Comparison of lornoxicam and diclofenac injections for post day case laparoscopic cholecystectomy pain relief, a prospective, randomized, single-blind, controlled study

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Abstract Background: The aim of the study was to compare and evaluate the efficacy and safety of Lornoxicam and Diclofenac injections in the management of post-laparoscopic cholecystectomy pain.

Methods: Sixty patients were enrolled in the study. The patients were randomly allocated to one of three groups (20 patients in each): Diclofenac (D, received 75 mg of diclofenac), Lornoxicam (L, received 16 mg of lornoxicam intravenously), and Controlled (C, received 5 ml of normal saline intravenously). Drugs were injected at the time of trocar’s holes closure. Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), respiratory rate (RR), oxygen saturation and pain score were recorded as a baseline and every 20 minutes post-operatively. The need for postoperative rescue analgesia was assessed per 0–10. Numerical Pain Scale at 0, 20, 40 and 60 minutes. Rescue analgesia was provided when patients had developed mild pain.
**Results:** Postoperatively, there was a significant increase in the mean of SBP, DBP, HR and RR in group C. The HR was significantly different between L and D groups. At 20 minutes 3 patients from C group requested rescue analgesia. At 40 minutes 9 patients from C group and 1 patient from D group suffered a mild pain for which rescue analgesia was given. At 60 minutes the numbers of patients in group C, D and L who received analgesia were 8, 2 and 1 respectively.

**Conclusion:** Both lornoxicam and diclofenac injections are safe and effective in treating post-laparoscopic cholecystectomy pain with bordering superiority of lornoxicam.

**Keywords:** Analgesia, diclofenac, laparoscopic cholecystectomy, lornoxicam, pain, postoperative.

**Introduction**

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.\(^1\) Postoperative pain is an undesirable event that may have an adverse effect on patients especially at recovery area. Laparoscopic cholecystectomy is a minimally invasive procedure which is carried out as a day case surgery.\(^2\) Pain and emesis are the two major postoperative complaints after day-case surgery. Post-laparoscopic cholecystectomy pain range from moderate to severe and originate from bed site of removed gallbladder, trocar’s holes and right diaphragm. Other factors are the peritoneal stretching and diaphragmatic irritation due to high intra-abdominal pressure caused by pneumoperitoneum. Both gallbladder bed and trocar’s holes manifested as abdominal pain.\(^3\)

Opioids which are used as analgesic of choice, is associated with dose-dependent adverse effects such as postoperative nausea and vomiting (PONV), sedation and respiratory depression, resulting in delayed discharge or prolonged hospital stay. Non-opioid analgesics, such as non-steroidal anti-inflammatory drugs (NSAIDs), are often used alone or as adjuncts to opioids because of fewer adverse effects compared to opioids alone.\(^4\)

Lornoxicam is a member of the oxicam subgroup of NSAID. It is a potent inhibitor of cyclo-oxygenase. Lornoxicam can be given by oral, IM and IV routes. In regards to renal and hepatic function, lornoxicam has a better profile compared to diclofenac and naproxen. It is completely metabolized to inactive metabolites and has a better GIT tolerability compared to selective COX2 inhibitors.\(^5\)\(^,\)\(^6\) Diclofenac sodium injection, which is the oldest NSAID in practice, is widely used. It has analgesic, anti-inflammatory, and antipyretic properties, and has been shown to be effective in treating a variety of acute and chronic pain and inflammatory conditions. As with all NSAIDs, diclofenac exerts its action via inhibition of prostaglandin synthesis by inhibiting cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). The pharmacologic activity of diclofenac goes beyond COX inhibition, and includes multimodal and, in some instances, novel mechanisms of action. Recently, a new formulation of the nonselective NSAID diclofenac sodium suitable for intravenous bolus injection has been developed using hydroxypropyl beta-cyclodextrin as a solubility enhancer.\(^7\)\(^,\)\(^8\)

**Materials and Methods**

The study was conducted in Aseer Central Hospital (ACH), Abha, KSA, from October 2016 to March 2017 as a prospective, single blind, controlled trial. Ethical approval was obtained from ACH Ethics and Internal Review Board (IBR) committee. Following informed written consent, a total of 60 male and female with age range from 24 - 54 years with American Society of Anesthesiologists (ASA) I and II classification were enrolled in the study. Patients with history of bronchial asthma, impaired renal or hepatic function, GI bleeding, peptic ulcer, intracranial bleeding or bleeding tendency, pregnancy, morbidly obese or having hypersensitivity to one of the drugs used were excluded from the study. Patients were randomly assigned to one of three groups with 20 patients in each (C, L, and D groups). L was the group which received 16 mg of lornoxicam intravenously;
D was the group which was given 75 mg of diclofenac injection intramuscularly, while C was the controlled group which received 5 ml of normal saline intravenously. Drugs were prepared and administered by the assigned anesthetists when surgeons started to close the trocars’ holes. Drugs were blinded from Post-Anaesthesia Care Unit (PACU) nurses. Monitoring of hemodynamic parameters were carried out as ordinary. Monitoring of the vital signs of patients were continued as usual. Recording of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (RR) and oxygen saturation were done at 0, 20, 40 and 60 minutes. Numerical Pain Scale (NPS) of 0–10 was used to assess pain at 0, 20, 40 and 60 minutes. Rescue analgesia was provided PRN when patients experienced mild pain (Score of 1 – 3 on NPS).

Data entry and analysis were performed using the Statistical Package for Social Sciences (SPSS version 21.0). Data were subjected to Chi Square test or one-way ANOVA test for statistical analysis. The quantitative data are presented as mean and standard deviation and the qualitative data as frequency. The Chi-square test was used for comparison of frequencies and one-way ANOVA were used for comparison of mean values among the three groups. The statistical significance was considered at p < 0.05.

**Results**

A total of 60 patients consisting of 20 in each group (L, D, and C groups) were included in the trial. The patients mean age was 38.6±7.91 in group L, 38.8±9.25 in group D and 38.65±8.54 in group C with no statistical differences. Other demographic characteristics including gender, weight, and ASA classification were also shown with no statistical differences as well as anesthesia duration (p value 0.854) (Table 1).

Table 1: The demographic characteristics and adverse effects among the groups.

<table>
<thead>
<tr>
<th></th>
<th>Group C (n = 20)</th>
<th>Group L (n = 20)</th>
<th>Group D (n = 20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Range, Mean</td>
<td>38.65±8.54</td>
<td>38.6±7.91</td>
<td>38.8±9.25</td>
<td>0.997</td>
</tr>
<tr>
<td>Gender: Male / Female</td>
<td>8/12</td>
<td>6/14</td>
<td>5/15</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>80.8±11.77</td>
<td>83.65±13.80</td>
<td>81.5±13.26</td>
<td>0.770</td>
</tr>
<tr>
<td>ASA I II</td>
<td>16 / 4</td>
<td>15 / 5</td>
<td>14 / 4</td>
<td></td>
</tr>
<tr>
<td>Duration of Anaesthesia</td>
<td>62.75±11.75</td>
<td>61.5±11.71</td>
<td>63.75±14.32</td>
<td>0.854</td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (10%)</td>
<td>0</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Shivering</td>
<td>4 (20%)*</td>
<td>0</td>
<td>1 (5%)</td>
<td>*0.0374</td>
</tr>
</tbody>
</table>

*C = Controlled, L = Lornoxicam, D = Diclofenac.* Significant p value - Chi Square and One-way ANOVA

Table 2 shows the means of baseline and postoperative SBP, DBP, HR, RR and oxygen saturation. The baseline parameters show no significant differences between the groups. The means of postoperative SBP revealed statically significant differences between all groups (p value < 0.001). Comparing group L and D, the p value was found 0.036 with a significant difference. The means of postoperative DBP between the groups showed a significant difference (p value = 0.037).

However, comparing group L with D there was no difference (p value = 0.394) (Table 2). The means of postoperative HR were significantly different between the groups (p value < 0.001). The highest increasing in the HR was shown in group C, while group L showed the lowest increasing. The difference between L and D group was statically significant (p value = 0.021) (Table 2). The differences in the means of postoperative RR between the groups were found statistically highly significant (p < 0.001).
However, between group L and D there was no difference ($p$ value = 0.575). None of the patients in all the groups developed hypoxia. The means of the oxygen saturation between the groups were not significantly different (Table 2).

### Table 2: The mean of pre- and postoperative parameters among the groups.

<table>
<thead>
<tr>
<th></th>
<th>Group C (n = 20)</th>
<th>Group L (n = 20)</th>
<th>Group D (n = 20)</th>
<th>$P$ value (L, D, C)</th>
<th>$P$ value (L, D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Blood Pressure</td>
<td>121.35±8.51</td>
<td>121.05±7.09</td>
<td>121.9±7.08</td>
<td>0.938</td>
<td></td>
</tr>
<tr>
<td>Diastolic Blood Pressure</td>
<td>75.45±7.59</td>
<td>74.95±5.93</td>
<td>76.45±7.03</td>
<td>0.783</td>
<td></td>
</tr>
<tr>
<td>Heart Rate</td>
<td>80.4±9.23</td>
<td>80±9.11</td>
<td>76.4±6.49</td>
<td>0.259</td>
<td></td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td>97.45±0.76</td>
<td>97.05±1.05</td>
<td>97.5±0.69</td>
<td>0.193</td>
<td></td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>15.5±0.95</td>
<td>15.5±1.19</td>
<td>15.65±1.27</td>
<td>0.892</td>
<td></td>
</tr>
</tbody>
</table>

Table 3 shows the needs for rescue analgesia. None of all patients needed analgesia up to 20 minutes from the end of anaesthesia. At 20 minutes 3 patients from C group requested rescue analgesia. At 40 minutes 9 patients from C group and 1 patient from D group suffered a mild pain for which rescue analgesia was given. At 60 minutes the numbers of patients in group C, D and L who received analgesia were 8, 2 and 1 respectively.

For rescue analgesia supplementation, the NPS of 0–10 was used to assess pain at 0, 20, 40 and 60 minutes. Analgesia was supplemented when a patient developed only mild pain (1-3 score).

### Table 3: Needs for rescue analgesia among the groups.

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Group C (n = 20)</th>
<th>Group L (n = 20)</th>
<th>Group D (n = 20)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>3 (15%)</td>
<td>0</td>
<td>0</td>
<td>0.0754</td>
</tr>
<tr>
<td>40</td>
<td>9 (45%)*</td>
<td>0</td>
<td>1 (5%)</td>
<td>0.0039</td>
</tr>
<tr>
<td>60</td>
<td>8 (40%)*</td>
<td>1 (5%)</td>
<td>2 (10%)</td>
<td>0.0305</td>
</tr>
</tbody>
</table>

Data were shown as mean ± SD (Standard Deviation). * Significant $p$ value. Chi Square test

### Discussion

A total of 60 patients consisting of 20 in each group (L, D, and C groups) were included in the trial. The patients mean age was 38.6±7.91 in L group, 38.8±9.25 in D group and 38.65±8.54 in C group with no statistically significant differences. Other demographic characteristics including gender, weight, and ASA classification was not statistically different. There was no statistical difference in anesthesia duration among all the groups.

Postoperative pain may be associated with deep vein thrombosis (DVT), pulmonary embolism, pneumonia, and delay in wound healing. Inadequate pain treatment may result in high morbidity and mortality as well as the cost of treatment and decreasing the quality of life. One of the important discharge criteria in day care anesthesia is postoperative pain management.$^{(9, 10, 11)}$

Lornoxicam, as well as diclofenac, have been used for postoperative pain relief in various...
surgical procedures. They are used either alone or in combination with other drugs as a multimodal regimen. Postoperative pain is distressing and may result in tachycardia and hypertension. In the study, the highest increase in the means of the postoperative SBP and HR were observed in group C, while group L showed the lowest increase in both mean SBP and HR. Lornoxicam has been successfully used in the prevention and treatment of postoperative pain. Following ENT procedure, 8 mg of lornoxicam was found to be compatible with 1 mg/kg of Tramadol in reducing the postoperative opioid requirement and consequently minimized the related adverse effects of the opioids.\(^\text{[12]}\) Das et al. found lornoxicam safe and effective compared with tramadol for relieving postoperative pain after operations on head and neck.\(^\text{[13]}\) Pre-emptive administration of lornoxicam in patients undergoing gynecological operations or thyroidectomy had shown better quality of postoperative analgesia and reducing postoperative opioids consumption.\(^\text{[14, 15]}\) Daglar et al. found that the lornoxicam and diclofenac both are similar in postoperative pain management and tolerability, following CABG operation.\(^\text{[16]}\) Galani et al. showed a slight greater efficacy of lornoxicam when they compared it with diclofenac in managing acute postoperative pain after spinal surgery. However, tolerability and safety were found similar.\(^\text{[17]}\) This is different from Bansal et al. when they compared 16 mg/day lornoxicam with 150 mg/day diclofenac sodium for postoperative pain relief in patients undergoing abdominal hysterectomy under general anaesthesia. They concluded the superiority of analgesic effect of diclofenac without any significant adverse events. However, to address these issues further, they recommended a long term multi-centric trials with more numbers of patients.\(^\text{[18]}\)

During the study, group C showed a significant difference from other groups regarding the mean of postoperative respiratory rate. Between lornoxicam and diclofenac there was no difference. None of the patients in all the groups developed hypoxia. Nalini and Ezhilramya compared twice daily, 8 mg of lornoxicam with 75 mg diclofenac in reliving the postoperative pain following mastoidectomy surgery under local anaesthesia. They concluded better analgesic properties and tolerability of lornoxicam.\(^\text{[19]}\) Rescue analgesia was given to patients per 0–10 NPS which was performed at 0, 20, 40 and 60 minutes. None of all patients needed rescue analgesia up to 20 minutes from the end of anaesthesia. At 20 minutes 3 patients from C group were given rescue analgesia. At 40 minutes 9 patients from group C and 1 patient from group D had experienced mild pain for which rescue analgesia was given. At 60 minutes the numbers of patients in group C, D and L who received analgesia were 8, 2 and 1 respectively. Lornoxicam, as well as diclofenac stated a significant reduction in postoperative rescue analgesia requirements. A single-blind, active-controlled, randomized study in June 2005 showed that postcardiac surgery pain may be treated with either diclofenac or lornoxicam. However, authors recommended further studies to assess the efficacy and safety of these drugs in postoperative analgesia for cardiac surgery patients.\(^\text{[20]}\) Postoperative pain relieve after cesarean section could be achieved effectively by administration of repeated IM injection of 75 mg diclofenac sodium (2 doses per day) without significant effects on uterine relaxation or bleeding during the first postoperative 48 hours.\(^\text{[21]}\) The effect of intravenous diclofenac on pain and recovery profile after day-case laparoscopy was assessed by Hovorka et al. They demonstrated the significant reduction in the need for postoperative analgesia in diagnostic laparoscopy patients.\(^\text{[22]}\) Tarkkila et al. found that parenteral ketorolac and diclofenac were similar for analgesia after maxillofacial surgery. However, they were insufficient alone.\(^\text{[23]}\) A study by Sener et al. demonstrated no superiority of lornoxicam compared with diclofenac, ketoprofen, and dipyrone during the management of acute postoperative pain after septoplasty.\(^\text{[24]}\)
Among all patients in the study groups, nausea was complained by 2 patients from group C and only 1 patient from group L with no patient from group D. The difference was not significant. The result showed a significance decrease in shivering by both diclofenac and lornoxicam. Nausea and vomiting are common following opioid analgesia and represent a significant cause of patient discomfort. Sometimes, intense pain may be accompanied by nausea or vomiting. Parenteral NSAIDs are effective in the treatment of patients complaining of a severe migraine associated with nausea and vomiting. Postoperatively, a single dose of sodium diclofenac suppository can provide satisfactory analgesia immediately as well as a decrease in shivering.\(^{(25,26,27)}\)

In conclusion, both lornoxicam and diclofenac injections are safe and effective in treating post-laparoscopic cholecystectomy pain. Lornoxicam injection shows bordering superiority when compared with diclofenac sodium in reducing the needs for rescue analgesia. However, more studies are needed to cover these issues up to discharging patients home.

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**Ethical clearance:** obtained  
**Informed consent form:** obtained

**References**


