20% reduction of SBP and/or DBP from baseline) rise in temperature, drowsiness, respiratory depression, itching and toxic effects of bupivacaine such as arrhythmias, respiratory depression, and restlessness, tremors, convulsions.

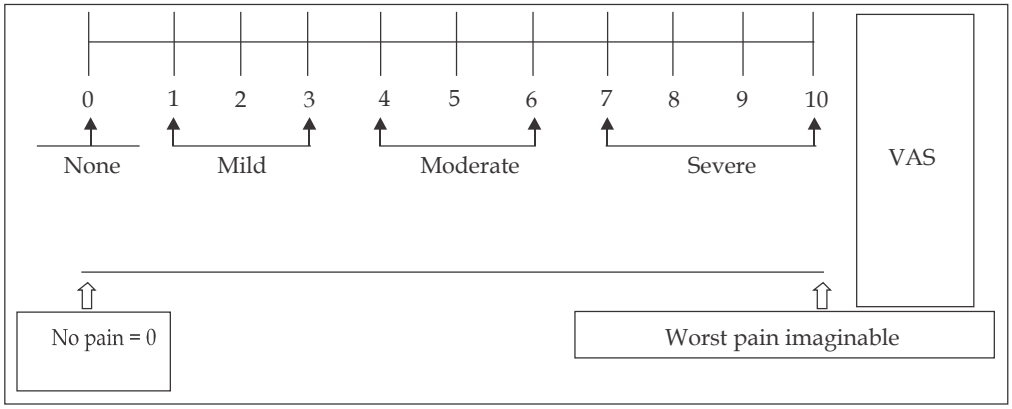


**Fig. 1:** Visualanalog scale

## Results

There was no statistically significant difference in age and weight between the two groups. Both groups had female population in greater proportions,accounting for 60% or more of the total study population in each group (Table 1).

Both the groups were comparable in terms of ASA status of either ASA I or II with 60–70% of the sample falling within ASA I Group (Table 2).

Sample population in both the study groups were comparable with respect to SBP, DBP, MAP, and HR with $p$ - value > 0.05 (Table 3).

Intraoperatively the differences in systolic blood pressure were not statistically significant throughout the period (Fig. 2).

There were no significant differences in diastolic blood pressures in both the groups throughout the intraoperative period (Fig. 3).

In Group BM, heart rate was recorded at 5 min interval and compared with baseline HR and found that the difference was statistically significant ($p$ <

**Table1:** Comparison of demographic details in between the two groups

| Parameters | | Group BM | Group BT | *t*-test |
|---|---|---|---|---|
| Age (years) | Mean | 36.63 | 36.90 | |
| | SD | 9.46 | 9.28 | 0.3891 |
| Weight (in kgs) | Mean | 66.96 | 65.33 | |
| | SD | 6.16 | 4.81 | 0.258 |
| Gender | | | | |
| Male | No. of patients | 12 | 10 | |
| | Percentages | 40% | 33.3% | 0.688 |
| Female | No of patients | 18 | 20 | |
| | Percentages | 60% | 66.6% | |

0.05). After instillation HR was slightly less than baseline and stable thereafter, in Group BM. There were no significant differences in heart rate in both the groups during intraoperative period (Fig. 4).

No significant differences were noted in SBP trends postoperatively between both the groups. No Significant differences in DBP were observed postoperatively. Postoperatively there were no significant differences between both the groups in terms of HR in the first 24 hrs.

Mean VAS scores though statistically significant at all intervals, lower in first 3hrs after instillation.

**Table 2:** ASA status comparision

| ASA physical status | Group BM | Group BT | *p* - Value (Fischer's Exact Test) |
|---|---|---|---|
| ASA I | 21(70%) | 18(60%) | |
| ASA II | 9(30%) | 12(40%) | 0.59 |
| Duration of surgery | 59.73/+-9.74 | 59.27/+-10.72 | 0.86 Not significant |
| Duration of anaesthesia | 76.73/+-10.41 | 74.70/+-8.19 | 0.40 Not significant |

**Table 3:** Preoperative hemodynamic data

| Parameters | SBP | DBP | MAP | HR |
|---|---|---|---|---|
| Group BM | 119.57±10.4 | 77.2±9.99 | 91.3±8.52 | 90.7±11.88 |
| Group BT | 123.07±10.5 | 78.53±7.95 | 93.5±6.98 | 92.3±12.94 |
| *p* value | 0.2708 | 0.57 | 0.28 | 0.62 |

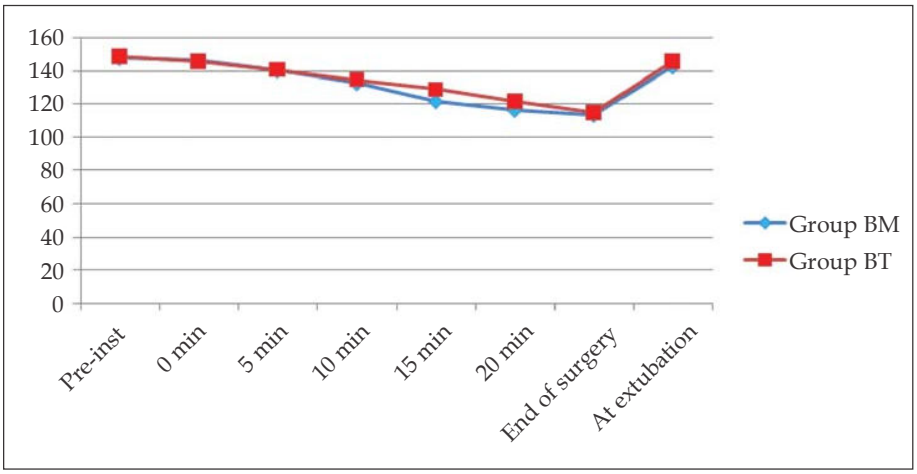


**Fig. 2:** Intraoperative systolic blood pressure

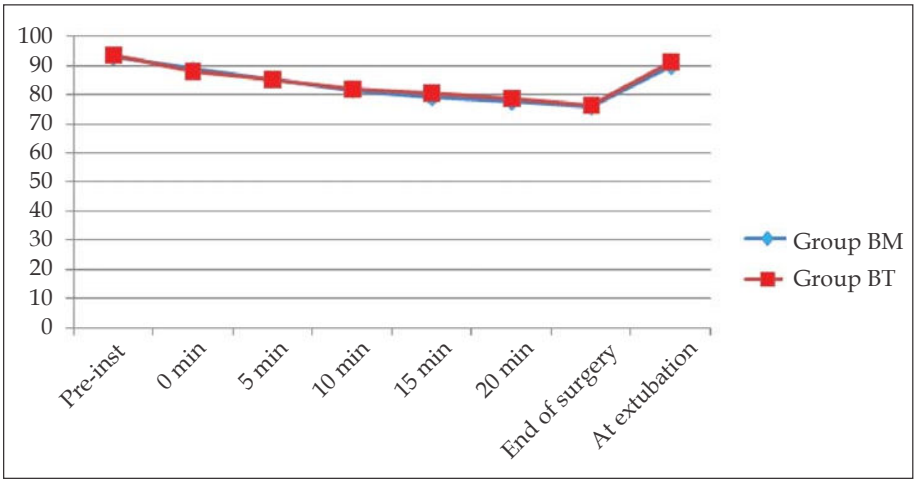


**Fig. 3:** Intraoperative diastolic blood pressure trend

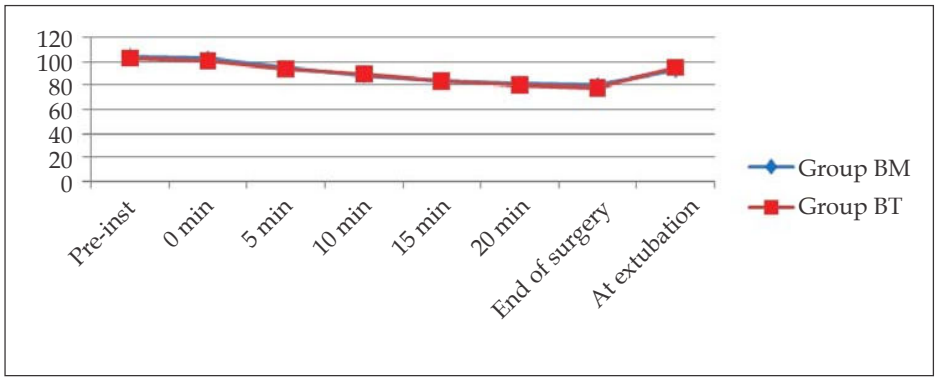


**Fig. 4:** Intraoperative heart rate trend between two groups

**Table 4:** VAS pain scores(values expressed in terms of mean and standard deviation and *p* values).

| **Time interval** | **VAS score** | | |
|---|---|---|---|
| **Post OP** | **Group BM** | **Group BT** | ***p* - Value** |
| 0 min | 1.73 ± 1.11 | 3.36 ± 1.56 | 0.0117 |
| 30 min | 2.03 ± 0.99 | 3.86 ± 1.19 | 0.0001 |
| 1 hr | 2.26 ± 1.14 | 3.43 ± 1.30 | 0.0005 |
| 2 hr | 2.5 ± 1.01 | 3.9 ± 1.21 | 0.0001 |
| 3 hr | 2.63 ± 1.32 | 4.4 ± 0.81 | 0.0001 |
| 4 hr | 1.96 ± 0.92 | 4.76 ± 1.43 | 0.0001 |
| 6 hr | 2.19 ± 0.80 | 2.96 ± 1.12 | 0.0035 |
| 8 hrs | 1.83 ± 1.14 | 2.76 ± 0.97 | 0.0005 |
| 12 hrs | 2.23 ± 1.25 | 2.93 ± 1.04 | 0.001 |
| 24 hrs | 1.77 ± 0.82 | 2.67 ± 1.42 | 0.022 |

It Increased after 3hrs and statistically significant. There was a slight increase in VAS scores 3 hrs of postoperative period in both the groups probably due to increasing intensity of pain and waning off of the effect of Bupivacaine. At 24 hrs the scores were reduced indicating reduction in intensity of postoperative pain (Table 4).

Mean Time taken for administration of rescue analgesia was 8.24 ± 0.51 hrs in Group BT and 4.06 ± 0.0.93 hrs in Group BM which was statistically significant ($p$ = 0.0001). Earliest and longest time of administering rescue analgesia in Group BM was required 7 and 9.1 hrs respectively and in Group BT was 2.2 and 6.2 hrsrespectively (Fig. 5).

Mean of Total rescue analgesic dose required in Group BM was 1.27 ± 0.61 mg *vs* 2.27 ± 1.14 mg in Group BT which was not very statistically significant ($p$ = 0.06). However, a total of 15 individuals in Group BT (50% of study group) and 8 individuals in Group BM (26.6% of study group) required 2$^{nd}$ dose of rescue analgesia in 24 hrs. This probably reflects the difference of efficacy in analgesia provided by Magnesium and Tramadol. There is no incidence of PONV in Group BM *vs* 13.3% in Group BT and was statistically not significant. ($p$ - value: 0.54). There are no complication in both groups (Fig. 6).

## Discussion

Laparoscopic surgeries being minimally invasive surgeries are associated with a relatively minor surgical trauma. They also have evolved as day

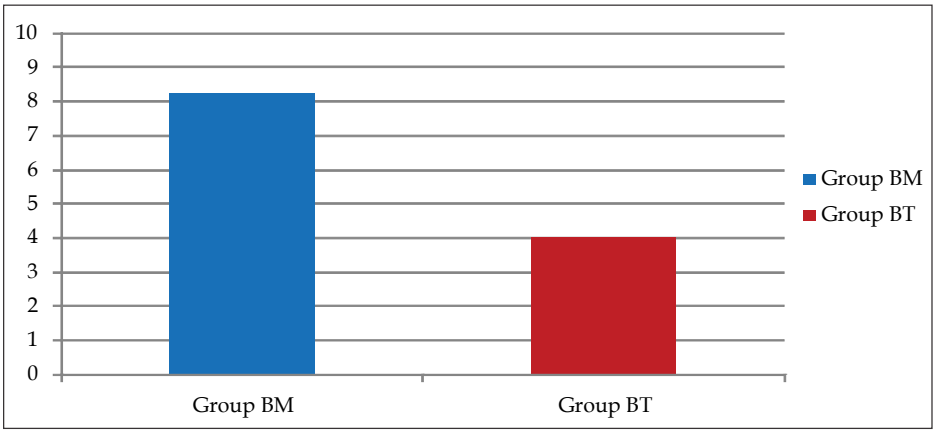


**Fig. 5:** Time required for first rescue analgesic (hrs) and total analgesic dose (Paracetamol) values expressed in terms of mean and standard deviation.

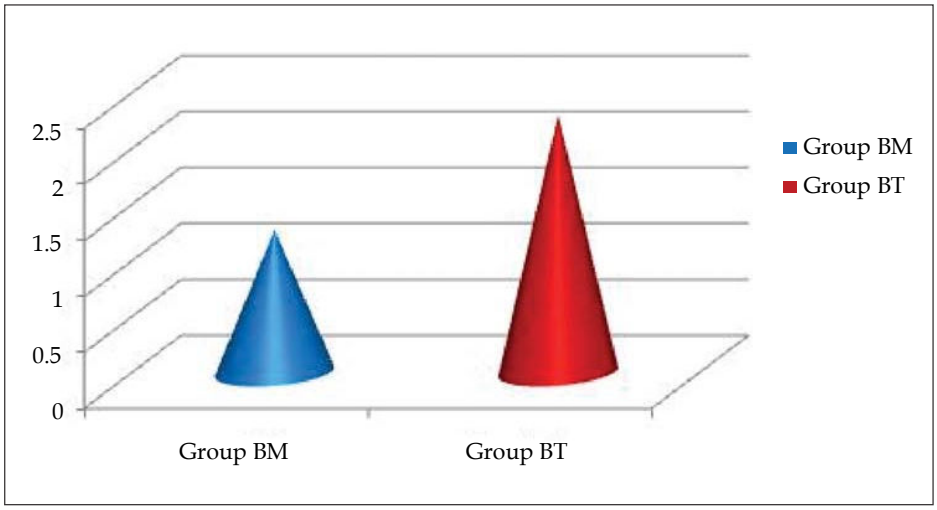


**Fig. 6:** Total dose of rescue analgesic

care surgeries owing to significantly reduced stress responses, postoperative pain and opioid requirements, improved postoperative pulmonary function, reduced overall morbidity resulting in rapid recovery, earlier ambulation thus, a reduced risk of DVT and a rapid return to normal activities. Top priorities for successfully discharging patients of day care surgeries are the four A's: Alertness, Analgesia, Ambulation and Alimentation. Excessive pain, nausea and vomiting and fatigue will delay the discharge. The success of fast tracking depends on effective pain management by simple techniques.

Postoperative pain in laparoscopic surgeries is multi-factorial in origin. Intraperitoneal infusion of normal saline at the end of the procedure is effective way to remove the carbon dioxide from the subdiaphragmatic area. The carbon dioxide gas between liver and diaphragm increases the space between them, producing tension of the peritoneal reflection and shoulder pain through mechanical irritation of the right phrenic nerve.The $37^0$C temperature of the infused normal saline improves the hypothermia caused by carbon dioxide gas used for pneumoperitoneum. The heating of the peritoneum reduces the freezing peritoneal irritation and thus abdominal and shoulder pain.

Bhardwaj et al., conducted study in patients undergoing laparoscopic cholecystectomy. He instilled 20 ml 0.5% bupivacaine only at the end of surgery in the Trendelburg position. Postoperatively they assessed for vital signs (heart rate, blood pressure and respiratory rate), pain scores (VAS, VRS and shoulder pain) and analgesic consumption. They found that it reduced postoperative cholecystectomy pain and analgesic consumption.[5] There is a contradictory opinion about when to administer the local anesthetic. Few authors suggested early instillation of intraperitoneal local anesthetics as it provides better control of postoperative pain when compared with instillation at the end of the surgery, but few others have contradicted this and suggested otherwise. In our study, we have instilled the study drugs intraperitoneally at the end of the surgery.

The efficacy of local anesthetic instillation in pain control has been demonstrated in numerous other studies in laparoscopic cholecystectomy. Some used bupivacaine 0.125% while others used 0.25% bupivacaineand found a good postoperative pain relief. Joris et al. studied the characteristics of pain after laparoscopic cholecystectomy and the effect of intraperitoneal instillation of 80 ml of 0.125% bupivacaine with adrenaline. A systematic review and meta-analysis for the effect of intraperitoneal local anesthetic in laparoscopic cholecystectomy was done and 12 out of 24 studies reported a significant improvement in pain during early postoperative period.[6] The results correlate well with the results claimed in our study.The present study, hypothesized that the use of more than one modality to prevent postoperative pain may be more efficacious, (Tables 1–3).

The underlying mechanism of attaining analgesia by $MgSO_4$ is thought to be due to the reduction of calcium influx to the cell by magnesium. Magnesium also antagonises N-methyl-D-aspartate (NMDA) receptors, which are critical for neuronal signalling as well as pain processing in the central nervous system, thus reducing postoperative pain as both somatic and visceral pain fiber are blocked.Conventionally in laparoscopic cholecystectomy, $MgSO_4$ is given in various routes such as an IV bolus, continuous infusion, epidural infusion and in the subarachnoid space. Recently it has been shown that intraperitoneal local anesthetics alone or in addition to $MgSO_4$ improved postoperative pain after laparoscopic cholecystectomy.

A second reason to choose this combined regimen is that the effectiveness of individual analgesics was enhanced by the additive or synergistic effect of two or more drugs that relieve pain by different mechanisms

Buyukakilli B et al. carried out a study on frog sciatic nerves and found a better conduction blockwith $MgSO_4$ plus bupivacaine but not with Tramadol and bupivacaine.[7] AdjuvantTramadol and Magnesium sulphate potentiates the impulse inhibition by local anesthetics supporting our findings. Golubovic et al. in their study reported that the analgesic effects of the intraperitoneal injection of bupivacaine and/or tramadol in patients with laparoscopic cholecystectomy were both effective for the treatment and management of pain after the surgery and there was less requirement of postsurgical analgesics.[8] In our study also, we found similar results with mild to moderate pain in the patients. However, in the patients with bupivacaine plus Magnesium sulphate, the pain was significantly lower, with not even one patient experiencing more than mild pain and discomfort.

Akinci SB et al. compared the effectiveness of tramadol given IV and intraperitoneally regarding the postoperative analgesia after laparoscopic cholecystectomy and found that IV tramadol produced a better postoperative analgesia than intraperitoneal dose of tramadol.[9] Shukla U et al.

compared the effectiveness of bupivacaine alone, bupivacaine with tramadol and intraperitoneal instillation of bupivacaine in combination with dexmedetomidine. They found that intraperitoneal instillation of bupivacaine in combination with dexmedetomidine was superior to other two in reducing postoperative pain.[10] Our study also showed, a significant difference in pain intensity in the early postoperative period and the number of patients in both the studies was similar.

The graphic representation also shows, a rise in pain scores in study groups after 3 hrs postoperatively indicating that the effect of bupivacaine instillation slowly wanes with time. And also, the pain scores at 24 hour were significantly lower in Group BM and BT indicating reduction in intensity of postoperative pain, Table 4. We found that in this study, in comparison with the patients belonging to Bupivacaine-Tramadol Group, the patients of Bupivacaine-Magnesium Sulphate Group experienced statistically significantly reduced VAS pain scores after 1, 2, 4, 6 and 24 h of surgery ($p< 0.05$). Our findings are in accordance with Yadava A et al.[11] Similar results were found in the study by Maharjan SK et al. They compared intraperitoneal instillation of bupivacaine, solely and in addition to $MgSO_4$ in a dose of 50 mg/kg and found that the patients receiving intraperitoneal bupivacaine with $MgSO_4$ at the end of the surgery had better pain relief for a period of 2–5 hours compared with patients who were given only intraperitoneal bupivacaine.[12] Time for first requirement of rescue analgesic is also more in Bupivacaine-Magnesium sulphate when compared to Bupivacaine-Tramadol group of patients 8.29 ± 0.75 *Vs* 4.03 ± 0.93, Fig. 5. Rania M. Alia et al. in their study comparing intraperitoneal instillation of Bupivacaine-magnesium sulphate in laparoscopic cholecystectomy for analgesic effect using 0.9% Normal saline in control group found that the first requirement for first rescue analgesia was 9.2±3 hrs.[13] These findings are almost comparable to present study.In their study, comparing analgesic efficacy of intraperitoneal bupivacaine and bupivacaine plus magnesium sulphate for postoperative pain relief after laparoscopic cholecystectomy found that there is longer pain free period of average 5.53 ±4.33 hours after surgery compared to 3.16 ± 1.59 hours in sole bupivacaine group.[13]

In our study, there was also reduction in total analgesic consumed over 24 hrs for which total rescue analgesia consumption in 24 h was analyzed, Fig. 6. BT Group had 2.390 g (2.39 g, mean) and BM Group had 1.27 g, mean) of paracetamol (rescue analgesia) consumption in 24 h which was statistically significant. ($p$=0.06). And found that total rescue analgesic requirement reduced by half compared to BT Group.Edmunds S et al. reported that when magnesium sulphate was used as an adjunct for anesthesia, it reduced the doses of analgesics required and their action was strengthened but there was no prolongation of analgesic effects.[14] None of the patients, belonging to either group complained of shoulder tip pain this study.

Instillation of drugs in Trendelenburg's position might facilitate intraperitoneal local anesthetic flow over the celiac plexus and phrenic nerve endings giving better results.

Out of 6 Randomized placebo controlled studies to check the effectiveness of Intraperitoneal local anesthetics, four reported reduced overall pain after intraperitoneal instillation of local anesthetics in patient undergoing laparoscopic cholecystectomy, Table 5. Our study showed effective analgesia, statistically significant difference during the first 24 hours. Our present study also showed, significant reduction in shoulder tip pain but it was in contradiction with the findings of Chundrigar et al.[15]

We also found that the addition of $MgSO_4$ to bupivacaine decreased the heart rate slightly less

**Table 5:** Randomized controlled studies on effect of intraperitoneal analgesia onshoulder tip and overall pain after laparoscopic cholecystectomy.

| First author and Ref. no. | No. of patients | Shoulder pain | Overall pain (incisional and visceral) |
|---|---|---|---|
| Chundrigar[15] | 58 | N | Y |
| Mraovic[16] | 80 | = | Y |
| Pasqualucci[17] | 109 | = | Y |
| Szem[18] | 55 | N | Y |
| Joris[6] | 40 | N | N |
| Raetzell[19] | 24 | N | N |

N-not significant difference from placebo;
Y-significant effect in the treatment group
=not investigated.

than baseline and became stable thereafter, when compared to patients who were given bupivacaine and tramadol after laparoscopic cholecystectomy, Fig. 2,3,4. Our findings are in agreement with that of Jee D et al.SBP was recorded at 5 minute intervals in both groups after the intraperitoneal instillation of study drugs.[20] When SBP during the observation period was compared with baseline SBP, the difference was found to be statistically insignificant ($p$>0.05). Similarly DBP was also recorded at 5 minute intervals in both groups and DBP during the observation period was compared with baseline DBP, the difference was found to be statistically insignificant ($p$> 0.05).

After intraperitoneal instillation of the study drugs, the HR was recorded at 5 min interval in BTGroup patientsand compared with baseline HR and found that the difference was not statistically significant ($p$> 0.05). In BM Group, HR was recorded at 5 min interval and compared with baseline HR and found that the difference was statistically significant ($p$ < 0.05). The HR after $MgSO_4$ plus bupivacaine instillation intraperitoneally was slightly less than baseline and stable thereafter. Jee D et al. in their study found a significant reduction in the mean arterial pressure was found with intravenous administration of Magnesium sulphate 50 mg/kg immediately before pneumoperitoneum, which was not found in our study.[20]

Maharjan SK et al. observed that there was no incidence of shoulder tip pain in patients receiving intraperitoneal bupivacaine solely compared to in addition to $MgSO_4$ in a dose of 50 mg/kg. There is 100% reduction in shoulder tip pain.[21] Rania M Alia et al. in their study found no significant difference in intraperitoneal magnesium sulfate group compared to 0.9% normal saline control group contradicting our study results though there is minimal shoulder pain.[13] Narchiet al. showed that intraperitoneal instillation of 100 mg bupivacaine did not cause toxicity.[22] This technique is safe with good pain relief in initial few hours. This drug possesses antiinflammatory activity that may further reduce pain when administered locally. Intraperitoneal instillation of 30 ml of 0.25% bupivacaine provides effective analgesia with plasma concentration below toxic levels (0.92–1.14 µg/ml). Several reports have revealed that the range of mean plasma concentration after plain intraperitoneal bupivacaine administration (100–150 mg) is well below the toxic concentration of 3 µg /ml.

In our study, we used lower doses (75 mg) of bupivacaine not more than 2 mg/kg body weight doses less than those believed to cause local anesthetic systemic toxicity, none of our patients exhibited features of toxicity such as arrhythmias, hypotension, delayed awakening. There is no record of clinical signs of local anesthetic systemic toxicity or signs of hypermagnesemia amongst all the previous studies. We recorded nausea and vomiting in four patients in the BT Group but not in any patient in the BM Group. There was no statistically significant difference in the proportion of patients with PONV. It would be more emetogenic potential of tramadol when compared to Magnesium sulphate. The results of Menteset al., who used preoperative infusion of $MgSO_4$ (50 mg/kg) in laparoscopic cholecystectomy, were in agreement with ours, as the incidence of nausea in the magnesium group was lower than in the control group.[23] Magnesium blocks NMDA receptors, which lie in both emetic pathways and structures associated with the final common pathway for vomiting. NMDA antagonists have the potential to be broad-spectrum antiemetics; however, there are no current data available on the direct effect of $MgSO_4$ on postoperative nausea and vomiting.

## Conclusion

Bupivacaine along with Magnesium sulphate instillation significantly reduced VAS pain scores over 24 hrs. Prolonged duration of analgesia was noted with Magnesium sulphate. Total analgesic required over 24 hrs was less with Magnesium use. No signs of drug allergy and toxicity were observed.

Thus, the intraperitoneal instillation of Bupivacaine-$MgSO_4$combination provides good analgesia in first 24 hours after surgery, with longer duration of pain free period when compared to Bupivacaine-Tramadol combination, with almost no side effects in both the groups.

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