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ORIGINAL ARTICLE

Intraperitoneal Hydrocortisone plus Bupivacaine administration For Pain Relief after Laparoscopic Cholecystectomy, A Comparison with Bupivacaine Alone

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Abstract

Introduction: shorter hospital stay and less pain in comparison to open surgery considered to be major benefits for laparoscopic cholecystectomy. We compared the effect of intraperitoneal hydrocortisone plus bupivacaine with bupivacaine alone on pain relief following laparoscopic cholecystectomy.

Methods: Sixty two patients participated in this double-blind, randomized clinical trial. Patients randomly received intraperitoneal instillation of either 100 mg bupivacaine in 250 ml normal saline (n=32) or 100 mg hydrocortisone plus 100 mg bupivacaine in 250 ml normal saline (n=30) before insufflation of CO_2 into the peritoneum. Abdominal and shoulder pain were evaluated using VAS postoperatively. The patients were also followed for postoperative analgesic requirements, nausea and vomiting, and return of bowel function.

We used independent Student *t*-test and Chi-square test and Mann-Whitney *U* tests with SPSS software to compare quantitative and qualitative variables, respectively. *P* value less than 0.05 was considered significant.

Results: Sixty patients completed the study. Patients in the hydrocortisone plus bupivacaine group had significantly lower abdominal and shoulder pain scores (11.72 vs 8.92 in the bupivacaine and bupivacaine plus hydrocortisone group, respectively; $P<0.01$). The patients were similar regarding analgesic requirements .The patients were similar with respect to return of bowel function, nausea and vomiting. No adverse reaction was observed in either group.

Conclusions: Intraperitoneal administrations of hydrocortisone plus bupivacaine can alleviate pain after laparoscopic cholecystectomy better than intraperitoneal bupivacaine alone.

Key Words: Cholecystectomy; Laparoscopy; Postoperative pain; intraperitoneal bupivacaine; intraperitoneal hydrocortisone

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Introduction

The treatment of choice for symptomatic cholelithiasis is laparoscopic cholecystectomy. Beside several benefits for laparoscopic cholecystectomy compared with open surgery, postoperative pain is still a common discontent after laparoscopic cholecystectomy. Prolonging hospital stay that lead to increased morbidity and delayed return to work are unwanted disadvantages that pain cause [1] Different methods have been tried 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. Except one study done by Sarvestani et al. that showed intraperitoneal hydrocortisone can reduce pain after laparoscopic cholecystectomy without significant side effects [10] there was not any other study evaluating the effect of intraperitoneal steroids on post operative laparoscopic cholecystectomy pain. On the other hand, steroids have also been used successfully for postoperative pain relief in combination to other modalities in different kinds of surgery [10-12] and different studies showed the addition of glucocorticoids to local anesthetics can prolong the onset and duration of nerve blockade that can reduce their effective dosage and side effects [13-15]. To the best of the author' knowledge, no study compare the intraperitoneal efficacy of glucocorticoids and local anesthesia combination with local anesthetics alone. The purpose of this study was to compare the intraperitoneal efficacy of glucocorticoids and local anesthesia combination with local anesthetics alone regarding 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 after laparoscopic cholecystectomy under general anesthesia.

Methods

62 patients of (American Society of Anesthesiologists) ASA physical status I-II scheduled for elective laparoscopic cholecystectomy were enrolled for this study, after approval of the local ethics committee (Etheic code: 483/T) and informed consent. 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. All of the patients received the same anesthesia. 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 2 O in oxygen and propofol 4-6 mg/kg/hr (to keep cerebral state index at 40-60) and remifentanyl 0.05-0.5μg/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(using block of four) to receive either instillation of 100 mg bupivacaine in 250 ml of normal saline or 100 mg hydrocortisone plus 100 mg bupivacaine 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 15(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 and Chi-square test and

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Mann-Whitney *U* tests to compare quantitative and qualitative variables, respectively. *P* value less than 0.05 was considered significant.

Results

Sixty patients completed the study. Two were excluded due to conversion to open cholecystectomy 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).

Data are presented as numbers or mean(±SD) 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 bupivacaine plus hydrocortisone group in the recovery room and at 6, 12, and 24 hours (Table 2).

The patients were similar regarding analgesic requirements in the recovery room, and at 6, 12 and 24 hours after operation (Table 3).

Frequency of nausea and vomiting, length of hospital stay, time of return of bowel function, time of unassisted ambulation, and time of oral intake were similar in both groups (Table 4).

Table 1: Patients data and operation characteristics

Data	Group		P-value
	Bupivacaine group	Bupivacaine and Hydrocortisone group	
Age (yr)	44.16(±8.39)	45.8(±2.93)	0.198
Sex(femle:male)	18:12	18:12	1.00
Weight(kg)	70.03(±9.60)	72.43(±9.26)	0.292
Height(cm)	162.2(±5.99)	162.3(±5.94)	0.929
Duration of surgery(min)	94.16(±11.22)	95.00(±9.46)	0.753

Table 2: Visual analogue abdominal pain scores in two groups

Time	Group		P-value
	Bupivacaine group	Bupivacaine and Hydrocortisone group	
In the recovery room(mg)	4.33(±0.84)	3.60(±0.89)	0.001
At 6 hours(mg)	3.33(±0.84)	2.60(±0.62)	0.001
At 12 hours(mg)	2.53(±0.57)	1.66(±0.60)	0.001
At 24 hours(mg)	1.53(±0.57)	1.06(±0.25)	0.004

Data are presented as mean (±SD)

Table 3: Postoperative meperidine requirements in the two groups

Time	group		P-value
	Bupivacaine group	Bupivacaine and Hydrocortisone group	
In the recovery room(mg)	40.00(±20.34)	31.66(±24.5)	0.56
At 6 hours(mg)	25.00(±25.42)	8.33(±18.95)	0.18
At 12 hours(mg)	15.00(±23.3)	1.66(±9.12)	0.15
At 24 hours(mg)	00	00	1.00

Data are presented as mean (±SD)

Table 4: Recovery variables between two groups

Time	Group		P-value
	Bupivacaine group	Bupivacaine and Hydrocortisone group	
Time of oral intake (hours)	12.7(±1.44)	12.20(±1.47)	0.241
Time of unassisted ambulation (hours)	14.66(±1.47)	14.26(±1.36)	0.287
Time of bowel function(hours)	18.96(±1.54)	17.76(±3.49)	0.051
Time of hospital stay(hours)	27.86(±1.87)	27.40(±1.86)	0.302

Data are presented as mean (±SD)

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Discussion

We showed that intraperitoneal administration of hydrocortisone plus bupivacaine can decrease pain without analgesic requirements after laparoscopic cholecystectomy more than intraperitoneal bupivacaine alone without significant side effects. Adequate postoperative pain relief is very important following day-case laparoscopic cholecystectomy [1]. 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 affect post laparoscopic cholecystectomy pain [16-21]. A number of techniques have been described for reducing post laparoscopy pain including: Preincisional infiltration and intraperitoneal instillation of levobupivacaine 0.25% [22]; intraperitoneal ropivacaine and a gas drain [23]; intraperitoneal levobupivacaine with epinephrine [24]; intraperitoneal application of bupivacaine plus morphine [25]; preincisional injection of bupivacaine [26]; pre-emptive intraperitoneal injection of ropivacaine [27]; and intraperitoneal lidocaine combined with intravenous or intraperitoneal tenoxicam. [28] It is suggested that post-laparoscopic cholecystectomy pain is multifactorial and methods for short term analgesia cannot improve postoperative functions or shortened hospitalization [29]. 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 [29]. The mechanism of analgesic effect of steroids is not well known. Sarvestani et al. Showed intraperitoneal hydrocortisone can reduce pain after laparoscopic cholecystectomy without significant side effects [10].

Prolonging the onset and duration of nerve blockade that can reduce their effective dosage and side effects by addition glucocorticoids to local anesthetics showed in different studies [13-15]. Some authors believe that there is a causative relationship between the suppression of inflammation by corticosteroids and the remarkably longer duration of effect [30]. The use of corticosteroids as an adjuvant to local anesthetic for nerve blocks rarely has been described, and Its mechanism of action is not clearly understood. One possibility is that prolongation of local anesthetic block occurs because of systemic effects of corticosteroids. Some authors believe that analgesic properties of corticosteroids are the result of their systemic effect [31, 32]. Unfortunately, a control group receiving parenteral administration of the same dose of hydrocortisone was not considered when this study was designed.

To the best of the author' knowledge, no study compare the intraperitoneal efficacy of glucocorticoids and local anesthesia combination with local anesthetics alone.

Adding a steroid to local anesthetic solution may not be indicated for all patients. For example, diabetic patients may experience hyperglycemia and patients with a continuing infectious process may be detrimentally affected by the anti-inflammatory effects of steroids.

The use of steroids to increase the duration of action of local anesthetics is not an indication of these drugs. This study led us to hypothesize that it may be useful in situations in which local anesthetics must be used with caution (e.g., hypertension, ischemic heart disease). Considering cardiovascular toxicity, lidocaine is safer than bupivacaine. Prolonging efficacy of local anesthetics by adding glucocorticoids help us local anesthetics in smaller doses. We used intraperitoneal hydrocortisone in combination with local anesthetic (bupivacaine) successfully to reduce pain following laparoscopic cholecystectomy. Although meperidine requirement was similar in both groups bur visual analogue pain scores are lower in hydrocortisone and bupivacaine group.

Conclusions

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

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