

# Patient controlled analgesia versus conventional analgesia for postoperative pain

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## ABSTRACT

**Purpose:** Patients may control postoperative pain by self-administration of intravenous opioids using devices designed for this purpose (patient controlled analgesia or PCA). This study set out to determine whether any of the two opioid administrations (i.e. PCA or conventional analgesia) would provide superior pain relief among patients undergoing laparoscopic cholecystectomy or not.

**Materials and Methods:** In a clinical trial the PCA group received self-administered intermittent intravenous morphine via PCA and the conventional group received intravenous Pethidine every 6 hours per day. The patients were assessed on an hourly basis for the first 4 hours after surgery, every 2 hours for the next 8 hours and every 4 hours for next 12 hours. Two methods were used in order to evaluate the degree of pain relief in patients: (1) facial pain scale; pain assessment based on the patient's appearance and (2) numerical rating scale; based on patient ratings of their pain.

**Results:** Forty eight patients (79.1% female, 20.1% male) with a mean age of  $45.7 \pm 10.7$  years old were enrolled into the study. During the first 24 hours after laparoscopic cholecystectomy, pain intensity based on facial pain scale was lower in the PCA group. However, the difference was significant only in the second hour (mean pain score in PCA group: 2.9, mean pain score in conventional group: 3.7,  $P = .007$ ). Also, the mean pain scores based on numerical rating scale were significantly lower in PCA group except for the first hour. Although it was not significantly lower than conventional group (mean pain score in PCA group: 4.2, mean pain score in conventional group: 4.6,  $P = .45$ ).

**Conclusion:** Intravenous PCA resulted in better postoperative pain reduction compared to intermittent bolus opioid delivery in laparoscopic cholecystectomy.

**Keywords:** cholecystectomy; postoperative pain; patient controlled analgesia; pain management; intravenous opioids.

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## INTRODUCTION

Analgesia is an essential part of postoperative care. However, 30-80% of patients complain about inadequate post-surgical pain relief.<sup>1</sup> Proper pain management, particularly postoperative pain that is normally perceived as nociceptive pain, is a major concern for

clinicians as well as for patients undergoing surgery.<sup>2</sup> Effective postoperative pain control is important to decrease the risk of postoperative complications, such as venous thromboembolism and nosocomial infections with early mobilization.<sup>3</sup> Intramuscular or intravenous administration of opioids has been used as the standard

method of treating postoperative pain. However, during the past few years, patient controlled analgesia (PCA) has been routinely used in postoperative care in many developed countries.<sup>4</sup>

PCA is usually used to deliver intermittent bolus doses of intravenous opioids postoperatively based on patients' demand. The dose is limited by a "lockout interval". It has also been used to administer other medications, for example following trauma or treating cancer pain, and to deliver non-opioids such as non-steroidal anti-inflammatory drugs.<sup>5-7</sup>

According to Williams and colleagues, intravenous PCA is considered the gold standard by which systematic opioids are delivered postoperatively. Unlike the traditional "as needed" analgesic regimens, intravenous PCA allows the clinician to compensate for several factors, including the wide inter- and intra-patient variability in analgesic needs, variability in serum drug levels, and administrative delays which might result in inadequate postoperative analgesia.<sup>8</sup>

Although PCA is regularly used in open cholecystectomy for postoperative pain management, its role in elective laparoscopic cholecystectomy has not been justified clearly.<sup>9</sup> Based on the authors investigations, assessment of the effect of this method (i.e. PCA) has been recommended by several studies.<sup>8</sup> Although many studies have been devoted to assessing PCA, to the authors' knowledge no report has yet been published concerning the comparison of PCA and conventional analgesia in laparoscopic cholecystectomy.

The aim of the present prospective study was to determine whether any of the two opioid administrations (i.e. PCA or conventional analgesia) would provide superior pain relief among patients undergoing laparoscopic cholecystectomy or not.

## MATERIALS AND METHODS

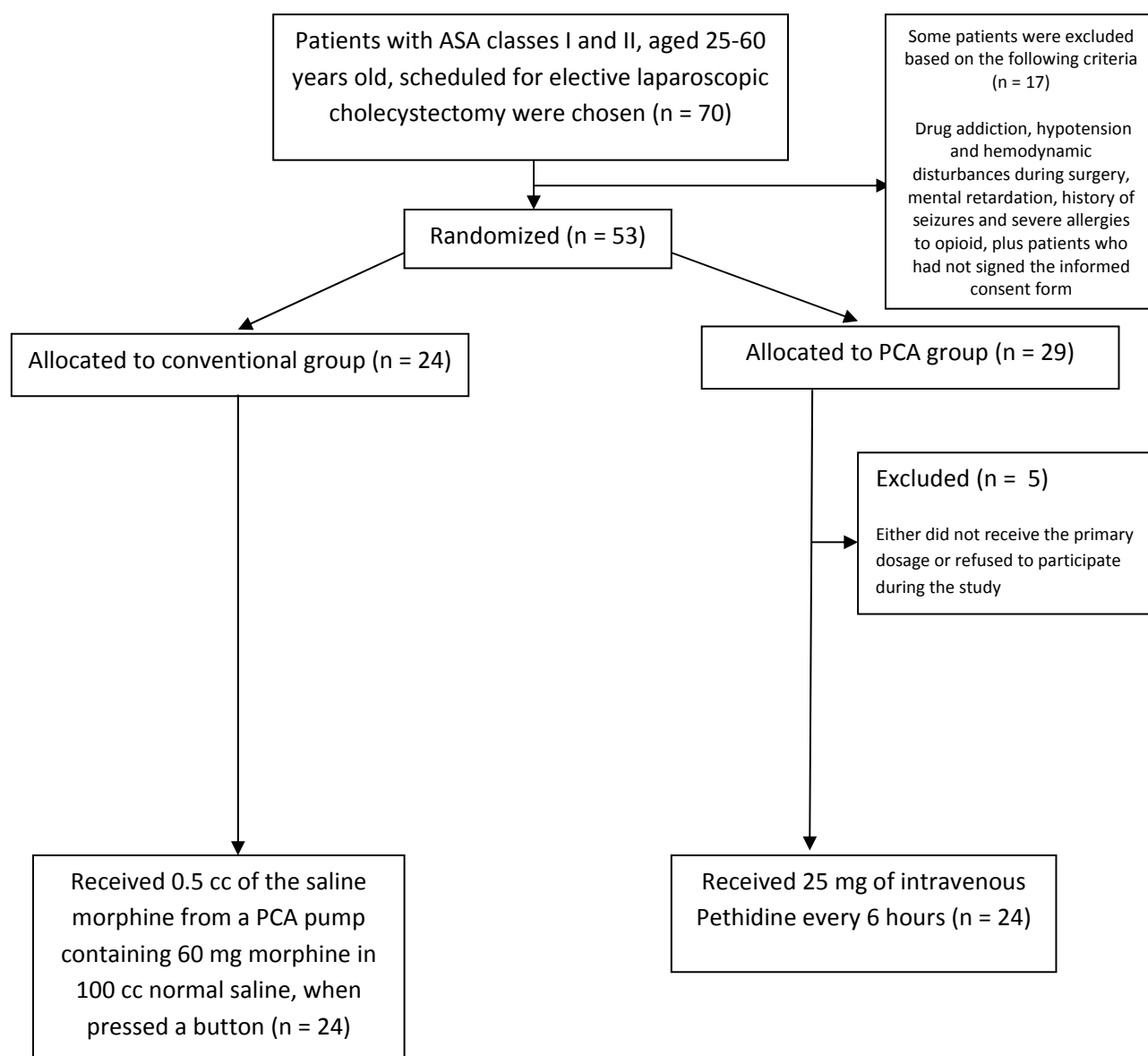
After gaining the approval of institutional ethics committee, patients (age range: 25-60 years old) were evaluated for having eligibility to be enrolled in this randomized prospective study. They were in American Society of Anesthesiology (ASA) classes I and II who had scheduled for elective laparoscopic cholecystectomy in a 9-month period. The intended participants were excluded if they had drug addiction, hypotension, and hemodynamic disturbances during surgery, mental retardation, history of seizures and severe allergies to opioid. Patients who had not signed the informed consent form were also excluded. Demographic data and history of underlying diseases were also recorded.

In this sense, 53 patients were allocated randomly (using a table of random numbers) into two groups to receive either PCA intravenous morphine or conventional intravenous Pethidine (Figure 1). The data of each group, consisting of 24 participants, were analyzed. Subjects in PCA group received instructions on how to use PCA. All participants underwent anesthesia with balanced technique. After premedication with 3 $\mu$ /kg Fentanyl and Midazolam slowly titrated to the desired effect of 1-3 mg, anesthesia was induced with 5-7 mg/kg thiopental followed by inhaled maintenance dose of Isoflurane 1.0-2.0% without N<sub>2</sub>O. Atracurium with an initial bolus dose of 0.3-0.6 mg/kg followed by continuous infusion rate of 0.3-0.6 mg/kg/hour was administered as muscle relaxant.

The patients received an injection of 0.1 mg/kg intravenous Morphine in the recovery room in order to control the immediate postoperative pain. No other analgesic was administered in the postoperative period.

The patients in PCA group received self-administered intermittent intravenous Morphine (Morphine 10 mg, Drau Paksh Industrial Co, Tehran, Iran) via Fonia infusion pump (Figure 2) after transfer to postoperative section. This pump (WZ-65523C-R) contained 100 mL of normal saline plus 60 mg of Morphine, releasing the solution at the basal rate of 2 mL per hour. When the pump button was pressed by the patient, 1 mL of the saline Morphine was administered to patients with a 15 minute lockout.<sup>10</sup> The conventional group received 25 milligrams of intravenous Pethidine (Pethidin 50 mg, Caspian Tumi Co, Tehran, Iran) every 6 hours per day after transfer to post-operative ward. This was the routine dosage for post-operative pain relief given by surgeons in our center.

Patients were assessed by the anesthesiologists on an hourly basis for the first 4 hours after surgery, every 2 hours for the next 8 hours and then every 4 hours for the next 12 hours. Two methods were used in order to evaluate the degree of pain relief in patients: (1) facial pain scale, pain assessment based on the patient's appearance, ranging from 0 (no pain) to 5 (the worst pain ever felt),<sup>11</sup> and (2) numerical rating scale based on patient ratings of their pain from 0 (lowest) to 10 (maximum pain imaginable).<sup>12</sup> Furthermore, other variables such as nausea, vomiting, systolic and diastolic blood pressure, intensity of sedation (Ramsay scale: 1, anxious, restless or both; 2, cooperative, orientated and tranquil; 3, responding to commands; 4, brisk response to stimulus; 5, sluggish response to stimulus; 6, no response to stimulus), respiratory rate, oxygen saturation and complaints of itching were also recorded. The recording of the measured items in patients



**Figure 1.** Flowchart of patient allocation.

was done by two trained staffs. The sample size was calculated based on the following formula:<sup>13</sup>

$$n = \frac{(Z_{1-\alpha/2} \sqrt{2\bar{P}(1-\bar{P})} + Z_{1-\beta} \sqrt{P_1(1-P_1) + P_2(1-P_2)})^2}{d^2}$$

In this formula  $\alpha$  (type 1 error) was 0.05,  $\beta$  (type 2 error) was 0.20,  $P_1$  (the effect of conventional method) was 20%,  $P_2$  (the effect of interventional method) was 70% or more (according to the authors' estimate) and (the difference in  $P_1$  and  $P_2$ ) was 50%. Therefore, 15 patients were needed in each group, at least for adequate power of study. Since the effects of conventional method and interventional method were estimated by the authors, the

number of patients was increased up to 24 in each group for more confidence. Descriptive data were presented as percentages and mean  $\pm$  standard deviation. Chi-square, independent sample t-test, Mann-Whitney  $U$  and Fischer's exact test were used to compare the two groups.  $P$  value of less than 0.05 was considered as statistically significant.

## RESULTS

Forty eight patients (79.1% female, 20.1% male) with a mean age of  $45.7 \pm 10.7$  years old were enrolled in this study in two groups. The mean age and weight of PCA group were  $46.6 \pm 10.52$  years old and



**Figure 2.** Fornia Pump (retrieved from: [www.rfornia.com](http://www.rfornia.com)).

75.9 ± 9.8 kg and for the conventional group they were 44.8 ± 11.15 years old and 72.2 ± 8.1 kg. There were no significant differences regarding demographics and underlying diseases, including hyperlipidemia, diabetes, cardiovascular and renal diseases, between the two groups (Table 1). Pain levels of patients in each group are summarized based on facial pain scale in Table 2 and numerical rating scale in Table 3.

Average consumption of opioid was 41 mg in the PCA group and 57.5 mg in the other group. Respiratory rate was significantly lower in the PCA group in the first hours after surgery but in the late hours of the first day, the difference was less pronounced. Mean arterial oxygen saturation was slightly higher in the group treated with Pethidine. The difference was statistically significant in the 8<sup>th</sup> and 10<sup>th</sup> hours post-surgery. Although systolic blood pressure was lower in the PCA group, significant difference was reported after eight hours. Diastolic blood pressure was significantly lower in the PCA group just in the 4<sup>th</sup>, 8<sup>th</sup>, 10<sup>th</sup> and 16<sup>th</sup> hours.

Nausea was more frequently reported in the

**Table 1.** Demographic data of the patients.

|                              | PCA Group | Conventional Group | P value |
|------------------------------|-----------|--------------------|---------|
| Age (mean)(years)            | 46.6      | 44.8               | .58     |
| Male                         | 6         | 4                  | .08     |
| Female                       | 18        | 20                 | .06     |
| Weight (mean)(kg)            | 75.9      | 72.1               | .16     |
| Hyperlipidemia (no.)         | 4         | 6                  | .47     |
| Cardiovascular disease (no.) | 2         | 0                  | .07     |
| Renal disease (no.)          | 2         | 0                  | .07     |
| Diabetic patients (no.)      | 0         | 2                  | .07     |
| Urinary catheter (no.)       | 8         | 3                  | .09     |
| Nasogastric tube (no.)       | 4         | 4                  | 1       |
| Smoking (no.)                | 4         | 6                  | .47     |

Key: PCA, patient controlled analgesia.

**Table 2.** Pain scores based on facial pain scale of the two groups.

| Mean Pain Score (Conventional Group) | Mean Pain Score (PCA Group) | Hour After Surgery | P value |
|--------------------------------------|-----------------------------|--------------------|---------|
| 3.8                                  | 3.5                         | 1                  | .38     |
| 3.7                                  | 2.9                         | 2                  | .007    |
| 3.1                                  | 2.6                         | 3                  | .15     |
| 3.1                                  | 2.7                         | 4                  | .32     |
| 2.8                                  | 2.6                         | 6                  | .43     |
| 2.8                                  | 2.7                         | 8                  | .08     |
| 3                                    | 2.8                         | 10                 | .82     |
| 3.1                                  | 2.8                         | 12                 | .11     |
| 2.6                                  | 2.1                         | 16                 | .06     |
| 2.6                                  | 2.1                         | 20                 | .06     |
| 2.6                                  | 2.1                         | 24                 | .06     |

Key: PCA, patient controlled analgesia.

**Table 3.** Pain scores based on numerical rating scale of the two groups.

| Mean Pain Score (Conventional Group) | Mean Pain Score (PCA Group) | Hour After Surgery | P value |
|--------------------------------------|-----------------------------|--------------------|---------|
| 4.6                                  | 4.2                         | 1                  | .45     |
| 5                                    | 3                           | 2                  | .003    |
| 4.2                                  | 2.5                         | 3                  | .002    |
| 4                                    | 2.6                         | 4                  | .03     |
| 3.2                                  | 2.1                         | 6                  | .02     |
| 4                                    | 2.2                         | 8                  | .001    |
| 3.5                                  | 2.3                         | 10                 | .01     |
| 3.4                                  | 1.6                         | 12                 | <.001   |
| 3.2                                  | 0.9                         | 16                 | <.001   |
| 3.1                                  | 1.2                         | 20                 | <.001   |
| 2.7                                  | 1.2                         | 24                 | <.001   |

Key: PCA, patient controlled analgesia.

conventional group in the first and fourth hours. Vomiting was likewise except that the difference was significant only in the first hour. Patient sedation scale in the two

groups was similar except for the 4<sup>th</sup> and 6<sup>th</sup> hours that had significant difference. None of the patients reported local or generalized pruritus between the two groups.

## DISCUSSION

The present study aimed to compare the effectiveness of intravenous PCA with conventional intravenous opioid administration in patients undergoing laparoscopic cholecystectomy. The main finding was that intravenous PCA provides better pain relief than the conventional method in spite of similar side-effects.

During the first 24 hours after laparoscopic cholecystectomy, pain intensity based on facial pain scale was lower in the PCA group. However, the difference was significant only in the second hour. In a study carried out by Chang and colleagues, the pain score in the first 24 hours after surgery was lower in the PCA group compared to the conventional group<sup>14</sup> Similar results were reported in several meta-analyses.<sup>4,15-17</sup> This difference may be explained by the changes in patients' facial expression which may be influenced by analgesic-related side-effects or factors such as hunger, bad positioning on bed and inconvenience due to urinary catheter. The authors have no suggestions about the significant differences in the second hour. Probably this scale is not suitable for assessment of pain score in this method. The scale used in the majority of studies is visual analogue scale which ranges from 0-100 mm. However, according to Liu and colleagues, statistically significant reduction in pain scores does not necessarily lead to clinical pain relief.<sup>18</sup> Some studies indicate that visual analogue scale may not accurately reflect the multidimensionality of acute pain as a one-dimensional instrument.<sup>19,20</sup> To address this issue, the authors asked the participants to rate their pain based on numerical rating scale. In this sense, the mean pain scores were significantly lower in PCA group except for the first hour. Several factors in first hour after surgery were used to justify this event, for example patient uneasiness.

Comparison of the side effects of the two techniques with previous studies showed conflicting results. In the present study, no respiratory depression was observed in either group which may be attributed to low dose opioids used in both groups. Although respiratory rate was significantly lower in PCA group in the first hours after surgery, the difference was less pronounced in the late hours of the first day. Mean arterial oxygen saturation was slightly higher in the group treated with intravenous Pethidine. This is in agreement with the results of Ballantyne and colleagues and Chang and colleagues.

<sup>14,16</sup> On the other hand, some authors have concluded that pulmonary complications were more frequently prevented with PCA than the conventional method.<sup>17</sup> Both systolic and diastolic blood pressures were lower in the PCA group. The difference was statistically significant after eight hours. However, these cardiovascular changes were not clinically important. Lower blood pressure without any circulatory depression in PCA method was also reported by Evans and colleagues.<sup>21</sup>

In spite of a higher incidence of pruritus in PCA method by Hudcova and colleagues and Liu and colleagues, none of the patients in our study complained of local or generalized pruritus.<sup>4,18</sup> This may be because of different doses of opioids used for intravenous PCA and conventional method in each study. Nausea and vomiting were more frequently reported in conventional group, but the difference was significant only in the first hour after laparoscopy. The incidence of nausea and vomiting seems to be similar with the use of PCA compared to traditional opioid administration methods in several systematic reviews.<sup>4,14,16,17</sup>

In a meta-analysis carried out by Liu and Wu, intravenous PCA resulted in greater use of opioid in the first 24 hours after surgery.<sup>18</sup> In our study, the average consumption of opioid was 41 mg in the treatment group and 57.5 mg in the conventional group. Of course, the exact amount of opioid use must be determined in each group by dose equivalent method for comparing the amount of drug use between the two groups, which was not in the interest of this study.

Providing Morphine, the patients' awareness and participation were our main limitations. The strategies to cope with them were to explain the advantages of this method, such as early mobilization and faster hospital discharge that can decrease the cost of hospital and patients, to the patients and staff. Finally, selecting the patients with laparoscopic cholecystectomy helped us, since these patients were more accessible than the others in our center and they were attentive after their surgery that was necessary for using PCA pump.

## CONCLUSION

Intravenous PCA resulted in better postoperative pain reduction compared to intermittent bolus opioid delivery after laparoscopic cholecystectomy. Studies with larger sample size are required to determine the safety of intravenous PCA. Cost-effective analysis and determining patient satisfaction may also help to confirm the effectiveness of intravenous PCA in post-operative pain control.

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**CONFLICT OF INTEREST**

None declared.

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