Dexamethasone and Pain After Laparoscopic Cholecystectomy: A Randomized Controlled Trial

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Received: 2024-11-29; Received in revised form: 2025-01-16; Accepted: 2025-03-07

Abstract

Background: Laparoscopic cholecystectomy is a surgical procedure used to remove the gallbladder in patients experiencing gallstones or acute cholecystitis. Pain is a common side effect of surgery.

Objective: This study evaluates the effectiveness of intraperitoneal dexamethasone injection from the umbilical port site in alleviating pain after laparoscopic cholecystectomy.

Methods: This research followed a triple-blind clinical trial that included 80 randomly selected patients who were hospitalized at Shahid Mohammadi Hospital in Bandar Abbas and deemed eligible for laparoscopic cholecystectomy. Patients were randomly divided into two groups, each containing 40 participants. In the test group, 8 mg of dexamethasone was injected into the intraperitoneal space through the umbilical port site during surgery, while no drug was administered in the control group. Pain scores were measured postoperatively using the VAS questionnaire at 6, 12, and 18 hours after surgery. The collected data were analyzed using SPSS version 21 statistical software, employing independent t-tests and chi-square tests.

Results: The experimental group exhibited significantly lower levels of nausea, vomiting, analgesic consumption, and pain compared to the control group ($p<0.000$).

Conclusions: Study confirmed that intraperitoneal dexamethasone infusion from the port site significantly reduced postoperative pain, nausea, vomiting, and the consumption of painkillers.

Keywords: Cholecystectomy, Laparoscopy, Dexamethasone, Intraperitoneal injection, Pain

Citation: Elyasinia F., Soroush A., Najjari Kh., Talebpour M., Barani AM, Eslamian R, Zabihi-Mahmoudabadi, H, Ahmadinasab M. **Dexamethasone and Pain After Laparoscopic Cholecystectomy: A Randomized Controlled Trial.** *Acad J Surg*, 2025; 8(1): 22-28.

Introduction

Laparoscopic cholecystectomy is a surgical procedure designed to remove the gallbladder in patients with conditions such as acute cholecystitis and gallstones [1]. Following laparoscopic cholecystectomy, two primary complications remain: pain and recovery duration [2]. Surgical procedures can result in acute pain due to the scope and location of the surgery, the patient's psychological and physiological history, and tissue injury [3].

Effective pain management is essential after surgery, as inadequate control can lead to increased morbidity, nausea, vomiting, urinary retention, oliguria, myocardial ischemia, delayed wound healing, and anxiety [4]. Assessing pain scores has shown that pregabalin intervention significantly reduces postoperative pain and fentanyl intake [5].

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Lowering pneumoperitoneum pressure to 8 mmHg, peritoneal irrigation with sodium bicarbonate, and active gas aspiration have also been found to effectively reduce pain [6-8]. Furthermore, dexamethasone has demonstrated efficacy in minimizing post-surgery pain among various pain management techniques [9].

Among various pain management techniques [9], one of the widely used corticosteroid drugs in clinical practice is dexamethasone [10]. Dexamethasone exerts its effects through multiple pathways, including the inhibition of neutrophil migration and the reduction of lymphocyte colony multiplication. In clinical practice, this drug has demonstrated effectiveness across various medical fields, including neurology, immunology, and surgery [11].

In laparoscopic cholecystectomy, using 8 mg of dexamethasone meaningfully decreased the occurrence of nausea and vomiting post-surgery [12].

Dexamethasone has demonstrated efficacy in reducing post-tonsillectomy pain when administered as either a single dose or as an extended infusion over 8-16 hours postoperatively, with minimal adverse effects [13,14]. Preoperative administration of 8-14 mg dexamethasone has been shown to reduce nausea, vomiting, and analgesic requirements during the first 24 hours following laparoscopic donor nephrectomy [15]. Similarly, intraperitoneal administration of 16 mg dexamethasone at the surgical site during gynecologic laparoscopy resulted in significant postoperative pain reduction [16]. A single intravenous dose of dexamethasone during anesthesia induction was associated with decreased pain scores, reduced opioid consumption, and lower incidence of postoperative nausea and vomiting following laparoscopic cholecystectomy [17].

On the other hand, pain scores and the duration of hospitalization did not vary between the groups receiving different doses of dexamethasone and ondansetron and the group receiving saline [18]. As presented above, pain management is essential after surgery, and despite existing evidence supporting the efficacy of dexamethasone in managing postoperative pain, some studies have not verified this data; consequently, more studies are needed to find the ideal administration route for this medication. Therefore, this study aims to explore the pain-relieving potential of intraperitoneal dexamethasone delivered through the umbilical port site in patients experiencing laparoscopic cholecystectomy.

Methods

Patients and study design

The efficacy of intraperitoneal dexamethasone in reducing postoperative pain following laparoscopic cholecystectomy was assessed through a parallel, randomized, controlled, single-center, triple-blinded clinical trial. The study population consisted of elective laparoscopic patients with indications for cholecystectomy who were referred to Shahid Mohammadi Hospital in Bandar Abbas in 2021 and were hospitalized in the participating service. Inclusion criteria encompassed any type of gallbladder disease that could be treated with laparoscopic cholecystectomy. Exclusion criteria included the use of analgesics within 24 hours before anesthesia, diabetes, immunodeficiency, current drug use, pregnancy or breastfeeding, mental retardation, and conversion from laparoscopy to laparotomy during surgery.

Before surgery, patients were informed about the method of drug administration and potential side effects. They entered the study after providing informed consent and were then divided into two groups. As mentioned in Figure 1, four patients did not meet the inclusion criteria, and three refused to participate in the study. A total of 80 patients were included in the randomization process. Both groups underwent surgery performed by the same team of surgeons. The procedures were conducted by highly experienced surgeons specializing in laparoscopic cholecystectomy.

The study received Ethics Committee approval with reference number IR.HUMS.REC.1399.454 on December 16, 2020, and was registered in the Iranian Registry of Clinical Trials under the title "Investigating the Effect of Intraperitoneal Injection of Dexamethasone from the Port Entry Site on Reducing Pain after Laparoscopic Cholecystectomy" (Trial ID Code: IRCT 57701). All interventions and evaluations were planned and supervised by the General Surgery Department of Hormozgan University of Medical Sciences in Bandar Abbas. Additionally, the university provided full sponsorship for this trial.

Study procedures

Using a convenience sampling method, 80 patients were randomly assigned to two groups of 40 using the random block allocation method. In the test group (case), 8 mg of dexamethasone (from Aburehyan and Zahrawi Pharmaceutical Companies) was injected into the intraperitoneal space via the umbilical port site during the operation, while in the other group, no dexamethasone was injected. Pain levels were assessed at 6, 12, and 18 hours post-surgery using the Visual Analog Scale (VAS). In the VAS score, pain severity is ranked from zero (no pain) to ten (worst possible pain). Additionally, we monitored the number of times

patients required analgesics and recorded any side effects. Furthermore, data on the frequency of vomiting and the duration of nausea were collected. Information on participants' age and weight was also gathered. Incomplete data sets were either excluded or recollected to ensure study clarity. The person responsible for data collection was unaware of the randomization. All procedures were performed under the supervision of the attending surgeon and followed a standardized protocol established before the surgery.

Data Outcome

The primary outcome of the study was that intraperitoneal injection of dexamethasone at the port site effectively reduced pain at 6, 12, and 18 hours post-surgery, as assessed using the Visual Analog Scale (VAS). Secondary endpoints included the number of patients who required analgesics, the duration of nausea, and the incidence of vomiting within the first 24 hours after surgery.

Randomizing and Blinding

We used random allocation software to divide the participants equally using the random block allocation method. Each block contained four participants, ensuring that patients were assigned to both groups at the same time intervals. A triple-blind study was conducted, in which the participants, the data collector, and the analyst remained unaware of the patient groups' randomization. All the processes were directed by the method writer.

Statistical Analysis

Based on the findings of a previous study [16], which demonstrated that intraperitoneal dexamethasone reduced analgesic requirements in patients following gynecological laparoscopy, we estimated a 5% reduction in analgesic dosage in the dexamethasone group compared to the placebo group. This reduction was considered the effect size for our study, leading to an estimated sample size of 40 patients per group, assuming a power of 90%. Additionally, quantitative data are presented as mean ± SD and analyzed using an independent t-test, while qualitative data are assessed using the chi-square test. A significance level of 0.05 was applied using SPSS Statistics, version 21.

Results

The descriptive data of the participants are presented in the following tables (Tables 1 and 2).

As shown in Figure 1, out of 87 patients with indications for laparoscopic cholecystectomy between January 6 and January 18, 2021, 80 participants were selected for the study. Seven patients were excluded: four did not meet the inclusion criteria, and three declined to participate. All 80 patients underwent randomization. The surgeries were performed at Shahid Mohammadi Hospital by the same team of surgeons. Due to the short follow-up period (24 hours), no patients were lost to follow-up, and all data were analyzed. The trial concluded upon reaching 40 participants in each group.

As shown in Table 1, the average age in the intervention group was 43.85 years, while in the control group, it was 41.95 years. Additionally, the average weight was 70.73 kg in the intervention group and 75.15 kg in the control group. Each group included 40 patients. All surgeries were performed by the same team of surgeons at Shahid Mohammadi Hospital.

Table 2 presents the mean and standard deviation of pain, nausea, vomiting, and analgesic administration variables for both groups. The average pain score at 6 hours post-surgery was 3.80 ± 1.60 in the test group and 6.95 ± 1.60 in the control group ($p < 0.000$, $t = -2.26$, 95% confidence interval [CI]). At 12 hours, the average pain score was 2.40 ± 1.42 in the test group and 6.15 ± 1.38 in the control group ($p < 0.000$, $t = -8.42$, 95% CI). After 18 hours, pain scores were 0.55 ± 0.82 in the test group and 5.9 ± 1.44 in the control

Table 1: Age and weight of the statistical population

Variable	Group	Patients	Mean	SD	Minimum	Maximum
Age	intervention	40	43.85	11.06	27	62
	Control	40	41.95	8.61	30	60
Weight	intervention	40	73.70	12.83	59	98
	Control	40	75.15	12.10	55	97

Table 2: mean and standard deviation of variables in the test group* Pain is evaluated for patients using the VAS scoring system.

Variable	Group	Patients	Mean	SD	T	df	Sig.
Pain (6 hours)	Test	40	3.80	1.60	-2.26	38	0.000
	Control	40	6.95	1.60			
Pain (12 hours)	Test	40	2.40	1.42	-8.42	38	0.000
	Control	40	6.15	1.38			
Pain (18 hours)	Test	40	0.55	0.82	-14.35	38	0.000
	Control	40	5.90	1.44			
Nausea	Test	40	0.95	0.94	-5.35	38	0.000
	Control	40	2.55	0.94			
Vomiting	Test	40	0.35	0.48	-7.52	38	0.000
	Control	40	1.85	0.74			
Analgesic	Test	40	1.00	0.56	-7.09	38	0.000
	Control	40	2.65	0.87			

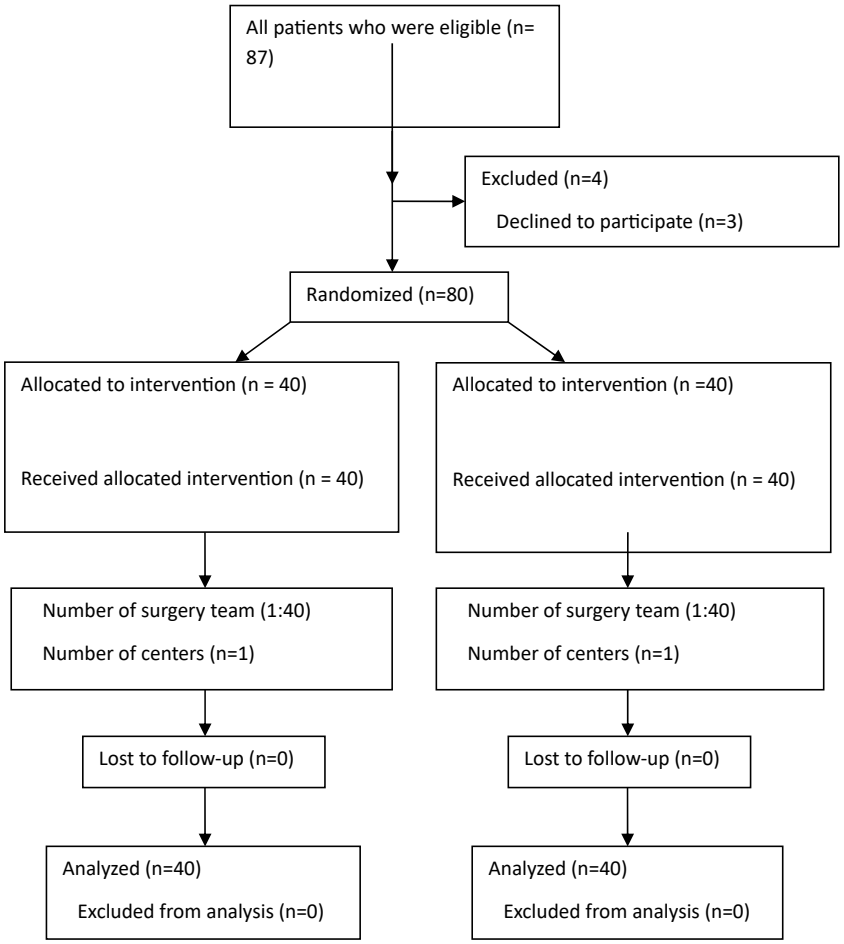

Fig. 1: Patients' flow diagram

group ($p < 0.000$, $t = -14.35$, 95% CI).

Furthermore, the mean duration of nausea (test: 0.95 ± 0.94, control: 2.55 ± 0.94) ($p < 0.000$, $t = -5.35$, 95% CI), the number of vomiting episodes (test: 0.35 ± 0.48, control: 1.85 ± 0.74) ($p < 0.000$, $t = -7.52$, 95% CI), and analgesic administration (test: 1.00 ± 0.56, control: 2.65 ± 0.87) ($p < 0.000$, $t = -7.09$, 95% CI) were significantly lower in the test group compared to the control group. These findings suggest that intraperitoneal dexamethasone injection effectively alleviates post-laparoscopic surgery pain, nausea, and vomiting.

All surgeries were successfully performed without complications. Patients' vital signs remained stable post-surgery, and no adverse effects or significant risks were observed.

Discussion

Our standard treatment choice for gallbladder stones in patients requiring surgery remains laparoscopic cholecystectomy. Although it has a few complications, it is still preferable to open surgery [19]. One-third of patients undergoing laparoscopic cholecystectomy experience considerable pain during the first day following surgery [20]. Several studies have demonstrated the effects of dexamethasone on postoperative pain and opioid consumption after surgery [21]. Thus, our study concludes that the intraperitoneal injection of dexamethasone from the umbilical port site reduces postoperative pain, nausea, vomiting, and analgesic consumption in patients undergoing laparoscopic cholecystectomy.

Kanwal Jamil et al. [22] evaluated the efficacy of dexamethasone in reducing pain after laparoscopic cholecystectomy. Unlike our study, dexamethasone in their trial was administered intravenously. In contrast, in our research, 8 mg of dexamethasone was injected directly into the umbilical port site, whereas in their study, dexamethasone was given at a dosage of 0.1 mg/kg combined with 5 ml of saline solution during anesthesia induction. Additionally, the statistical population in their study was larger than in ours. For pain assessment, Visual Analog Scale (VAS) scores were recorded at two, six, twelve, and twenty-four hours post-surgery in their study, whereas we measured pain scores three times after surgery. Ultimately, their findings were consistent with the outcomes of our study.

In a study conducted by Thue Bisgaard et al. [23], the effects of preoperative dexamethasone on surgical outcomes were assessed. This placebo-controlled trial involved 88 patients, a sample size comparable to ours, with an injection dose of 8 mg administered 90 minutes before surgery. Unlike our study, additional variables evaluated included pulmonary function and C-reactive protein (CRP). The findings of this study support our data, indicating reduced pain, nausea, and vomiting.

Ahmadreza Mohtadi et al. [17] conducted a trial exploring the analgesic effects of dexamethasone in patients undergoing laparoscopic cholecystectomy. A total of 122 participants were classified into case and control groups: in the intervention group, general anesthesia was administered, and dexamethasone at a dosage of 0.1 mg/kg was given intravenously, whereas in the control group, normal saline was used instead of dexamethasone. Our study evaluated pain scores at 6, 12, and 18 hours post-surgery, while this study measured pain scores at five time points within 24 hours following arrival in the post-anesthesia care unit (PACU). Both studies utilized the Visual Analog Scale (VAS). According to the collected data, the average pain severity at the beginning and end of the 24-hour period after admission to the unit was similar between the two groups. However, mean postoperative pain severity at two, six, and twelve hours after arrival in PACU was significantly lower in the dexamethasone group compared to the control group ($P < 0.05$).

While most studies support the analgesic effect of dexamethasone, Mokhtar Elhakim et al. [18] demonstrated in a randomized controlled trial that the combination of 8 mg dexamethasone and 4 mg ondansetron effectively reduces nausea and vomiting after laparoscopic cholecystectomy; however, it does not significantly reduce postoperative pain.

The pain-relieving effect of dexamethasone is well-documented in various types of surgeries, including joint arthroplasty and other clinical procedures similar to ours. This effect is achieved through the suppression of peripheral phospholipase and the reduction of cyclooxygenase and lipoxygenase activity [24-26]. Although glucocorticoids suppress the immune system, a study by Tomás B. Corcoran et al. [27] found no significant incidence of surgical site infections within 30 days postoperatively in patients undergoing non-cardiac surgery [28]. Our study specifically examined this property of dexamethasone in laparoscopic cholecystectomy, focusing on its administration via port site injection into the intraperitoneal space.

One limitation of our study was its small sample size. Future research could address this issue by incorporating a larger population. Another limitation was the presence of uncontrolled variables, such as the financial and social status of the participants' families. Additional constraints included sample loss, the limited duration of follow-up, and the reliance on a questionnaire for pain assessment.

Conclusion

The study found that administering 8 mg of intraperitoneal dexamethasone after laparoscopic cholecystectomy significantly reduces postoperative pain, nausea, and vomiting. Additionally, it decreases the need for analgesics. Overall, dexamethasone injection via the umbilical port site enhances recovery following the procedure.

Clinical Trial Registration Code

This interventional study, as a randomized, single-blinded clinical trial, has been registered on Iran's clinical trials website (ID No.: IRCT20240711062392N1).

Conflict of Interests Statement

The authors declare that they have no competing interests.

Data Availability

The dataset presented in this study is available upon request from the corresponding author during submission or after publication.

Ethical Approval

This project was reviewed by the Ethics Committee of Hormozgan University of Medical Sciences and approved by the Ethics Committee based on the sent documents (ID No.: IR.HUMS.REC.1399.454).

Funding/Support

The authors received no financial support from public or private sources.

Informed Consent

Written informed consent was obtained.

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