Incidence and Risk Factors of Moderate to Severe Pain in 24 hours after Laparoscopic Cholecystectomy

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ABSTRACT

Objective: Laparoscopic cholecystectomy (LC) is considered to cause no significant pain. However, the literature reveals 58%-87% incidence of moderate to severe post-operative after this procedure. The objectives of this study were 1) finding the incidence of moderate to severe pain during the first 24 hours after LC surgery, and 2) identifying risk factors for it.

Methods: In a retrospective study the charts of 245 patients ≥ 18 years of age with LC surgery at Siriraj Hospital in 2008 were reviewed. Cases with conversion to open cholecystectomy were excluded. Insufficient documentation (pain score recorded < 5 times within the first 24 hours) was also an exclusion criterion. Demographic data and peri-operative anesthetic and surgical characteristics including outcome and pain therapy were recorded.

Results: Two hundred and forty LC cases (67 male, 163 female) with diagnosis of calculus of gall bladder, acute or chronic cholecystitis, and cholangitis met the criteria. The incidence of moderate to severe pain (NRS 4-10) within the first 24 hours was 76.7%. Risk factors of relevant post-operative pain with statistical significance were not identified. However, patients receiving NSAIDs tended to have less pain. In 30 patients with persistent moderate to severe pain up to 48 hours post-operatively, post-operative vomiting and prolonged surgery (> 60 minutes) were significant risk factors.

Conclusion: Within the limitations of a retrospective study, we conclude that in LC surgery giving NSAIDs and antiemetic drugs prophylactically may lead to a better pain control, especially in prolonged surgical cases.

Keywords: Laparoscopic cholecystectomy

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INTRODUCTION

Laparoscopic cholecystectomy (LC) was first introduced in 1985 and became rapidly popular. The procedure almost completely replaced the traditional open cholecystectomy. The endoscopic approach leaves 3-4 small wounds at the abdomen. Patients with LC are reported to have faster recovery profile and less pain when compared with the conventional method.[1,2] However, recent studies demonstrate an incidence of moderate to severe pain after LC between 58%[3] to 87%.[4,5] Ekstein et al[6] reported post-operative pain score after LC being higher than after exploratory laparotomy surgery. Post-operative pain has its maximum usually during the first 6-8 hours after surgery, and then gradually decreases within 2-3 days.[4,7] More than 60% of the patients require analgesics.[8-10] Risk factors for post-operative pain after LC mainly concern on the individual patient, surgical factors and patients post-operative condition. In particular female gender,[11,12] patients pain tolerance and anxiety about pain,[4,11,13] multiple incisions for trocar insertion or extension of incisions are reported as risks. In addition post-operative nausea/vomiting leads to higher pain score. However, data are conflicting, as shown by Bisgaard et al.[4,7] The authors demonstrated that severity of pain after LC was not influenced by gender, age, weight, pathology at their biliary tract, extension of incisions, or perioperative blood loss.

Laparoscopic cholecystectomy is the most common procedure in general surgery service performed at Siriraj Hospital. The incidence of moderate to severe pain was yet unknown as were the risk factors related to it. Therefore this study was performed to answer these two questions for

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the first 24 post-operative hours. In addition the frequency and severity of nausea and vomiting as well as analgesic side effects were recorded.

MATERIALS AND METHODS

After ethical approval from the Siriraj Institutional Review Board (Si.491/2009), we retrospectively reviewed 245 charts of patients who underwent LC surgery at Siriraj Hospital in 2008. Exclusion criterions were age < 18 years, surgery converted to open cholecystectomy, and insufficient data: numerical rating pain score (NRS) recorded < 5 times within the first 24 hours.

All patients had received standard general anesthesia. The drugs used for induction, maintenance, muscle relaxation and analgesia were at anesthetists discretion and included thiopental, propofol, sevoflurane, isoflurane, atracurium, cisatracurium, vecuronium, fentanyl, and meperidine. Six percent of the patients received 40 mg Dynastat^{R} (parecoxib) intravenously during the operation. Most patients received intravenous antiemetic prophylaxis, either ondansetron (4 or 8 mg) alone or in combination with metoclopramide (10 mg) and dexamethasone (5 or 10 mg). A four-trocar technique of laparoscopic cholecystectomy was used and the gallbladder was extracted via an umbilical incision in all patients. Performance of pneumoperitoneum was standardized using carbon dioxide and keeping the intraabdominal pressure < 14 mmHg. At completion of surgery the surgeon infiltrated the wounds with about 20 ml 0.25% bupivacaine. All patients were extubated at the end of the operation and moved to the post anesthesia care unit (PACU). Immediate post-operative complications such as pain, nausea/vomiting, and/or respiratory depression were noted. Pain was usually treated with intermittent intravenous opioids (mostly meperidine) in order to maintain NRS < 4 and sedation score ≥ 2. After transferral to a surgical ward patients received pain and antiemetic medication as per surgeon's orders. At Siriraj Hospital, patients are usually allowed to receive oral acetaminophen on demand every 6 hours with additional analgesics such as opioids and/or NSAIDs. Post-operative pain level reported by patients used a numerical rating scale (NRS) ranging from 0-10 (0 = no pain, 10 = worst pain imaginable) which was recorded by the surgical ward nurse as the fifth vital signs.

Demographic data including age, gender, ASA physical status, body weight, body mass index (BMI), surgical diagnosis, premedication, and anesthetic technique and agents used were recorded. The outcome data included NRS at 1, 2, 3, 4, 6, 8, 10, 12 hours after surgery and then every 4 hours until hospital discharge, maximal pain score in 0-6 hours, 6-12 hours, 12-24 hours, and 24-48 hours post-operatively. In addition analgesics consumption, complications of treatment (respiratory depression, nausea, vomiting, pruritus and urinary retention), and antiemetics for post-operative nausea/vomiting were recorded. Patients with any of the complications mentioned above were further inspected on their severity and response to treatment. Then they were classified into 4 groups; 0 = no side effect, 1 = mild effect, no need for treatment, 2 = symptom relieved by simple treatment, and 3 = symptom not relieved by simple treatment.

Results are reported as mean ± SD. Data were analyzed by using SPSS program version 13.0 Inc, Chicago, IL, USA. Descriptive analysis was used for demographic data. Chi-square or Fisher exact test which were used to compare outcome differences between groups, and a p-value < 0.05 was considered statistically significant.

RESULTS

Two hundred and forty patients (63 males, 167 females) met the criteria, most were less than 60 years of age, and ASA physical status was I to III. One single emergency case occurred. Most of them were discharged 24 to 48 hours post-operatively. There were 41 patients with delayed discharge (> 72 hours), all of them for surgical reasons.

Eighty eight percent of the diagnoses were cholelithiasis. Patients' characteristics have been presented in Table 1. The incidence of moderate to severe pain within the first 24 hours after LC was 76.7%, and sixty five patients (27.1%) had severe pain (NRS 8-10). Only 24 percent of the patients had mild pain. Pain management after surgery usually included intermittent morphine (1-4 mg) or meperidine (25 mg) intravenously for NRS > 7. Average opioid consumption per patient during the entire hospital stay was 5.22 mg morphine (or morphine equivalent). The dosage ranged from 0 mg to 55 mg. On demand all patients were allowed to receive oral acetaminophen 500-1000 mg every 6 hours. Adjuvant to opioid and acetaminophen 30% of the patients got 120 mg oral Arcoxia^{R} (etoricoxib) once a day.

NSAIDs, given either intra-operatively (intravenous 40 mg Dynastat^{R}) or post-operatively (120 mg oral Arcoxia^{R}) significantly reduced the incidence of moderate to severe pain within the first 24 hours (Table 2). Inflammation of the hepatobiliary system (acute/chronic cholecystitis, cholangitis), and post-operative vomiting were risk factors for severe post-operative pain (Table 3). There were 30 patients with prolonged moderate to severe pain until 48 hours post-operatively. The risk factors in this group were prolonged surgery (> 60 minutes) and post-operative vomiting (Table 4).

The side effects of pain therapy have been presented in Table 5. Nausea was the most common side effect (18.4 percent of the studied population). Patients who developed complications were mostly treated successfully by adequate medication or simple procedures (such as urinary catheterization). However, there was one patient with respiratory depression not responding to naloxone who required intubation and temporary mechanical ventilation.

TABLE 1. Demographic data of 240 Laparoscopic Cholecystectomy cases.

Patients characteristics	n (%)
Female	163 (72.1)
Age < 60 yr	146 (60.8)
ASA status 1	79 (32.9)
2	133 (55.4)
3	28 (11.7)
BMI < 30 kg/m^2	213 (88.8)
Diagnosis	
Cholelithiasis	213 (88.8)
Acute cholecystitis	18 (7.5)
Chronic cholecystitis	7 (2.9)
Acute cholangitis	2 (0.8)

TABLE 2. Risk factors of moderate to severe pain in the first 24 hours post-operative.

Risk factor	Mild pain n (%)	Moderate to severe pain n (%)	p-value
Number of cases	56	184	
Female	36 (64.3)	137 (74.5)	0.137
Age < 60 yr	50 (28)	64.1 (118)	0.058
ASA 3-4	14.3 (8)	10.9 (20)	0.486
Inflammation†	7.1 (4)	12.5 (23)	0.267
NSAIDs	32.1 (59)	26.4 (26)	0.049*
Prolonged operation‡	58.9 (33)	62 (114)	0.684
Post-operative nausea	12.5 (7)	20.1 (37)	0.198
Post-operative vomiting	7.1 (4)	30 (16.3)	0.085
Morphine (or equivalent) dose	1.95 mg	6.01 mg*	

† = Diagnosis of acute/chronic cholecystitis or acute cholangitis
‡ = Surgical time longer than 60 minutes
* = Calculated by N = 183 cases (one out of 184 cases had unusual opioid consumption of 44 mg and we omitted this case)

TABLE 3. Risk factors of severe pain in the first 24 hours post-operative.

Risk factor	Mild to moderate pain n (%)	Severe pain n (%)	p-value
Number of cases	175	65	
Female	69.2(121)	80 (52)	0.096
ASA 3-4	12 (21)	10.7 (7)	0.792
Inflammation†	8.5 (15)	18.4 (12)	0.031*
NSAIDs	37.7 (66)	29.2 (19)	0.222
Prolonged operation‡	57.7 (101)	70.7 (46)	0.065
Post-operative nausea	16 (28)	24.6 (16)	0.125
- vomiting	10.8 (19)	23 (15)	0.016*

† Diagnosis of acute/chronic cholecystitis or acute cholangitis
‡ = Surgical time longer than 60 minutes

TABLE 4. Risk factors of persistent moderate to severe pain in the 0-48 hours post-operative.

Risk factor	Mild pain group n (%)	Moderate to severe pain; n (%)	p-value
Number of cases	210	30	
Female	72 (150)	77 (23)	0.55
ASA 3-4	13 (27)	4 (1)	0.129
Inflammation†	10 (21)	20 (6)	0.121
NSAIDs	26.7 (8)	36.7 (77)	0.284
Prolonged operation‡	58 (121)	87 (26)	0.002*
Post-operative nausea	17 (35)	30 (9)	0.077
Vomiting	13 (26)	74 (8)	0.048*

† = Diagnosis of acute/chronic cholecystitis or acute cholangitis
‡ = Surgical time longer than 60 minutes

DISCUSSION

The incidence of moderate to severe pain after LC surgery in the first 24 hours at Siriraj Hospital was high (76.7%).[3-5] In most cases, the pain subsided within 24 hours, which is again similar to other investigators[7]. Pain treatment in our patients seemed to be inadequate, as 47% who had moderate to severe pain within the first 24 hours did not receive any opioids.

The procedure-specific post-operative pain management (PROSPECT) recommendation for post-operative pain management after LC was released in 2007, and the full details are described elsewhere.[14,15] In summary, pre-operative cox-2 inhibitors, gabapentin, and dexamethasone, as well as local anesthetics infiltration at trocar sites and/or intra-peritoneal instillation of long acting local anesthetics have been proven to reduce post-operative pain in these patients. Intra-operative low pressure carbon dioxide insufflations followed by saline lavage is recommended. General anesthesia is the technique of choice. Systemic opioids or NSAIDS can be used intra-operatively. Most recommended systemic analgesics for treatment of post-operative pain are NSAIDs and acetaminophen, with opioids as rescue medication. However, there is no study reporting accurately the effect on pain control when strictly following the PROSPECT recommendations. Other investigators[16,17] proposed suggestions on how to improve the quality of post-operative pain management for this particular type of

TABLE 5. Side effects of pain therapy.

Side effects	0 n (%)	1 n (%)	2 n (%)	3 n (%)
Respiratory depression	236 (98.3)	1 (0.4)	2 (0.8)	1 (0.4)
Nausea	196 (81.7)	10 (4.2)	34 (14.2)	0
Vomiting	206 (85.8)	8 (3.3)	26 (10.8)	0
Pruritus	237 (98.8)	1 (0.4)	2 (0.4)	0
Urinary retention	236 (98.3)	3 (1.3)	1 (0.4)	0

0 = No side effect
1 = Mild effect, no need for treatment
2 = Symptom relieved by simple treatment (small bolus dose of iv naloxone for respiratory depression, antiemetic drug for nausea/vomiting, single catheterization for urinary retention)
3 = Symptom not relieved by simple treatment (one case with severe respiratory depression required endotracheal intubation)

surgery, and the details were quite similar to PROSPECT. Pain after laparoscopic cholecystectomy is a result of various impacts such as tissue injury, abdominal distension, local trauma secondary to gall bladder removal, chemical irritation of the peritoneum, and the application of pneumoperitoneum.[7,10] Three types of pain typical for LC can be distinguished, visceral (in the abdomen), somatic (at the wounds), and referred pain of right shoulder. The maximum post-operative pain is usually within the first 8 hours after surgery,[10] with visceral pain being the most common.[10,18] Referred pain is less common and usually lasts no longer than 48 hours post-operatively.[10] The methods proven to reduce shoulder pain are intra-peritoneal saline lavage and intra-peritoneal local anesthetics instillation.[10,14] Local wound infiltration with bupivacaine is performed at our institution as this technique is recommended to reduce pain at the trocar sites.[10,14] Due to a lack of data in some charts, we could not gain accurate information about the type of post-operative pain in all patients. As a consequence this study cannot contribute to the question what pain management is particularly suitable to some kind of pain.

It is well known that female patients have a significantly higher intensity of pain than male patients,[10] something we could not demonstrate in our study. This may be due to the small number of patients enrolled compared with previous reports.[10] Post-operative pain score in patients with biliary tract inflammation was higher, which was most likely because they already have significant pain pre-operatively. Prolonged surgical time led to longer lasting high pain intensity, probably as a consequence of the degree of tissue injury. Patients with post-operative vomiting/nausea had post-operative pain scores significantly above average and also longer duration of pain. Antiemetic prophylaxis performed routinely may provide benefit for this operation.

NSAIDs are increasingly used for post-operative pain treatment in many surgical procedures including LC. We do not have this strategy yet. In the group of patients who had severe pain within the first 24 hours no NSAIDs was prescribed at all. Supported by our data, we suggest giving NSAIDs routinely after LC to improve pain management thus reducing the number of patients suffering from severe pain within the first 24 hours.

SUMMARY

Pain intensity after laparoscopic cholecystectomy is significantly greater than expected after so called "patient-friendly" surgery. Patients with biliary tract inflammation, prolonged surgery, post-operative vomiting, and no NSAIDs (either prophylactic or prescribed on demand) were at risk for relevant pain or prolonged pain. From this retrospective study, giving NSAIDs and antiemetic prophylaxis as a routine treatment in patients undergoing laparoscopic cholecystectomy might be helpful in order to provide better pain control, especially in prolonged surgical cases. However, future prospective randomized study in the same patient setting should be performed to get definite conclusions.

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