







## ORIGINAL ARTICLE

# POSTOPERATIVE PAIN SCORE USING INTRAPERITONEAL LOCAL ANESTHETIC BUPIVACAINE VERSUS PLACEBO AFTER LAPAROSCOPIC CHOLECYSTECTOMY: A RANDOMIZED CONTROL TRIAL

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## ABSTRACT

**Background:** Intraperitoneal injection of bupivacaine has been used for treatment of pain following laparoscopic surgeries. The objective of this study was to compare the pain score using intraperitoneal local anesthetic bupivacaine versus placebo after laparoscopic cholecystectomy at 1, 6, 12, 18 and 24 hours respectively.

**Materials & Methods:** This randomized control trial was conducted in Department of General Surgery, Indus Hospital Karachi, Pakistan from July 2020 to January 2021. All adult patients undergoing laparoscopic cholecystectomy were eligible. Sixty patients were randomly allocated to experimental (bupivacaine=30) and placebo (normal saline=30) groups. At the end of surgery, 20 ml bupivacaine 0.5% in experimental group and 20 ml normal saline in placebo group were administered in gall bladder fossa. Postoperative pain was measured by 11-points Visual Analogue Scale at 1, 6, 12, 18 and 24 hours as five research variables. All hypotheses were verified by independent samples t-test.

**Results:** Experimental group included 5 (16.67%) men and 25 women (83.33%). Placebo group included 3 (10%) men and 27 women (90%). Each group included 14 (46.67%) patients in age group 19-40 and 16 (53.33%) in age group 41-65 years. Mean pain score was similar in experimental and placebo groups at 1 hour (3.63 vs. 3.87), 6 hours (3.87 vs. 4.10), 12 hours (3.53 vs. 3.37), 18 hours (2.50 vs. 2.77) and 24 hours (1.80 vs. 2.00) respectively.

**Conclusion:** Mean postoperative pain scores using intraperitoneal local anesthetic bupivacaine versus placebo after laparoscopic cholecystectomy at 1, 6, 12, 18 and 24 hours respectively were similar.

**KEY WORDS:** Cholecystectomy; Laparoscopic Cholecystectomy; Postoperative Pain; Bupivacaine; Normal Saline; Peritoneum.

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## 1. INTRODUCTION

**1.1 Background:** Cholecystectomy is one of the routinely performed surgeries for gall stones. As compared to open cholecystectomy, laparoscopic cholecystectomy is more acceptable in terms of postoperative results like pain, recovery time,

cosmetic and morbidity. Despite of these facts, patients undergoing laparoscopic cholecystectomy experiences significant component of pain. This pain can occur at shoulder region due to diaphragmatic stretching or it can be felt in the abdomen. Abdominal pain has two components, i.e. visceral pain which is associated with dissection of gall bladder, injury to nerve endings in peritoneum, release of inflammatory mediators, irritation of peritoneum by blood, bile spillage & CO<sub>2</sub> and parietal pain which is associated with injury at port sites.

Various treatment modalities are available for controlling pain after laparoscopic cholecystectomy. One of them is injection of local anesthetic intraperitoneally. Intraperitoneal injection of lignocaine, bupivacaine, ropivacaine & levobupivacaine have been used long for the treatment of postoperative

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pain following laparoscopic surgical & gynecologic procedures.<sup>1</sup>

Szem, et al.<sup>2</sup> carried double-blinded placebo-controlled randomized, trial in New York, USA in May 1995 including 26 cases in bupivacaine group and 29 patients in placebo group (normal saline). Mean pain score was statistically significantly lower ( $p < 0.05$ ) at 0-6 hours postoperatively in bupivacaine group  $3.4 \pm 0.5$  than placebo group  $4.7 \pm 0.5$ . After 6 hours, the mean pain score was same for both the groups.

Papagiannopoulou, et al.<sup>3</sup> carried double-blind randomized trial in Thessaloniki, Greece in December 2002. He assigned 57 patients into Levobupivacaine group ( $n=19$ ), Ropivacaine group ( $n=20$ ) and placebo group ( $n=18$ ) with normal saline infusion postoperatively. Mean pain score at 2 hours postoperatively was significantly lower ( $p = < 0.001$ ) in Levobupivacaine group  $2.42 \pm 0.76$  than in placebo group  $4.05 \pm 1.6$ . At 4 hours postoperatively mean pain score was also significantly lower ( $p = < 0.001$ ) in Levobupivacaine group  $1.05 \pm 0.84$  than in placebo group  $4.94 \pm 1.34$ . Mean pain score at 24 hours postoperatively was also significantly lower ( $p = < 0.001$ ) in Levobupivacaine group  $0.57 \pm 0.76$  than in placebo group  $2.33 \pm 0.68$ .

Das, et al.<sup>4</sup> from Mumbai, Maharashtra, India in a randomized, prospective, double blinded study for the period from January 2012 to December 2014, divided 90 patients into 3 groups with 30 patients in each group and pain was assessed by numerical rating scale (NRS). At interval 0-20 minutes, the difference was not statistically significant ( $p > 0.05$ ) in mean pain score between bupivacaine group and control (normal saline) group. The mean NRS score at 2 hours was statistically lower ( $p < 0.05$ ) in bupivacaine group (0.8) than control group (2.2). The mean pain score at 8 hours was also statistically lower ( $p < 0.05$ ) in bupivacaine group (5.0) than in control group (5.6). At 12 hours, both bupivacaine and control groups had mean NRS score  $> 5$  and both groups were given IV analgesics with no statistical difference.

Vijayaraghavalu, et al.<sup>5</sup> from Chennai, India in a randomized, double-blind prospective study from June 2020 to December 2020 found that mean pain score in bupivacaine group was 1.56 at zero hour, 1.99 at 2 hours, 2.11 at 4 hours, 2.45 at 6 hours, 3.36 at 12 hours, and 3.53 at 24 hours, while it was 3.46 at zero hour, 3.83 at 2 hours, 3.90 at 4 hours, 4.22 at 6 hours, 4.32 at 12 hours, and 4.38 at 24 hours in normal saline group. At zero, 2, 4, and 6 hours the bupivacaine group had statistically significant lower pain score as compared to normal saline group. At 12 and 24 hours, the mean VAS score was same in the two groups.

**1.2 Research Problems (RPs) & Knowledge Gaps (KGs):** Unawareness about the difference between the mean postoperative pain score using

intraperitoneal local anesthetic bupivacaine vs. placebo after laparoscopic cholecystectomy at 1, 6, 12, 18 and 24 hours respectively were our five RPs. Unavailability of data about these problems were our five KGs.

**1.3 Research Questions (RQs 1-5):** What is the difference between the mean postoperative pain score using intraperitoneal local anesthetic bupivacaine vs. placebo after laparoscopic cholecystectomy at 1, 6, 12, 18 and 24 hours respectively?

**1.4 Research Objectives (ROs 1-5):** To compare the postoperative pain score using intraperitoneal local anesthetic bupivacaine versus placebo after laparoscopic cholecystectomy at 1, 6, 12, 18 and 24 hours respectively.

### 1.5 Research (Null) Hypotheses

**H<sub>01</sub>:** Mean postoperative pain score using intraperitoneal local anesthetic bupivacaine is same as placebo after laparoscopic cholecystectomy at 1 hour.

**H<sub>02</sub>:** Mean postoperative pain score using intraperitoneal local anesthetic bupivacaine is same as placebo after laparoscopic cholecystectomy at 6 hours.

**H<sub>03</sub>:** Mean postoperative pain score using intraperitoneal local anesthetic bupivacaine is same as placebo after laparoscopic cholecystectomy at 12 hours.

**H<sub>04</sub>:** Mean postoperative pain score using intraperitoneal local anesthetic bupivacaine is same as placebo after laparoscopic cholecystectomy at 18 hours.

**H<sub>05</sub>:** Mean postoperative pain score using intraperitoneal local anesthetic bupivacaine is same as placebo after laparoscopic cholecystectomy at 24 hours.

**1.6 Significance:** This study will provide us important data about the efficacy of these two drugs. It will guide and help the surgeons and gynecologists that which drug provides better pain relief in laparoscopic cholecystectomy and other procedures involving peritoneal cavity.

## 2. MATERIALS AND METHODS

**2.1 Design, setting and duration:** This randomized control trial was carried out in the Department of General Surgery, Indus Hospital Karachi, Pakistan from July 10, 2020 to January 9, 2021. The project was started after approval from the Indus Hospital Ethical Committee. Also informed consent was received from all the patients before inclusion.

**2.2 Sampling and randomization:** All adult patients with age 18-65 years and candidates for laparoscopic cholecystectomy were eligible. Patients having severe renal, cardiovascular, hematologic or hepatic diseases, those with pre-existing psychiatric illness or neurologic diseases or having history of alcohol or drug abuse were not eligible. Sixty cases were allocated randomly by toss to experimental (bupivacaine) and placebo (normal saline) groups; 30 patients to each group.

**2.3 Procedure, intervention and follow up:** All patients were trained on Visual Analogue Scale (VAS). All cases were operated under general anesthesia using propofol 2mg/kg with 1% isoflurane, with intermittent doses of muscle relaxant. At the end of surgery, 20 ml bupivacaine 0.5% in the experimental group and 20 ml normal saline in the placebo group were administered under direct vision into the sub-diaphragmatic space in the gall bladder fossa. Patients were monitored hourly for 3 hours by ECG, SpO<sub>2</sub> & blood pressure. Patients in both groups were given two tablets paracetamol orally at 1 hour postoperatively and then three times per day. In bupivacaine group no rescue analgesia was required, while eight patients in the placebo group were given rescue analgesia as inj. tramadol 2mg/kg I/V. Postoperative pain was measured at 1, 6, 12, 18 and 24 hours by a doctor on duty and a trained nurse.

**2.4 Data collection instrument and plan:** Pain was measured on 11-points (0-10) Visual Analogue Scale<sup>6-7</sup> (VAS); zero means no pain and 10 means maximum imaginable pain. VAS is 10-cm long strip pasted on the patient's chart. At each point in 24-hours follow up, separate strip was used. Sex (men & women), age groups (up to 40 years & > 40 years) and age in years were three matching variables, while postoperative pain at 1, 6, 12, 18 and 24 hours were five research variables. Data for sex and age groups was measured on nominal scale, while for five research variables it was measured on interval (numeric) scale.

**2.5 Data analysis plan:** Sex and age groups were analyzed by count and percentage. The five research variables were analyzed by mean, SD, minimum, maximum & range, with 95% CI. All the five hypotheses were tested through independent samples

t-test.<sup>8-9</sup> using IBM SPSS Statistics v. 22 at alpha .05.<sup>10</sup>

### 3. RESULTS

**3.1 Sample description:** Thirty patients in experimental group included 5 (16.67%) men and 25 women (83.33%), while 30 patients in placebo group included 3 (10%) men and 27 women (90%); almost with same proportion.

Experimental group included 14 (46.67%) patients in age group 19-40 years and 16 (53.33%) in age group 41-65 years, while the placebo group also included 14 (46.67%) patients in age group 19-40 years and 16 (53.33%) in age group 41-65 years; having equal proportion.

The mean age was  $41.47 \pm 11.467$  (19-65, range 46, 95%CI 37.18-45.75) years in experimental group, while it was  $41.27 \pm 9.599$  (21-58, range 37, 95%CI 37.68-44.85) years in placebo group; both closely similar.

Based on ASA status, the experimental group included 24 (80%) patients in ASA-I and 6 (20%) in ASA-II, while the placebo group included 22 (73.33%) patients in ASA-I and 8 (26.67%) in ASA-II; having almost similar proportion.

**3.2 Descriptive statistics & estimation of parameters:** Mean pain score was similar in experimental (bupivacaine) and placebo (normal saline) groups at 1, 6, 12, 18 and 24 hours as their confidence intervals are overlapping. (Table 3.2)

### 3.3 Testing of hypotheses

**3.3.1 H<sub>01</sub>:** H<sub>01</sub> could not be rejected, showing that the mean postoperative pain scores using intraperitoneal bupivacaine vs. placebo 1 hour after laparoscopic cholecystectomy were statistically not different. (Table 3.3.1)

**Table 3.2: Postoperative pain score using intraperitoneal bupivacaine and placebo after laparoscopic cholecystectomy**

Variables	Groups	Sample Statistics					95% CI of Mean	
		Mean	Min.	Max.	Range	SD	Lower	Upper
Pain score at 1 hour	Experimental (n=30)	3.63	1	7	6	1.790	3.00	4.30
	Placebo (n=30)	3.87	1	8	7	1.871	3.23	4.54
Pain score at 6 hours	Experimental (n=30)	3.87	1	7	6	1.279	3.41	4.35
	Placebo (n=30)	4.10	1	7	6	1.348	3.62	4.58
Pain score at 12 hours	Experimental (n=30)	3.53	2	8	6	1.525	3.00	4.13
	Placebo (n=30)	3.37	1	5	4	0.964	3.03	4.72
Pain score at 18 hours	Experimental (n=30)	2.50	1	4	3	0.861	2.21	2.82
	Placebo (n=30)	2.77	1	5	4	1.006	2.41	3.12
Pain score at 24 hours	Experimental (n=30)	1.80	0	4	4	0.997	1.45	2.14
	Placebo (n=30)	2.00	0	4	4	0.947	1.66	2.34

**Postoperative pain score after laparoscopic cholecystectomy.**

**3.3.2 H<sub>02</sub>:** H<sub>02</sub> could not be rejected, showing that the mean postoperative pain scores using intraperitoneal bupivacaine vs. placebo 6 hour after laparoscopic cholecystectomy were statistically not different. (Table 3.3.2)

**3.3.3 H<sub>03</sub>:** H<sub>03</sub> could not be rejected, showing that the mean postoperative pain scores using intraperitoneal bupivacaine vs. placebo 12 hour after laparoscopic cholecystectomy were statistically not different. (Table 3.3.3)

**3.3.4 H<sub>04</sub>:** H<sub>04</sub> could not be rejected, showing that the mean postoperative pain scores using intraperitoneal bupivacaine vs. placebo 18 hour after laparoscopic cholecystectomy were statistically not different. (Table 3.3.4)

**3.3.5 H<sub>05</sub>:** H<sub>05</sub> could not be rejected, showing that the mean postoperative pain scores using intraperitoneal bupivacaine vs. placebo 24 hour after laparoscopic cholecystectomy were statistically not different. (Table 3.3.5)

**Table 3.3.1: Postoperative pain score using intraperitoneal bupivacaine vs. placebo 1 hour after laparoscopic cholecystectomy**

Groups	Mean	SD	Difference of means	95%CI of difference		t value	d.f.	p-value (2-tailed)
				Lower	Upper			
Experimental (n=30)	3.63	1.790	-.233	-1.180	.713	-.494	58	.623
Placebo (n=30)	3.87	1.871						

**Table 3.3.2: Postoperative pain score using intraperitoneal bupivacaine vs. placebo 6 hour after laparoscopic cholecystectomy**

Groups	Mean	SD	Difference of means	95%CI of difference		t value	d.f.	p-value (2-tailed)
				Lower	Upper			
Experimental (n=30)	3.87	1.279	-.233	-.913	.446	-.688	58	.494
Placebo (n=30)	4.10	1.348						

**Table 3.3.3: Postoperative pain score using intraperitoneal bupivacaine vs. placebo 12 hour after laparoscopic cholecystectomy**

Groups	Mean	SD	Difference of means	95%CI of difference		t value	d.f.	p-value (2-tailed)
				Lower	Upper			
Experimental (n=30)	3.53	1.525	.167	-.493	.826	.506	58	.615
Placebo (n=30)	3.37	0.964						

**Table 3.3.4: Postoperative pain score using intraperitoneal bupivacaine vs. placebo 18 hour after laparoscopic cholecystectomy**

Groups	Mean	SD	Difference of means	95%CI of difference		t value	d.f.	p-value (2-tailed)
				Lower	Upper			
Experimental (n=30)	2.50	0.861	-.267	-.751	.217	-1.103	58	.275
Placebo (n=30)	2.77	1.006						

**Table 3.3.5: Postoperative pain score using intraperitoneal bupivacaine vs. placebo 24 hour after laparoscopic cholecystectomy**

Groups	Mean	SD	Difference of means	95%CI of difference		t value	d.f.	p-value (2-tailed)
				Lower	Upper			
Experimental (n=30)	1.80	0.997	-.200	-.702	.302	-.797	58	.429
Placebo (n=30)	2.00	0.947						

#### 4. DISCUSSION

Laparoscopic cholecystectomy is widely accomplished, elective procedure. It has replaced open cholecystectomy being a gold standard procedure.<sup>11</sup> Postoperative pain is relatively less in laparoscopic cholecystectomy as compared to open surgery but still it may cause significant amount of morbidity and can cause delay in discharge of patients.<sup>12</sup> Patients frequently experience significant amount of pain post operatively in laparoscopic cholecystectomy on the day of surgery.

Normal saline intraperitoneal infiltration postoperatively causes reduction in visceral and referred pains by diluting inflammatory markers. It also replaces gas above the liver and it reduces space between the liver and diaphragm; whereas bupivacaine is a highly potent and longer acting local anesthetic.<sup>13</sup> Intraperitoneal injection of local anesthetic agents alone or with opioids in combination helps in the reduction of postoperative pain and analgesics consumption following laparoscopic cholecystectomy.<sup>14-15</sup> In a recent study conducted in Turkey and Poland, the effects of analgesia along with intraperitoneal instillation of bupivacaine in pain relieving is more pronounced.<sup>16-17</sup>

**H<sub>01</sub>:** In our study, the mean pain score was similar ( $p=.623$ ) in experimental ( $3.63\pm 1.790$ ) and placebo groups ( $3.87\pm 1.871$ ) at 1 hour. Similarly, Das, et al.<sup>4</sup> from Mumbai, India found that at 0-20 minutes, the difference in mean pain score was not statistically different ( $p\text{-value}>0.05$ ) between the bupivacaine and control (normal saline) groups.

Opposite findings are shown by the following three studies at 2 hours period. Vijayaraghavalu, et al.<sup>5</sup> from Chennai, India reported that the mean pain score was less ( $p=0.04$ ) in bupivacaine ( $1.99\pm 0.92$ ) than placebo group ( $3.83\pm 1.39$ ) at 2 hours. Das, et al.<sup>4</sup> from Mumbai, India found that mean NRS score at 2 hours was significantly lower ( $p\text{-value}<0.05$ ) in bupivacaine than control group (0.8 vs. 2.2). Papagiannopoulou, et al.<sup>5</sup> from Thessaloniki, Greece found that Mean pain score at 2 hours postoperatively was significantly lower ( $p\text{-value}<0.001$ ) in Lev group  $2.42\pm 0.76$  than in placebo group  $4.05\pm 1.6$ .

**H<sub>02</sub>:** In our study, the mean pain score was similar ( $p=.494$ ) in experimental ( $3.87\pm 1.279$ ) and placebo groups ( $4.10\pm 1.348$ ) at 6 hours. Opposite findings are given by Vijayaraghavalu, et al.<sup>5</sup> from Chennai, India who reported that the mean pain score was less ( $p=0.04$ ) in bupivacaine ( $2.45\pm 1.11$ ) than placebo group ( $4.22\pm 1.26$ ) at 6 hours. Likewise, Szem, et al.<sup>2</sup> from New York, USA found that mean pain score was significantly lower ( $p\text{-value}<0.05$ ) at 0-6 hours postoperatively in bupivacaine group  $3.4\pm 0.5$  than placebo group  $4.7\pm 0.5$ .

**H<sub>03</sub>:** In our study, the mean pain score was similar ( $p=.615$ ) in experimental ( $3.53\pm 1.525$ ) and placebo groups ( $3.37\pm 0.964$ ) at 12 hours. In line to our study,

Vijayaraghavalu, et al.<sup>5</sup> from Chennai, India reported that the mean pain score was similar ( $p=.1$ ) in bupivacaine ( $3.36\pm 1.18$ ) and placebo groups ( $4.32\pm 1.14$ ) at 12 hours. Likewise, Das, et al.<sup>4</sup> from Mumbai, India found that at 12 hours both bupivacaine and control groups had mean NRS score  $>5$  and both groups were given IV analgesics with no significant difference between the two groups. Likewise, Szem, et al.<sup>2</sup> from New York, USA found that after 6 hours, the mean pain score was same in both the groups.

**H<sub>04</sub>:** In our study, the mean pain score was similar ( $p=.275$ ) in experimental ( $2.50\pm 0.861$ ) and placebo groups ( $2.77\pm 1.006$ ) at 18 hours. No study from literature was retrieved having same or different results.

**H<sub>05</sub>:** In our study, the mean pain score was similar ( $p=.429$ ) in experimental ( $1.80\pm 0.997$ ) and placebo groups ( $2.00\pm 0.947$ ) at 24 hours. Similarly, Vijayaraghavalu, et al.<sup>5</sup> from Chennai, India reported that the mean pain score was similar ( $p=.7$ ) in bupivacaine ( $3.53\pm 1.04$ ) and placebo groups ( $4.38\pm 1.17$ ) at 24 hours. In contrary, Papagiannopoulou, et al.<sup>3</sup> from Thessaloniki, Greece found that mean pain score at 24 hours postoperatively was significantly lower ( $p\text{-value}<0.001$ ) in Lev group  $0.57\pm 0.76$  than in placebo group  $2.33\pm 0.68$ .

#### CONCLUSION

In our study, Mean postoperative pain scores using intraperitoneal local anesthetic bupivacaine versus placebo after laparoscopic cholecystectomy at 1, 6, 12, 18 and 24 hours respectively were similar.

#### REFERENCES

1. Choi GJ, Kang H, Baek CW, Jung YH, Kim DR. Effect of intraperitoneal local anesthetic on pain characteristics after laparoscopic cholecystectomy. *World J Gastroenterol* 2015;21(47):13386-95.7. <https://doi.org/10.3748/wjg.v21.i47.13386>
2. Szem JW, Hydo L, Barie PS. A double-blinded evaluation of intraperitoneal bupivacaine vs saline for the reduction of postoperative pain and nausea after laparoscopic cholecystectomy. *Surg Endosc* 1996;10(1):44-8. <https://doi.org/10.1007/s004649910011>
3. Papagiannopoulou P, Argiriadou H, Georgiou M, Papaziogas B, Sfyra E, Kanakoudis F. Preincisional local infiltration of levobupivacaine vs ropivacaine for pain control after laparoscopic cholecystectomy. *Surg Endosc* 2003;17(12):1961-4. <https://doi.org/10.1007/s00464-002-9256-1>
4. Das NT, Deshpande C. Effects of intraperitoneal local anaesthetics bupivacaine and ropivacaine versus placebo on postoperative pain after laparoscopic cholecystectomy: a randomised double blind study. *J Clin Diagn Res* 2017;11(7):UC08-UC12. <https://doi.org/10.7860/JCDR/2017/26162.10188>
5. Vijayaraghavalu S, Sekar EB. A comparative study on the postoperative analgesic effects of the intraperitoneal instillation of bupivacaine versus

- normal saline following laparoscopic cholecystectomy. *Cureus* 2021;13(3): e14151. <https://doi.org/10.7759/cureus.14151>
6. Visual analog scale. Physiopedia [accessed 2022 June 22]. Available at: [https://www.physio-pedia.com/Visual\\_Analogue\\_Scale](https://www.physio-pedia.com/Visual_Analogue_Scale)
  7. Delgado DA, Lambert BS, Boutris N, McCulloch PC, Robbins AB, Moreno MR, et al. Validation of digital visual analog scale pain scoring with a traditional paper-based visual analog scale in adults. *J Am Acad Orthop Surg Glob Res Rev* 2018;2(3):e088. <https://doi.org/10.5435/JAAOS-Global-D-17-00088>
  8. Zar JH. *Biostatistical Analysis*. 5th ed. Englewood Cliffs, New Jersey: Prentice-Hall, Inc. p.127.
  9. Pegano M, Gauvreau K. *Principals of Biostatistics*. 2nd ed. Boston, MA, USA: Cengage Learning; 2000. p.349-52.
  10. IBM SPSS Statistics for Windows, Version 22.0, released 2013, IBM Corp., Armonk, NY [cited 2022 Apr 10]. Available at: <https://www.ibm.com/support/pages/how-cite-ibm-spss-statistics-or-earlier-versions-spss>
  11. Jensen K, Kehlet H, Lund CM. Post-operative recovery profile after laparoscopic cholecystectomy: a prospective, observational study of a multimodal anaesthetic regime. *Acta Anaesthesiol Scand* 2007;51:464-71. <https://doi.org/10.1111/j.1399-6576.2006.01251.x>
  12. Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and prevention. *J Pain Res* 2017;10:2287-98. <https://doi.org/10.2147/JPR.S144066>
  13. Tsimoyiannis EC, Siakas P, Tassis A, Lekkas ET, Tzourou H, Kambili M. Intraperitoneal normal saline infusion for postoperative pain after laparoscopic cholecystectomy. *World J Surg* 1998;22:824-8. <https://doi.org/10.1007/s002689900477>
  14. Boddy AP, Mehta S, Rhodes M. The effect of intraperitoneal local anesthesia in laparoscopic cholecystectomy: A systematic review and meta-analysis. *Anesth Analg* 2006;103:682-8. <https://doi.org/10.1213/01.ane.0000226268.06279.5a>
  15. Kahokehr A, Sammour T, Srinivasa S, Hill AG. Systematic review and meta-analysis of intraperitoneal local anesthetic for pain reduction after laparoscopic gastric procedures. *Br J Surg* 2011;98:29-36. <https://doi.org/10.1002/bjs.7293>
  16. Karaaslan D, Sivaci RG, Akbulut G, Dilek ON. Pre-emptive analgesia in laparoscopic cholecystectomy: A randomized controlled study. *Pain Pract* 2006;6:237-41. <https://doi.org/10.1111/j.1533-2500.2006.00092.x>
  17. Barczyński M, Konturek A, Herman RM. Superiority of preemptive analgesia with intraperitoneal instillation of bupivacaine before rather than after the creation of capnoperitoneum for laparoscopic cholecystectomy: A randomized, double-blind, placebo-controlled study. *Surg Endosc* 2006;20:1088-93. <https://doi.org/10.1007/s00464-005-0458-1>

**CONFLICT OF INTEREST**

Authors declare no conflict of interest.  
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**AUTHORS' CONTRIBUTION**

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	ANZ, LR
Acquisition, Analysis or Interpretation of Data:	ANZ, LR, GK, GA, AH, AI
Manuscript Writing & Approval:	ANZ, LR, GK, GA, AH, AI

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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