Does the opioid-sparing effect of rectal diclofenac following total abdominal hysterectomy benefit the patient?

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Background. The aim of this prospective, double-blind, randomized, placebo-controlled clinical trial was to investigate the opioid-sparing effects of rectal diclofenac following total abdominal hysterectomy.

Methods. Forty ASA I–II patients, aged 20–60 yr, were randomized to receive identical-looking suppositories of either diclofenac 75 mg or placebo, twice daily. All patients were given a standardized anaesthetic, with intravenous morphine via a patient-controlled analgesia device and either diclofenac or placebo for postoperative analgesia.

Results. The median 24 h morphine consumption (interquartile range) was significantly higher ($P=0.02$) in the placebo group [59 (45–85) mg] than in the diclofenac group [31 (14–65) mg]. In comparison with the placebo group, there were significant reductions in total pain score in the diclofenac group at rest ($P=0.04$) and on movement ($P<0.01$). Total (SD) sedation score was significantly lower ($P=0.04$) in the diclofenac group [90 (73) mm] than in the placebo group [148 (89) mm]. Total (interquartile range) nausea score was significantly lower ($P<0.01$) in the diclofenac group [14 (0–53) mm] than in the placebo group [64 (30–109) mm]. There was no significant difference between the two groups of patients in episodes of vomiting or number of rescue antiemetics.

Conclusions. Rectal diclofenac reduces morphine consumption, improves postoperative analgesia, and reduces the incidence of adverse effects such as sedation and nausea.

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Pain in the postoperative period is a critical factor that impedes recovery from surgery and anaesthesia. Despite the fact that total abdominal hysterectomy (TAH) is usually performed through a Pfannenstiel incision, patients still experience much abdominal pain during the first 24 h after surgery. At our institution, the current standard analgesic for this group of patients is intravenous morphine via a patient-controlled analgesia (PCA) device. The consumption of morphine is high, particularly in the initial postoperative period. Morphine can cause adverse effects such as sedation, nausea and vomiting. Other methods of analgesia that have morphine-sparing effects are therefore required so that postoperative morbidity can be minimized.

Diclofenac is a non-steroidal anti-inflammatory analgesic that may reduce morphine consumption after TAH. The aim of the study was to assess if decreased morphine consumption is associated with a reduction in sedation and nausea and vomiting, in addition to improved analgesia. Elimination of these adverse effects is important to facilitate recovery from surgery.

Methods and results

After obtaining local institutional Research Ethical Committee approval and informed patient consent, we studied 40 ASA I–II patients, aged 20–60 yr, scheduled for TAH. Patients were excluded if the hysterectomy was indicated for malignancy, or if there was a history of chronic pain, continuous usage of analgesic drugs, inability to tolerate diclofenac, or inability to use the PCA device.

All patients were given a standardized anaesthetic comprising propofol 2–4 ml kg$^{-1}$, a non-depolarizing
neuromuscular blocking drug, morphine 10 mg i.v. and prochlorperazine 12.5 mg i.m. Their lungs were ventilated with nitrous oxide and isoflurane in oxygen, via a tracheal tube. At the end of surgery, residual neuromuscular blockade was antagonized with neostigmine 2.5 mg with glycopyrrolate 500 µg.

Patients were allocated randomly to receive either diclofenac or placebo. Identical looking suppositories of diclofenac 75 mg and placebo were prepared by our pharmacy. Each patient was allocated to a numbered container holding four matching suppositories. The first suppository was given after induction of anaesthesia. Subsequently, suppositories of the same content were given on three occasions, at 12 hourly intervals.

In the postoperative period, assessments were made by a member of staff blinded to the treatment, on awakening of the patient and then at 8, 12 and 24 h. Sedation, nausea and pain at rest and on movement (deep inspiration) were assessed on linear analogue scales ranging from 0 mm for wide awake, no nausea, and no pain, to 100 mm for very drowsy, worst possible nausea, and worst pain imaginable. Patients who were too drowsy to assess themselves were scored as 100 mm for sedation and 0 mm for nausea by the observer. In addition, the number of instances of vomiting and the number of doses of rescue antiemetic were recorded. Morphine consumption was recorded by the PCA device.

We considered that in order to avoid the potential adverse effects of morphine, diclofenac should be able to reduce morphine consumption in the postoperative period by 50%; this reduction was considered clinically important because smaller reductions in morphine consumption have not been associated with improvements in the number of adverse effects. From a previous study on non-steroidal anti-inflammatory drugs, it was estimated that to have an 80% chance of detecting a reduction in morphine consumption from 38 mg to 19 mg in the first 24 h after surgery, 16 patients per group would be required.

Data were analysed in Excel 2000 and SPSS 9.5. To assess the cumulative adverse effects over the 24 h period, pain scores at rest and on movement, sedation scores, nausea scores, number of vomiting episodes, and number of antiemetic administrations were summed from the values taken on awakening, and at 8, 12 and 24 h. Data were assessed for normality using the Kolmogorov–Smirnov test. Data were analysed using the chi-squared test, t-test and Mann–Whitney test, as appropriate. P<0.05 was considered statistically significant.

Of 40 patients, six did not complete the study. In the diclofenac group, one patient had a midline incision and another patient withdrew herself from the study. In the placebo group, at least one suppository was omitted in two patients, one patient had insufficient pain relief, and haematemesis occurred in one patient.

There was no significant difference between the groups in weight and ASA status of the remaining patients. The median morphine consumption in the first 24 h and total pain scores at rest and on movement were significantly higher in the placebo group than in the diclofenac group. Although there were no significant differences between the groups in the number of vomiting episodes and number of doses of rescue antiemetics in the first 24 h after surgery, there were smaller scores for total sedation and total nausea in the diclofenac group (Table 1).

**Table 1** Baseline characteristics and results. Age, weight, duration of surgery, total pain at rest and on movement, and sedation are expressed as mean (SD); 24 h morphine consumption, total nausea, total vomiting episodes, and total antiemetic administrations are expressed as median (interquartile range); ns, not significant.

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=16)</th>
<th>Diclofenac (n=18)</th>
<th>P</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>44 (00–00)</td>
<td>46 (00–00)</td>
<td>ns</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74 (17)</td>
<td>71 (8)</td>
<td>ns</td>
</tr>
<tr>
<td>ASA III</td>
<td>8/9</td>
<td>12/6</td>
<td>ns</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>65 (19)</td>
<td>75 (21)</td>
<td>ns</td>
</tr>
<tr>
<td>24 h morphine consumption (mg)</td>
<td>59 (45–85)</td>
<td>31 (14–65)</td>
<td>0.02</td>
</tr>
<tr>
<td>Total pain at rest (mm)</td>
<td>132 (55)</td>
<td>85 (72)</td>
<td>0.04</td>
</tr>
<tr>
<td>Total pain on movement (mm)</td>
<td>213 (76)</td>
<td>130 (94)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total sedation (mm)</td>
<td>148 (89)</td>
<td>90 (73)</td>
<td>0.04</td>
</tr>
<tr>
<td>Total nausea (mm)</td>
<td>64 (30–109)</td>
<td>14 (0–53)</td>
<td>&lt;0.01</td>
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<tr>
<td>Total vomiting episodes</td>
<td>0 (0–0)</td>
<td>0 (0–1)</td>
<td>ns</td>
</tr>
<tr>
<td>Total antiemetic adm</td>
<td>1 (0–2)</td>
<td>1 (0–1)</td>
<td>ns</td>
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</tbody>
</table>

**Comment**

We have found that rectal diclofenac was associated with significant 24 h morphine-sparing effects in comparison with placebo. In addition, total pain, sedation and nausea scores were significantly lower in the diclofenac group than in the placebo group. However, there was no significant difference between the two groups in vomiting or consumption of rescue antiemetic.

The morphine-sparing effects of diclofenac in our study concur with the findings of other studies. However, although previous studies have demonstrated that diclofenac had morphine-sparing effects, this was not associated with a reduction in sedation and nausea. This inability to detect a significant difference may have been related to the categorical scoring system used to measure sedation and nausea, in contrast, we assessed sedation and nausea using linear analogue scales.

Our results concur well with another study in which ketorolac 30 mg i.v. reduced both morphine consumption and sedation on the first postoperative evening. In this study, assessments were also made using a standardized linear analogue scale.

Tenoxicam is another non-specific cyclo-oxygenase inhibitor that is given intravenously. In a clinical trial involving 45 patients undergoing TAH, however, tenoxicam 20 mg or 40 mg i.v. was not found to produce a significant reduction in fentanyl consumption via PCA, pain scores or side-effects such as nausea.
We conclude that diclofenac as prescribed in our study can be recommended, for it provides morphine-sparing analgesia and improves postoperative adverse effects such as sedation and nausea. These are important considerations in facilitating recovery from surgery and anaesthesia.

References