Postoperative pain after abdominal hysterectomy: a randomized, double-blind, controlled trial comparing continuous infusion vs patient-controlled intraperitoneal injection of local anaesthetic

A. Perniola*, F. Fant, A. Magnuson, K. Axelsson and A. Gupta

1 Department of Anesthesiology and Intensive Care and 2 Clinical Epidemiology and Biostatistical Unit, Clinical Research Centre, Örebro University Hospital, School of Health and Medical Sciences, Örebro University, SE-701 85 Örebro, Sweden

* Corresponding author. E-mail: perniola.d@gmail.com

Editor’s key points

- Effective analgesic techniques that reduce opioid consumption may improve postoperative recovery.
- There is evidence that intraperitoneal (i.p.) local anaesthetics can be effective.
- This study compared continuous with intermittent patient-controlled i.p. levobupivacaine (PCiPA) for postoperative analgesia.
- PCiPA resulted in similar pain control, reduced opioid consumption and improved gastrointestinal function.
- Further work is needed to evaluate this potentially beneficial analgesic technique.

Background. Local anaesthetics (LA) injected intraperitoneally have been found to decrease postoperative pain. This double-blind randomized study was performed comparing continuous infusion or patient-controlled intraperitoneal (i.p.) bolus injection of LA. The primary endpoint was supplemental opioid consumption during the first 24 postoperative hours.

Methods. Two multi-hole catheters were placed intraperitoneally at the end of the surgery in 40 patients undergoing elective abdominal hysterectomy. The patients were randomized into two groups: Group P: patients self-injected 10 ml of levobupivacaine 1.25 mg ml⁻¹ via the i.p. catheter as needed, maximum once per hour, and had continuous saline infusion 10 ml h⁻¹ into the second catheter. Group C: patients received a continuous infusion of 10 ml h⁻¹ of levobupivacaine 1.25 mg ml⁻¹ intraperitoneally through one catheter and 10 ml saline as bolus as needed via the other. Ketobemidone was administered intravenously as rescue medication.

Results. Total ketobemidone consumption during 0–24 h was lower in Group P compared with Group C (mean 23.1 vs 35.7 mg, P = 0.04). No differences in the median pain scores were found between the groups. Earlier return of gastrointestinal (GI) function was found in Group P vs Group C (mean 1.5 vs 2.2 days, P < 0.01), which also resulted in earlier home-readiness (mean 1.9 vs 2.7 days, P = 0.04).

Conclusions. A statistically significant opioid-sparing effect was found when patient-controlled levobupivacaine was administered intraperitoneally as needed compared with continuous infusion. This was associated with a faster return of GI function and home-readiness. There was, however, a wide confidence interval in the primary endpoint, opioid consumption.

Keywords: abdominal hysterectomy; local anaesthetics; postoperative pain

Accepted for publication: 11 August 2013

It is estimated that one woman in 10 undergoes hysterectomy in Sweden. Abdominal hysterectomy is associated with moderate-to-severe postoperative pain. Traditional methods for postoperative pain management include opioids administered systemically using patient-controlled i.v. analgesia (PCA), or neuroaxially via epidural or spinal injections. However, pain relief, specifically on movement, is not always adequately controlled when using PCA, despite moderate–large doses of morphine. This is associated with side-effects such as postoperative nausea and vomiting (PONV), tiredness, pruritus, headache, and constipation. Therefore, epidural or intrathecal analgesia may be considered by some to be the gold standard for pain management after abdominal surgery, and leads to enhanced and prolonged postoperative analgesia. Although concerns remain regarding complications after central blocks, specifically in older patients, recent evidence suggests that these are extremely rare. There has been recent interest in alternative methods for analgesia with minimal side-effects and a trend towards movement from central blocks towards other peripheral and less invasive methods for pain relief. One such technique is wound infiltration, intraperitoneal (i.p.) administration of...
Intraperitoneal local anaesthetics for pain relief after abdominal hysterectomy

local anaesthetics (LA), or both.8–11 Continuous i.p. infusion of LA has been reported to result in a 30–40% morphine-sparing effect and a reduction in postoperative nausea.12 Several studies have shown that patient-controlled bolus administration of LA during neuraxial or peripheral nerve block gives better postoperative analgesia compared with continuous infusions.13–17 Therefore, we decided to test the hypothesis that patient-controlled i.p. analgesia (PCipA) with LA would reduce pain intensity and thereby supplemental opioid consumption compared with continuous infusion of LA.

The primary aim was therefore to analyse rescue analgesic consumption during 0–24 h after operation after abdominal hysterectomy in patients receiving continuous LA infusion compared with intermittent patient-controlled i.p. injections. The secondary outcomes were analgesic consumption during 0–4 h, pain intensity, incidence of nausea and vomiting, maximum expiratory pressure, time to mobilization, and length of hospital stay, and also health-related quality of life at 1 and 3 months.

Methods
This study was registered in an international registry, clinicaltrials.gov (identification number NCT01492075) before patient recruitment. The study was performed at the Department of Anaesthesiology and Intensive Care and the Department of Gynaecological Surgery, University Hospital, Örebro, Sweden, and monitored by an external organization not involved in any way with the study. This unit is a quality-based organization located within the hospital and monitors clinical trials. After approval from the Regional Ethics Committee, Uppsala, oral and written informed consent was obtained from 40 patients (ASA status I–II), aged 40–65 yr undergoing elective abdominal hysterectomy with or without salpingo-oophorectomy in this randomized, double-blind study. The exclusion criteria were: patients undergoing surgery for suspected gynaecological cancer, patients on chronic analgesic medication, those with known allergy to LA, patients participating in another clinical study, and those who had difficulty in understanding Swedish.

Randomization and blinding
On the day of surgery, the Hospital Pharmacy randomized patients into two groups (20 in each group) using computer-generated randomized numbers inserted into sealed opaque envelopes and marked 1–40. All personnel involved in patient management were fully blinded to the method of analgesia until the study was completed.

Anaesthesia and surgery
All patients were premedicated with midazolam 0.1 mg kg\(^{-1}\) orally and paracetamol 1 g was given orally every 6 h with the first dose at the time of premedication. Anaesthesia was induced with fentanyl 1–2 \(\mu\)g kg\(^{-1}\) and propofol 1–2 mg kg\(^{-1}\) intravenously. Tracheal intubation was performed after muscle relaxation with rocuronium 0.5 mg kg\(^{-1}\) and anaesthesia was subsequently maintained with sevoflurane 1–3% and oxygen 33% in air. End-tidal CO\(_2\) was maintained between 4.5 and 5.5 kPa using mechanical ventilation in a low-flow breathing system with CO\(_2\) absorber. Monitoring included non-invasive arterial pressure, heart rate, peripheral oxygen saturation, end-tidal gas monitoring, ECG, and muscle relaxation using the train-of-four stimulation. Sevoflurane concentration was adjusted in order to maintain adequate anaesthetic depth, assessed clinically, and fentanyl was given intermittently intravenously when required for analgesia during the operation. Muscle relaxation was reversed at the end of surgery using glycopyrrolate (0.5 mg) and neostigmine (2.5 mg). Hysterectomy was performed using either a lower-abdominal midline incision or a Pfannenstiel incision, depending on the choice of the operator taking into consideration the size of the uterus and expected surgical difficulty.

Catheter insertion and postoperative pain management
Before closing the peritoneum, two multi-hole catheters were inserted percutaneously by the surgeon; one catheter was tunneled from the left side and the other from the right side, about 1–2 cm lateral to the abdominal incision and the tip of the catheters was placed supravaginally as described previously.2 The catheters were not fixed intraperitoneally. In all patients, levobupivacaine 1.25 mg ml\(^{-1}\) (20 ml) was injected subcutaneously along both sides of the incision before skin closure by the surgeon; an additional 20 ml was injected via one of the catheters into the peritoneal cavity. The pharmacy sent (i) one blinded bag, containing 500 ml of levobupivacaine 1.25 mg ml\(^{-1}\) or placebo (normal saline) and (ii) one elastomeric pump (On-Q Pain BusterR, ref PS125071; I-Flow Corp., Lake Forest, CA, USA) containing 500 ml of levobupivacaine 1.25 mg ml\(^{-1}\) or placebo (normal saline). When the patient arrived in the post-anaesthesia care unit (PACU), the infusions were set up, connected, and started by one of the co-authors immediately as described below. The time of start of infusion was considered \(t=0\).

Group P: PCipA with LA. The patients self-administered 10 ml of levobupivacaine via the first i.p catheter as required (maximum once per hour) during the first 48 h after the operation via an electronic pump (Abbot GemStar, Abbot Laboratories, North Chicago, IL, USA) over 10 min. Normal saline was infused at 10 ml h\(^{-1}\) via the second i.p catheter using the elastomeric pump.

Group C: continuous i.p. infusion of LA. Patients received a continuous infusion of levobupivacaine 10 ml h\(^{-1}\) intraperitoneally through the first catheter via the elastomeric pump and saline as bolus injection via the second i.p. catheter using the electronic pump. After 48 h, the i.p. bolus/infusion was stopped and both catheters were removed.

Rescue medication and postoperative ward
All patients received 2–4 mg ketobemidone intravenously, an opioid analgesic equipotent with morphine,18 intermittently by the staff nurse if pain was >3 on the numerical rating scale (NRS) (0, no pain; 10, worst imaginable pain). Analgesics were administered on patient request, irrespective of whether...
the pain was >3 at rest, on sitting, or during coughing. The patients were observed in the PACU until the day after the surgery. In the case of severe postoperative nausea or vomiting (PONV) not relieved by anti-emetics, the nursing staff were allowed to administer non-steroidal anti-inflammatory drugs (NSAIDs) for pain management in order to reduce opioid-induced PONV.

**Recording and measurements**

In addition to the routine postoperative protocols, the following parameters were recorded:

- **Pain and analgesia:** pain at the site of the incision, ‘deep’ (visceral) pain, and pain on coughing at 1, 4, 12, 24, and 48 h were measured using NRS. Rescue analgesic (ketobemidone) consumption was measured during 0–4, 0–24, and 24–48 h.
- **Side-effects:** nausea, vomiting, or both (0–4, 4–24, and 24–48 h) were recorded on a yes/no score; anti-emetic consumption during 0–24 and 24–48 h was also recorded. Sedation (before operation, at 4, 24, and 48 h) was recorded by nurses using a 0–10 scale (0, awake; 10, verbally arousable).
- **Expiratory muscle function:** this was measured before and 24 and 48 h after the operation using maximum expiratory pressure (P_{\text{emax}}) (MicroMedical, Moreton-in-Marsh, UK), in a similar way as described in previous studies. P_{\text{emax}} was measured twice by asking the patient to blow rapidly using the full abdominal force after a maximal inspiration while in the semi-reclining position. The best of two measurements was recorded.
- **Recovery parameters:** the ability to walk with and without support, time to start drinking, eating, and time to return of gastrointestinal (GI) function (bowel movement or passing flatus), postoperative home-readiness, and length of hospital stay were recorded once a day by nurses in the gynaecological ward. Standardized home-readiness criteria were used that have been described previously. LA toxicity: the nurses were informed about the common signs and symptoms of LA toxicity and the patients told to inform the nurses of any side-effects and symptoms.
- **Health-related quality of life:** this was measured using the written form of SF-36 questionnaire before and 1 and 3 months after the operation in both groups and the patients were asked to return it by post. The SF-36 is a validated health survey consisting of 36 questions that measure eight health concepts and has been translated and validated into the Swedish language. A higher score indicates an improved level of function.

**Statistics**

In a previous study, the mean [standard deviation (SD)] total morphine consumption during 0–24 h was found to be 30 mg (SD 17) in patients receiving continuous i.p. LA. Our hypothesis was that this could be reduced by 50% to a mean value of 15 mg (SD 8) in patients receiving PCipA with LA.

The sample size was calculated using the unpaired two-sided t-test. Assuming $\beta=0.2$ (power 80%) and $\alpha=0.05$, we determined that we would require 28 patients (14 per group) in order to achieve statistical significance for the primary endpoint. We recruited 40 patients in order to achieve adequate power in the case of missing data or patient drop out.

The mean and sd are used to summarize continuous variables, while categorical variables are presented as numbers (%). Unpaired t-test with 95% confidence intervals (CIs) and P-values was used to analyse differences between study groups for morphine consumption and the other continuous variables distributed approximately normally with or without log transformation. The Shapiro–Wilks test was used to evaluate normal distribution and if non-normality was found, log-transformation was performed before statistical evaluation. The results were then transformed back to original scale and the effect parameter is therefore the ratio of geometric means. The results are presented as the mean ratios together with 95% CI. Owing to multiple comparisons when evaluating the primary endpoint, 0–24 h ketobemidone consumption, the Bonferroni–Holm correction was applied. The $\chi^2$ test or Fisher’s exact test when appropriate was used for categorical variables and odds ratio (OR) with normal approximated 95% CI was calculated. Owing to some missing values, a mixed model with autoregressive covariance structure was used to analyse pain on incision, deep pain, and pain on coughing, and also for assessment of sedation, $P_{\text{emax}}$, and when analysing dimensions of SF-36. Study groups and time points were fixed effects and patients were random effect in this mixed model. None of the mixed models used found an overall statistically significant difference between study groups. The marginally mean differences between groups at different time-points with 95% CI and P-values are presented. When normality assumption was not valid, and log transformation did not help, sensitivity analysis was performed using the Mann–Whitney U-test, but because no different conclusions could be made from the analyses, these results are not presented. Two-tailed P-value of <0.05 was considered to be statistically significant. All statistical analyses were performed using the SPSS version 17 (Chicago, IL, USA).

**Results**

Of the 40 patients initially randomized into the study, no patient was excluded and all patients completed the study (Fig. 1). The patient characteristic data in the two groups, the operation performed, and intraoperative fentanyl consumption are shown in Table 1.

The rescue analgesic ketobemidone consumption was statistically significantly greater in Group C compared with Group P during 0–24 h and during 0–4 h after operation (Table 2). No significant difference in ketobemidone consumption was seen between the groups during the time period 24–48 h. The number of patients given NSAID as rescue medication during 0–24 h did not differ significantly between the groups (Table 2).

The intensity of postoperative pain on the NRS is shown in Figure 2A–C. In general, the median pain scores were <5 in all groups, except during coughing when the median scores
reached ~7 in the early postoperative period. No significant differences were seen between the groups in NRS pain score at any time point during the 48 h study period.

The total volume of levobupivacaine administered after the first 24 postoperative hours was statistically significantly lower in Group P (180 ml) than in Group C (240 ml) (P<0.01).

The recovery times and time to home-readiness are shown in Table 3. A statistically significant difference between the groups was found in the return of GI function, which was shorter in Group P compared with Group C. The mean time to home-readiness was statistically significantly shorter in Group P compared with Group C, while the length of hospital stay did not differ significantly between the groups. Expiratory muscle function, measured as maximum expiratory pressure (P_{E_{max}}), decreased at 4 h compared with preoperative values in both groups, and gradually recovered over time during 48 h. However, no statistically significant differences were found between the groups at any time point (Table 3). The incidence of PONV and the number of patients who received anti-emetics did not differ between the groups. The sedation scores between the groups were similar (Table 4) and no differences were seen between the groups in any of the parameters of the health-related quality of life (SF-36), or the average score in SF-36 at 1 or 3 months after surgery (Fig. 3).

Discussion

In this study, we found a statistically significant opioid-sparing effect when patients self-administered bolus doses of levobupivacaine compared with those having a continuous infusion of...
LA. Furthermore, there was a faster return of GI function and a shorter time to home-readiness when intermittent injection of LA was used.

Pain after abdominal hysterectomy arises from several structures that are traumatized during surgery and includes somatic pain from the incision site, and pain from deeper structures including muscle pain and peritoneal and visceral pain. Although the magnitude of pain from each component is difficult to define, pain from the incision site is often relatively mild in comparison with deeper pain from the muscles and peritoneum. Specifically, pain on mobilization and during coughing is multifactorial and can be very severe in the early postoperative period.

We studied patients undergoing abdominal hysterectomy since this is a procedure associated with moderate-to-severe postoperative pain, specifically in the early postoperative period. We found a low supplementary analgesic consumption during the first 24 h after i.p. administration of levobupivacaine in both groups, confirming our previous studies.

### Table 1: Patient characteristic data, duration of anaesthesia and operation, and fentanyl consumption are shown as mean (sd) except age (range). All other data are shown as numbers (ASA physical status) or n (%) as appropriate. Group P, patient-controlled i.p. analgesia; Group C, continuous i.p. analgesia

<table>
<thead>
<tr>
<th>Group</th>
<th>Group P (n = 20)</th>
<th>Group C (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>48 (38–65)</td>
<td>51 (40–63)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73 (12)</td>
<td>68 (9)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168 (5)</td>
<td>165 (6)</td>
</tr>
<tr>
<td>ASA physical status (I/II)</td>
<td>15/5</td>
<td>17/3</td>
</tr>
<tr>
<td>Duration of operation (min)</td>
<td>119 (26)</td>
<td>121 (29)</td>
</tr>
<tr>
<td>Duration of anaesthesia (min)</td>
<td>156 (27)</td>
<td>156 (29)</td>
</tr>
<tr>
<td>Type of operation</td>
<td>Total hysterectomy</td>
<td>12 (60%)</td>
</tr>
<tr>
<td></td>
<td>Salpingo-oophorectomy</td>
<td>8 (40%)</td>
</tr>
<tr>
<td>Type of incision</td>
<td>Pfannenstiel</td>
<td>3 (15%)</td>
</tr>
<tr>
<td></td>
<td>Lower midline</td>
<td>17 (85%)</td>
</tr>
<tr>
<td></td>
<td>Intraoperative fentanyl (µg)</td>
<td>318 (74)</td>
</tr>
</tbody>
</table>

### Table 2: Analgesic consumption. All data are shown as mean (sd) except number of patients n (%) for NSAIDs. Data are analysed by the unpaired t-test or Fisher exact test as appropriate. Group P, patient-controlled i.p. analgesia; Group C, continuous i.p. analgesia. *A mean ratio is the difference between two means on a relative scale, that is, mean ratio of 1.56 interprets as 56% higher geometric mean in Group C compared with Group P. Following the Bonferroni–Holm correction for multiple comparisons, for details, see text. †Group C vs P; results are presented as odds ratio (95% CI)

|                         | Group P (n = 20) | Group C (n = 20) | Group C/P, mean difference (95% CI) | Group C/P, mean ratio* (95% CI) | P-values | Corrected P-values† |
|---|------------------|------------------|-------------------|-----------------------------------|-------------------------------|-----------|---------------------|
| Ketobemidone in mg 0–4 h (range) | 13.4 (7.1) (4–28) | 21.0 (12.6) (8–59) | 7.6 (1.0–14.1)                  | 1.56 (1.09–2.22)            | 0.015     | 0.045               |
| Ketobemidone in mg 0–24 h (range) | 23.1 (13.8) (8–48) | 35.7 (20.2) (10–81) | 12.6 (1.5–23.6)                 | 1.58 (1.07–2.32)            | 0.021     | 0.042               |
| Ketobemidone in mg 24–48 h (range) | 3.1 (4.2) (0–12) | 6.3 (8.6) (0–31) | 3.2 (1.1–7.5)                   | 1.84 (0.97–3.48)          | 0.060     | 0.060               |
| NSAID (0–24 h) [n (%)] | 3 (15%)          | 4 (22%)          | 1.4 (0.2–11.1)                 | †                          | 1.00      |                     |
in a block of more free afferent nerve endings within the peritoneum compared with a continuous infusion of 10 ml over 60 min. The reason why patients in both groups reported moderate to severe pain on coughing when they could request further analgesia (LA or opioids) is unclear. It is possible that analgesic supplementation was requested only during pain at rest and not during mobilization/coughing. Additionally, in our experience, some patients may have severe nausea or vomiting from opioid supplementation and accept pain on coughing rather than constant nausea.28

The health-related quality-of-life questionnaire (SF-36) did not show any differences between the groups after operation, which may be not surprising since we did not find any difference in postoperative pain intensity between the groups. The faster recovery of GI function in patients receiving LA via PCipA may have resulted in a shorter time to home-readiness. The shortened time to recovery of bowel function after patient-controlled i.p. administration of LA may be due to the opioid sparing which was evident in the present study. We found no major complications when using i.p. LA, including infection,
and no patient had any signs or symptoms of LA toxicity, which is in accordance with our earlier studies.21 2

Study limitations

The patient-controlled i.p. analgesia group received more intraoperative fentanyl, and therefore, the reduction in the 0–4 ketobemidone consumption in this group may reflect on the higher intraoperative fentanyl given. Furthermore, the wide CI of ketobemidone consumption during the first 24 h suggests caution in concluding that the primary endpoint of this study was clinically significant. However, the finding that some secondary endpoints such as return of GI function and home-readiness favour the patient-controlled i.p. method would suggest that there is some impact of reduced opioid consumption on recovery parameters. We did not measure plasma concentration of levobupivacaine in this study, which would be of interest in understanding the mechanism of action of LA. The PCiP with LA made it almost impossible to correctly schedule blood sampling. However, in our earlier study using higher doses of levobupivacaine via continuous i.p. infusion, we found a dose-dependent increase in plasma concentration.

Table 3 Postoperative functional recovery and respiratory function. All data are shown as mean (so) unless otherwise shown and analysed by the unpaired t-test except $P_{\text{Emax}}$, which was analysed by using mixed model. $P_{\text{Emax}}$, maximum expiratory pressure; Group P, patient-controlled i.p. analgesia; Group C, continuous i.p. analgesia; GI, gastrointestinal

<table>
<thead>
<tr>
<th>Time to walk with help (h)</th>
<th>Group P (n=20)</th>
<th>Group C (n=20)</th>
<th>Group C vs P, mean difference (95% CI)</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4 h</td>
<td>21 (4), n=19</td>
<td>22 (3), n=19</td>
<td>0.4 (−1.8 to 2.8)</td>
<td>0.68</td>
</tr>
<tr>
<td>24 h</td>
<td>23 (6), n=19</td>
<td>25 (6), n=18</td>
<td>2.2 (−2.1 to 6.6)</td>
<td>0.30</td>
</tr>
<tr>
<td>48 h</td>
<td>16 (7), n=17</td>
<td>15 (8), n=17</td>
<td>−1.4 (−6.8 to 3.9)</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Table 4 Side-effect and complications. All results are shown as number of patients n (%) except sedation which is presented as mean (so). PON, postoperative nausea; POV, postoperative vomiting. The $\chi^2$ test or Fisher exact test was used as appropriate except sedation which was analysed using mixed model. NE, not estimated; Group P, patient-controlled i.p. analgesia; Group C, continuous i.p. analgesia. *Group C vs P is presented as mean difference (95% CI)

<table>
<thead>
<tr>
<th>Postoperative nausea (PON)</th>
<th>Group P (n=20)</th>
<th>Group C (n=20)</th>
<th>Group C vs P, odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4 h</td>
<td>10 (50%)</td>
<td>5 (25%)</td>
<td>0.3 (0.1–1.3)</td>
<td>0.10</td>
</tr>
<tr>
<td>4–24 h</td>
<td>2 (10%)</td>
<td>2 (10%)</td>
<td>1.0 (0.1–7.9)</td>
<td>1.00</td>
</tr>
<tr>
<td>24–48 h</td>
<td>1 (5%)</td>
<td>0</td>
<td>NE</td>
<td>1.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Postoperative vomiting (POV)</th>
<th>Group P (n=20)</th>
<th>Group C (n=20)</th>
<th>Group C vs P, odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4 h</td>
<td>3 (15%)</td>
<td>1 (5%)</td>
<td>0.3 (0.03–3.1)</td>
<td>0.60</td>
</tr>
<tr>
<td>4–24 h</td>
<td>2 (10%)</td>
<td>1 (5%)</td>
<td>0.5 (0.04–5.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>24–48 h</td>
<td>0</td>
<td>0</td>
<td>NE</td>
<td>1.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total PON or POV</th>
<th>Group P (n=20)</th>
<th>Group C (n=20)</th>
<th>Group C vs P, odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–48 h</td>
<td>11 (55%)</td>
<td>6 (30%)</td>
<td>0.3 (0.1–1.3)</td>
<td>0.11</td>
</tr>
<tr>
<td>0–24 h</td>
<td>16 (80%)</td>
<td>17 (85%)</td>
<td>1.4 (0.3–7.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>24–48 h</td>
<td>4 (20%)</td>
<td>3 (15%)</td>
<td>0.7 (0.1–3.6)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sedation (NRS)*</th>
<th>Group P (n=20)</th>
<th>Group C (n=20)</th>
<th>Group C vs P, odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 h</td>
<td>4.8 (2.5), n=18</td>
<td>4.4 (2.7), n=19</td>
<td>−0.4 (−2.2 to 1.4)</td>
<td>0.65</td>
</tr>
<tr>
<td>24 h</td>
<td>4.0 (2.4), n=19</td>
<td>4.3 (3.2), n=20</td>
<td>0.4 (−1.3 to 2.2)</td>
<td>0.61</td>
</tr>
<tr>
<td>48 h</td>
<td>3.5 (3.0), n=17</td>
<td>3.1 (2.4), n=17</td>
<td>−0.3 (−2.1 to 1.6)</td>
<td>0.77</td>
</tr>
</tbody>
</table>
but no systemic toxicity due to the low level of free LA in the plasma. Another limitation of this study was that we did not verify catheter position by contrast injection. Therefore, we do not know the exact position of the catheter tip or if there was catheter migration during mobilization. Finally, we did not use a patient-controlled analgesia pump intravenously, which allows the correct assessment of analgesic requirement after operation since it would have been difficult for patients to handle two PCA devices, one for i.p. LA and the other for i.v. injection of opioids as rescue medication.

**Conclusions**

We found that the patient-controlled i.p. analgesia with LA resulted in statistically significant lower ketobemidone consumption compared with continuous infusion both during the initial postoperative phase and during 0–24 h after operation. Because of the large confidence intervals in ketobemidone consumption, the clinical relevance for this is uncertain. However, the lower ketobemidone consumption did translate into quicker return of GI function and earlier home-readiness. Future studies should focus on identifying the mechanism of analgesic effect of LA administered intermittently intraperitoneally.

**Authors’ contributions**

A.P.: contributed towards designing the study, data collection, statistical analysis, and writing the manuscript. F.F.: contributed towards data collection and critical comments in the writing of the manuscript. A.M.: contributed towards all statistical analysis and discussion on presentation of results. K.A.: contributed towards designing the study, data confirmation, and critical comments in the writing of the manuscript. A.G.: contributed towards designing, data interpretation, and writing of the manuscript.
Acknowledgements

We would like to thank the personnel in the operating theatres and those in the postoperative and gynaecological wards for their help and attention during the various phases of this study. Special thanks to Ingegård Wilhelmsson for her help with the data collection and with patient recruitment.

Declaration of interest

None declared.

Funding

This study was supported partly by funds obtained from the Research Committee, Örebro County Council, Örebro, Sweden.

References