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Original Article

Efficacy of Preoperative Single Dose Intravenous Dexamethasone in Laparoscopic Cholecystectomy: A Randomized Double-Blind Placebo-Controlled Trial

Phaiwit Sriphatphiriyakun, MD
Yada Chumongkhon, MD
Department of Surgery, Suratthani Hospital, Thailand

Abstract

Background: Postoperative pain following laparoscopic cholecystectomy (LC) is complex and influenced by multiple factors. Dexamethasone has been investigated for its potential to reduce postoperative pain and nausea, but its efficacy remains controversial.

Materials and Methods: This prospective, randomized, double-blind, controlled trial included 108 patients undergoing elective LC. Patients were randomly assigned to receive either 5 mg dexamethasone (study group) or 1 ml normal saline (control group) 1–2 hours before surgery. Postoperative pain was assessed using the Visual Analog Scale (VAS) at 0, 2, 6, 12, and 24 hours. Data on analgesic use, postoperative nausea and vomiting (PONV), complications, and length of hospital stay were also collected. Statistical analyses were conducted using SPSS, with a p-value < 0.05 considered significant.

Results: No statistically significant differences in VAS scores were observed between the dexamethasone and control groups at any time point. Morphine use was similarly low in both groups (2.0 ± 2.9 mg vs. 2.2 ± 3.6 mg, $p > 0.05$), with about half of the patients requiring no morphine. PONV was less frequent in the dexamethasone group (5.7% vs. 11.1%), but the difference was insignificant. Length of hospital stay was identical in both groups (2.3 ± 0.5 days).

Conclusion: Dexamethasone did not significantly reduce postoperative pain or morphine use in LC patients with low baseline pain scores. Although PONV was less frequent in the dexamethasone group, the difference was not statistically significant. Future studies with larger sample sizes and standardized postoperative care are needed to clarify its role in LC pain management.

Keywords: Laparoscopic cholecystectomy, Dexamethasone, Postoperative pain

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Corresponding author: Phaiwit Sriphatphiriyakun, MD, Department of Surgery, Suratthani Hospital, Thailand; E-mail: phaiwit3050@gmail.com

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Introduction

Approximately one-fifth of the population has gallstones, and about 20-30% of these individuals require surgical intervention.[1] Both open and laparoscopic cholecystectomy are standard treatments for gallstone disease. Since the introduction of laparoscopic surgery in the 1980s, this technique has become increasingly popular due to its benefits, including smaller incisions, reduced blood loss, less postoperative pain, shorter hospital stays, and fewer major wound complications.[2]

While laparoscopic surgery can reduce postoperative pain, many patients still require strong opioids for pain control. The pain mechanism is complex and involves factors such as incisional (somatic) pain, visceral pain, and referred pain, which are unpredictable. Maximum pain is typically observed on the first day after surgery and gradually decreases over the following days.[3]

The exact cause of post-laparoscopic cholecystectomy pain remains unclear, although the most likely causes include peritoneal inflammation due to carbon dioxide (CO2) and peritoneal stretching.[4-5] Various techniques have been studied to minimize pain, such as preoperative administration of analgesics, local anesthetics, intraperitoneal irrigation with bupivacaine, and suctioning residual gas from the peritoneum before closure.[6-10]

Dexamethasone, with its anti-inflammatory properties and ability to block neural discharge and nociceptor C-fiber transmission, has shown promise in reducing postoperative pain and postoperative nausea and vomiting. Several studies,[11-15] including one conducted in Thailand,[16] have demonstrated the benefits of dexamethasone in postoperative pain reduction without increasing infection rates or delaying wound healing. However, some other trials[17-18] reported no significant reduction in postoperative pain among LC patients receiving dexamethasone, and meta-analyses[19] show that dexamethasone provides small but statistically significant analgesic benefits. We question whether the pain-reducing effects of dexamethasone justify its routine use, particularly given that other non-steroidal anti-inflammatory drugs (NSAIDs) or opioids are also effective for pain control. This raises the debate of whether dexamethasone should be reserved only for patients at high risk for PONV rather than being a blanket recommendation for all undergoing laparoscopic cholecystectomy.

This study aims to evaluate the effectiveness of a single preoperative dose of intravenous dexamethasone in reducing postoperative pain, analgesic requirements, and postoperative nausea and vomiting (PONV) in patients undergoing laparoscopic cholecystectomy. Additionally, the study seeks to identify any associated complications and assess whether the administration of dexamethasone improves overall clinical outcomes following surgery.

Material and Methods

This study is a prospective, randomized, double-blind, controlled trial. The study protocol and methodology were approved by the institutional review board, and written informed consent was obtained from all participants.

Inclusion criteria:

1. Patients scheduled for elective laparoscopic cholecystectomy at Suratthani Hospital
2. Age between 20 and 60 years
3. ASA class I or II

Exclusion criteria:

1. Emergency or urgent cases
2. Conversion to open surgery
3. Patients who required routine use of steroids, other immunosuppressive drugs, or NSAIDs
4. Placement of a drainage tube

A total of 143 patients were included in the study and allocated using a computer-based random integer generator. They were randomly assigned to one of two study groups by research assistants who were not involved in outcome assessment. Patients, surgeons, anesthesiologists, residents, nurses, and the primary researcher remained blinded to group assignments until the end of the study. The intervention group received 5 mg of dexamethasone 1-2 hours before skin incision, while the control group received 1 ml of normal saline (NSS) instead.

LC was performed by multiple surgeons in Surathani Hospital using their preferred technique. Thirty-five patients were excluded due to conversion to open surgery (16 patients), drainage tube placement (13 patients), incomplete data, or surgery cancellation (6 patients). This left 54 patients in each group (Figure 1).

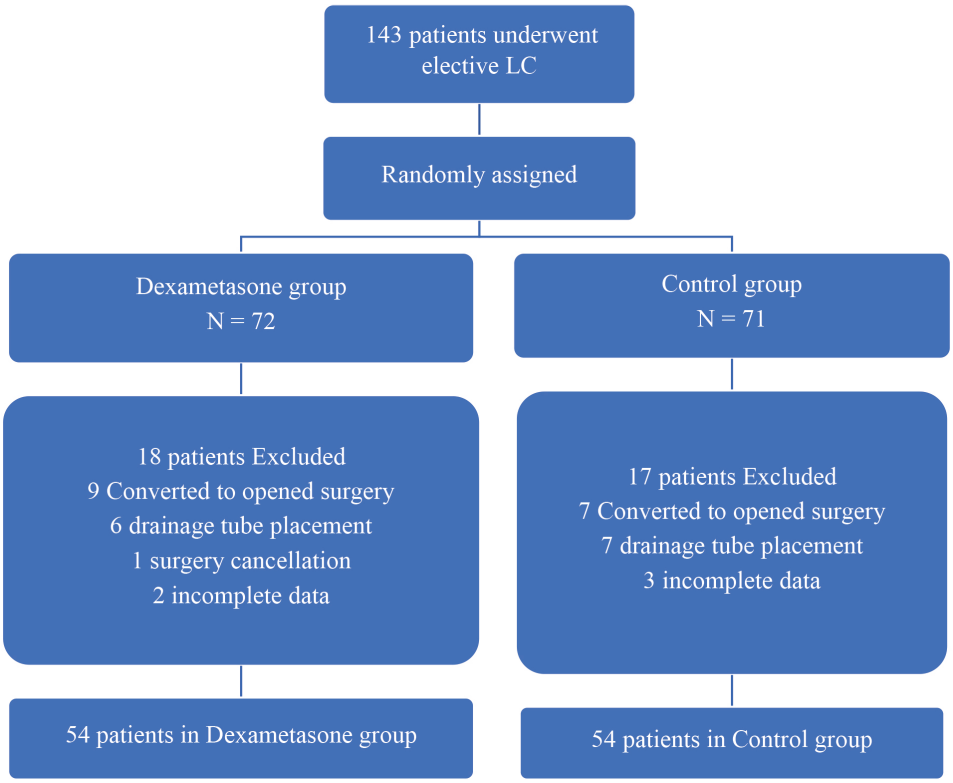

Figure 1 Flow chart

All patients received standardized care, including paracetamol 500 mg orally, as needed every 6 hours, and morphine 2 mg intravenously, as needed every 2 hours, without the use of other analgesics. Postoperative pain was assessed using the Visual Analog Scale (VAS) at 2, 6, 12, 24, and 48 hours after surgery. Additional data collected included the use of antiemetics (e.g., metoclopramide, ondansetron) over 48 hours, complications (e.g., nausea/vomiting, surgical site infection, sedation, respiratory depression), length of hospital stay, bile culture results, and pathology findings.

We use the sample size formula for a two-group comparison (assuming equal group sizes) based on postoperative pain data at 2 hours from Archana Har et al. study.[20]

$$n = \frac{2 \bullet (Z_{\alpha/2} + Z_{\beta})^2 \bullet \sigma^2}{\Delta^2}$$

Significance level (α) = 0.05 (Z = 1.96)
Power ($1 - \beta$) = 0.80 (Z = 0.84)
Estimated standard deviation (σ) = 2.3
Minimum detectable effect size (Δ) = 1.4
n = 49.45

Data were analyzed using SPSS, version 28. Means/medians and standard deviations were calculated for quantitative variables (e.g., age, pain scores), while frequencies and percentages were calculated for qualitative variables (e.g., gender). Differences in patient characteristics were analyzed using a chi-square test for categorical variables (e.g., sex, ASA class, prior surgeries or procedures, local anesthetic use, number of laparoscopic ports, PONV, SSI, bile culture results, pathology) and Student's t-test for continuous variables (e.g., age, BMI, total postoperative opioid use, pain scores, operative/recovery time, length of stay). Statistical significance was set at a p-value < 0.05.

Results

A total of 108 patients were included in the study, with 54 patients assigned to the control group and 54 patients assigned to the study group (dexamethasone group). There were no statistically significant differences between the two groups in terms of age, sex, BMI, ASA classification, diagnosis, history of ERCP, or operative time. However, a higher proportion of patients in the study group had a history of previous abdominal surgery (45% vs. 27%, $p > 0.05$) (Table 1).

The mean postoperative pain scores (VAS) in the study group were 3.4 ± 2.8, 3.7 ± 1.4, 3.5 ± 1.5, 2.8 ± 1.3, and 2.7 ± 1.2 at 0, 2, 6, 12, and 24 hours after surgery, respectively. These scores were not significantly different from the control group, which recorded scores of 3.6 ± 2.7, 3.9 ± 1.4, 3.4 ± 1.4, 2.8 ± 0.9, and 2.5 ± 1.1 at the same time points ($p > 0.05$). Similarly, morphine usage was comparable between the two groups (2.0 ± 2.9 mg in the study group vs. 2.2 ± 3.6 mg in the control group, $p > 0.05$) (Table 2).

Postoperative nausea and vomiting (PONV) were less frequent in the study group (5.7% vs. 11.1%), although the difference was not statistically significant. The length of hospital stay was identical in both groups, averaging 2.3 ± 0.5 days. One patient in the study group experienced a superficial surgical site infection at the umbilical port, but this was not significantly different between the groups. No other complications were reported.

Table 1 Patient demographic data

	Group		*P*-value
	Study (N = 54)	Control (N = 54)	
Mean age: year (Mean ± SD)	42.5 ± 10.8	43.9 ± 10.7	0.501
Sex: n (%)			0.681
Male	11 (20.8)	13 (24.1)	
Female	42 (79.2)	41 (75.9)	
BMI: kg/m² (Mean ± SD)	27.4 ± 5.1	26.5 ± 4.7	0.344
ASA class: %			0.634
I	25 (47.2)	23 (42.6)	
II	28 (52.8)	31 (57.4)	
Diabetes malitus	12	13	0.687
Previous abdominal Sx: n (%)	24 (45.3)	15 (27.8)	0.005
Previous ERCP	16 (30.2)	9 (16.7)	0.098
Number of ports: n (%)			0.277
3 ports	20 (37.7)	26 (48.1)	
4 ports	33 (62.3)	28 (51.9)	
Diagnosis			0.413
Symptomatic Gallstone	27	31	
History of cholecystitis	7	8	
Gallstone pancreatitis	3	4	
History of CBD stone	17	11	
Gallbladder polyp	0	2	
Operative time - min (Mean ± SD)	78.4 ± 38.9	69.3 ± 30.1	0.387

Table 2 Outcome

	Group		*P*-value
	Study (N = 54)	Control (N = 54)	
Visual Analogue Pain Score			
0 hr	3.4 ± 2.8	3.6 ± 2.7	0.825
2 hr	3.7 ± 1.4	3.9 ± 1.4	0.594
6 hr	3.5 ± 1.5	3.4 ± 1.4	0.772
12 hr	2.8 ± 1.3	2.8 ± 0.9	0.749
24 hr	2.7 ± 1.2	2.5 ± 1.1	0.454
Total morphine use-mg (Mean ± SD)	2.0 ± 2.9	2.2 ± 3.6	0.864
Postop. nausea/vomiting: n (%)	3 (5.7)	6 (11.1)	0.310
Surgical site infection: n (%)	1 (5.7)	0 (0.0)	0.311
Length of stay-day (Mean ± SD)	2.3 ± 0.5	2.3 ± 0.5	0.915
Pathology report: n (%)			0.547
Acute cholecystitis	2 (3.7)	2 (3.7)	
Chronic cholecystitis	46 (86.8)	44 (81.5)	
Acute & Chronic cholecystitis	5 (9.4)	6 (11.1)	
Benign neoplasm	0 (0.0)	2 (3.7)	

Discussion

Postoperative pain after laparoscopic cholecystectomy (LC) is complex and unpredictable. While several studies have investigated the role of dexamethasone in reducing postoperative pain, its effectiveness remains controversial. Many randomized controlled trials,[11-15] including one conducted in Thailand,[16] have shown that patients administered dexamethasone required less postoperative morphine and reported significantly lower pain scores compared to control groups. However, other trials[10,21] reported no significant reductions in postoperative pain among LC patients receiving dexamethasone. The optimal time of dexamethasone injection is 1–2 hours before surgery to diffuse across the cell membrane and minimize pain and inflammation.[19]

In our study, we found no statistically significant differences in pain scores (VAS) at any time point or in the total dose of analgesic drugs used. This discrepancy may be due to our study's overall lower pain scores compared to other studies. The average pain scores in our study ranged from 3-4 during the first 6 hours post-surgery to 2-3 at 12-24 hours. Similarly, the total morphine dose was minimal, averaging 2.0 ± 2.9 mg in the study group and 2.2 ± 3.6 mg in the control group. Notably, about half of the patients in both groups did not require morphine at all. When compared with other studies, for example, Petra-Evelyn et al.,[21] reported higher postoperative pain scores immediately after surgery (VAS score: 6.9 ± 1.2 vs. 7.5 ± 1.6; $P = 0.001$) and at 6 hours post-operation (VAS score: 5.2 ± 1.0 vs. 6.5 ± 1.4; $P = 0.000$). Similarly, Bisgaard T et al.,11 reported VAS scores of 4.1 and 5.2 in the control group vs. 3.3 and 3.5 in the dexamethasone group at 6 and 12 hours, respectively. These findings suggest that our population may have a higher pain tolerance, potentially diminishing the observable benefits of dexamethasone on postoperative pain.

Regarding postoperative nausea and vomiting (PONV), the incidence was lower in the study group (5.7%) compared to the control group (11.1%), although the difference was not statistically significant ($p > 0.05$). A meta-analysis of 17 placebo-controlled studies demonstrated that combining a 5-HT3 receptor antagonist and a single dose of dexamethasone can reduce PONV. However, the routine use of this combination remains debated, with some studies suggesting it should be reserved for patients with a history of severe nausea and vomiting.[12,18]

In our study, one patient in the study group experienced a superficial surgical site infection at the umbilical port, which caused delayed wound healing. However, this was not significantly different between the groups and is consistent with findings from other studies.[11-18] From a meta-analysis,[19] it was noted that blood sugar levels in the dexamethasone group were significantly higher at 24 hours after surgery. However, our study did not routinely monitor perioperative blood sugar levels in non-diabetic patients. No hyperglycemic crisis was observed in the 12 diabetic patients in the study group and the 13 patients in the control group.

There are several limitations to our study. First, the sample size was relatively small, and the study was conducted at a single center, limiting the findings' generalizability. Second, there were confounding factors, including differences in baseline patient characteristics, particularly the higher prevalence of previous abdominal surgery in the study group. Additionally, there was no standardized perioperative care protocol, including surgical technique, choice of anesthesia, and type of anesthetic drugs used in the induction and maintenance phases. Management of PONV depended on the attending surgeons and anesthesiologists. Future studies with larger sample sizes, consideration of prior abdominal surgeries, and standardized postoperative care protocols are needed to draw more definitive conclusions.

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Conclusion

This prospective randomized double-blind controlled trial demonstrated that dexamethasone did not significantly reduce postoperative pain scores or analgesic use following laparoscopic cholecystectomy in our study population. The overall low pain scores and minimal analgesic requirements suggest that the high pain tolerance in this population may have diminished the measurable benefits of dexamethasone. Although there was a lower incidence of postoperative nausea and vomiting (PONV) in the dexamethasone group, the difference was not statistically significant. Further studies with larger sample sizes, standardized postoperative care protocols, and consideration of baseline patient characteristics, such as prior abdominal surgeries, are warranted to evaluate better dexamethasone's efficacy in managing postoperative pain and PONV in laparoscopic cholecystectomy patients.

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