ORIGINAL ARTICLE

Intraperitoneal hydrocortisone for pain relief after laparoscopic cholecystectomy

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ABSTRACT

Background: Laparoscopic cholecystectomy is associated with shorter hospital stay and less pain in comparison to open surgery. The aim of this study was to evaluate the effect of intraperitoneal hydrocortisone on pain relief following laparoscopic cholecystectomy. **Methods:** Sixty two patients were enrolled in a double-blind, randomized clinical trial. Patients randomly received intraperitoneal instillation of either 250 ml normal saline (n=31) or 100 mg hydrocortisone in 250 ml normal saline (n=31) before insufflation of CO_2 into the peritoneum. Abdominal and shoulder pain were evaluated using VAS after surgery and at 6, 12, and 24 hours postoperatively. The patients were also followed for postoperative analgesic requirements, nausea and vomiting, and return of bowel function. **Results:** Sixty patients completed the study. Patients in the hydrocortisone group had significantly lower abdominal and shoulder pain scores (10.95 vs 12.95; $P<0.01$). The patients were similar regarding analgesic requirements in the recovery room. However, those in the hydrocortisone group required less meperidine than the saline group (151.66 (±49.9) mg vs 61.66 (±38.69) mg; $P=0.00$). The patients were similar with respect to return of bowel function, nausea and vomiting. No adverse reaction was observed in either group. **Conclusion:** Intraperitoneal administration of hydrocortisone can significantly decrease pain and analgesic requirements after laparoscopic cholecystectomy with no adverse effects.

Key words: *Cholecystectomy, intraperitoneal hydrocortisone, laparoscopy, postoperative pain*

INTRODUCTION

Laparoscopic cholecystectomy is the treatment of choice for symptomatic cholelithiasis. Although there are clear benefits compared with open surgery, postoperative pain is still a common complaint after laparoscopic cholecystectomy. Pain can prolong hospital stay and lead to increased morbidity, which is particularly important in centers performing this operation as a day-case procedure.[1] Different methods have been proposed to relieve postoperative pain following laparoscopic cholecystectomy.[2-4]

Administration of intraperitoneal local anesthetics alone[5-7] or in combination with nonopioid analgesics[8,9] have been used to reduce postoperative pain following laparoscopic cholecystectomy. This might reduce adverse effects of opioids'

On the other hand, steroids have also been used successfully for postoperative pain relief in different kinds of surgery.[10-12]

The purpose of this study was to assess the effect of intraperitoneal hydrocortisone to reduce postoperative pain after laparoscopic cholecystectomy under general anesthesia. The primary outcome was to compare pain scores. The secondary outcomes included postoperative analgesic requirements, frequency of nausea and vomiting, length of hospital stay, time of return of bowel function, time of unassisted ambulation, and time of oral intake.

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METHODS

After approval of the local ethics committee and informed consent, 62 patients of ASA physical status I-II scheduled for elective laparoscopic cholecystectomy were recruited for the study. The exclusion criteria were chronic pain diseases other than gallstone disease, use of opioids,

tranquilizers, steroids, NSAIDs, and alcohol, patients with acute cholecystitis, allergy to corticosteroids, neuromuscular diseases and bleeding disorders.

After receiving 5 ml/kg crystalloids, preoxygenation with 100% O_2 for 3 minutes, 2 μg/kg of fentanyl and 0.05 mg/kg of midazolam, anesthesia was induced with thiopenthal 5 mg/kg followed by 0.15 mg/kg of cisatracurium to facilitate endotracheal intubation. Anesthesia was maintained with 60% N_2O in oxygen and propofol 4-6 mg/kg/hr (to keep cerebral state index at 40-60) and remifentanyl 0.05-0.5 μg/kg/min (to maintain mean arterial blood pressure and pulse rates within 20% of the baseline). All patients received 1 μg/kg of fentanyl 5 minutes before the end of operation to reduce postoperative pain.

After receiving the standard anesthesia and before insufflations of CO_2, the patients were randomized to receive either instillation of 250 ml of normal saline or 100 mg hydrocortisone in 250 ml normal saline into the peritoneum by a surgical scrub nurse who was blind to the study. The patients were then rotated into Trendelenburg, anti-Trendelenburg, left and right lateral decubitus, and finally supine positions (each for 2 minutes). Nasogastric tube was inserted for all patients after induction and was removed at the end of the surgery. All surgical procedures were performed by a single surgeon. During laparoscopy, intra-abdominal pressure was maintained at 14 mmHg. Carbon dioxide was carefully evacuated at the end of surgery by manual compression of the abdomen with open trocars. Ten milliliters of bupivacaine 0.25% was injected in laparoscopy entering sites. Patients were followed by a blind investigator for postoperative abdominal and shoulder pain using VAS based on a 0-10 scale (with 0 meaning no pain and 10 meaning the most intense pain ever experienced), postoperative analgesic requirements, presence of nausea and vomiting, time of unassisted ambulation, time of oral intake and time of return of bowel function in the recovery room and at 6, 12 and 24 hours after operation. Time of return of bowel function was defined as the time from end of anesthesia until presence of intestinal sound or first passage of flatus.

We used intramuscular meperidine 0.5 mg/kg and 1 mg/kg as rescue analgesic for VAS 4-7, and 8-10, respectively.

Using SPSS software for Windows, version 11(SPSS Inc, Chicago, IL, USA), arithmetic mean and standard deviation values for different variables were calculated and statistical analyses were performed for each group. We used independent Student *t*-test to compare continuous variables exhibiting normal distribution, and Chi-square test and Mann-Whitney *U* test for noncontinuous variables. *P* value less than 0.05 was considered significant.

RESULTS

Sixty patients completed the study. Two were excluded since conversion to open cholecystectomy was necessary in both cases because of dense inflammatory adhesions. There were no statistically significant differences between the two groups in terms of demographic data and duration of surgery [Table 1].

The patients were similar with respect to factors likely to increase postoperative pain including: Bile spillage from punctured gallbladder, difficult dissection due to adhesions from previous surgery, bleeding, need to cholangiography, injury to bowels or other organs, and insertion of drain.

The abdominal and shoulder pain scores were significantly lower in the hydrocortisone group in the recovery room and at 6, 12, and 24 hours postoperatively (total scores 10.95 vs 12.95 in the hydrocortisone and saline group, respectively; $P<0.01$) [Table 2].

The patients were similar regarding analgesic requirements in the recovery room. Nevertheless, patients in the saline group required more meperidine than the hydrocortisone group (151.66 (±49.9) mg vs 61.66 (±38.69); $P=0.00$)] [Table 3].

The patients were similar with respect to frequency of nausea and vomiting, length of hospital stay, time of return

Table 1: Patients data and operation characteristics

	Saline group	Hydrocortisone group	*P* value
Age (yr)	44.5 (±3.64)	44.6 (±3.32)	0.971
Sex (female:male)	18:12	19:11	0.991
Weight (kg)	69.7 (±8.22)	72.2 (±7.94)	0.236
Height (cm)	162 (±5.75)	162 (±5.45)	0.963
Duration of surgery (min)	93.5 (±9.65)	93.8 (±10.3)	0.898

Data are presented as numbers or mean (±SD)

Table 2: Visual analog pain scores in the two groups

Group time	Saline group	Hydrocortisone group	*P* value
In the recovery room	4.73 (±0.9)	4.23 (±0.77)	0.025
At 6 hours	3.73 (±0.9)	3.13 (±0.73)	0.007
At 12 hours	2.76 (±0.77)	2.26 (±0.58)	0.006
At 24 hours	1.73 (±0.69)	1.33 (±0.47)	0.012

Data are presented as mean (±SD)

of bowel function, time of unassisted ambulation, and time of oral intake [Table 4].

DISCUSSION

We demonstrated that intraperitoneal injection of hydrocortisone can reduce pain and analgesic requirements following laparoscopic cholecystectomy without significant side effects.

Provision of adequate postoperative pain relief is of considerable importance following day-case laparoscopic cholecystectomy.[1] Pain after laparoscopic cholecystectomy is affect by several factors including patient demographics, nature of underlying disease, surgical factors, volume of residual gas, type of gas used for pneumoperitoneum, and the pressure created by the pneumoperitoneum.[13-18] A number of techniques have been described for reducing postlaparoscopy pain including: Preincisional infiltration and intraperitoneal instillation of levobupivacaine 0.25%;[19] intraperitoneal ropivacaine and a gas drain;[20] intraperitoneal levobupivacaine with epinephrine;[21] intraperitoneal application of bupivacaine plus morphine;[22] preincisional injection of bupivacaine;[23] pre-emptive intraperitoneal injection of ropivacaine;[24] and intraperitoneal lidocaine combined with intravenous or intraperitoneal tenoxicam.[25] It is suggested that post-laparoscopic cholecystectomy pain is multifactorial and methods for short term analgesia cannot improve postoperative functions or shortened hospitalization.[26]

It has been shown that glucocorticoids can play a crucial role in the regulation of inflammatory responses through both genomic and nongenomic mechanisms and therefore may reduce pain.[27] Among corticosteroids, dexamethasone has been used widely to reduce postoperative pain.[28-30] The mechanism of analgesic effect of steroids is not well known.

The proposed mechanisms include: Suppression of tissue levels of bradykinin and the release of neuropeptides from nerve endings; reduction in prostaglandin production resulting in inhibition of the synthesis of the cyclooxygenase isoform-2 in peripheral tissues and in the central nervous system; and inhibition of other mediators of inflammatory hyperalgesia, for example, tumor necrosis factor-a, interleukin-17b, and interleukin-6.

The effect of intraperitoneal corticosteroids on pain after elective laparoscopic cholecystectomy has not been investigated. We assumed that early postoperative pain was mainly generated by irritation of the peritoneum, and the application of corticosteroids may attenuate this pain.

We used intraperitoneal hydrocortisone successfully to reduce pain following laparoscopic cholecystectomy. Although meperidine requirement was similar in both groups in the recovery room, patients in the hydrocortisone group required less analgesic afterwards. This might be attributed to short analgesic effect of intraoperative remifentanil.

In conclusion, our study showed that intraperitoneal injection of hydrocortisone before gas insufflation in laparoscopic cholecystectomy can reduce postoperative pain with no significant postoperative adverse effect.

Table 3: Postoperative meperidine requirements in the two groups

Group time	Hydrocortisone group	Saline group	*P* value
In the recovery room (mg)	40.00 (20.34)	41.66 (18.95)	0.25
At 6 hours (mg)	21.66 (25.22)	46.66 (12.68)	00
At 12 hours (mg)	00	41.66 (18.95)	00
At 24 hours (mg)	00	20.00 (24.99)	00

Data are presented as mean (±SD)

Table 4: Recovery variables between two groups

	Saline group	Hydrocortisone group	*P* value
Time of oral intake (hours)	13.1 (±1.7)	12.3 (±1.49)	0.082
Time of unassisted ambulation (hours)	14.4 (±1.45)	14.6 (±1.49)	0.664
Time of bowel function (hours)	20.8 (±2.3)	18.6 (±1.49)	0.000
Length of hospital stay (hours)	28.6 (±1.27)	27.5 (±1.88)	0.016

Data are presented as mean (±SD)

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