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Preoperative epidural fentanyl reduces postoperative pain after upper abdominal surgery

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Abstract
Forty patients, American Society of Anesthesiology (ASA) physical status 1–2, undergoing subtotal gastrectomy were enrolled in this study. The patients were allocated to two groups with or (group P) and without (group C) preoperative epidural fentanyl 100 μg. Postoperatively, all patients received continuous infusion of the study solution, containing fentanyl 30 μg·ml^{-1} and 2 mg/ml bupivacaine, at a rate of 0.7 ml·h^{-1} for 72 h. The scores on the Prince Henry Hospital self-assessed pain scale (PHPS) were recorded at 0, 4, 12, 24, 48, and 72 h after the surgery. We compared the total rescue doses of analgesics during each period of 24 h until 72 h postoperatively. Although the total rescue doses of analgesics were not different between the groups, the median PHPS score was lower in group P than in group C, except at 0 h after the surgery. Preoperative epidural fentanyl 100 μg may increase the analgesic potency of postoperative epidural low-dose infusion of bupivacaine with fentanyl.

Key words Postoperative analgesia · Epidural analgesia · Bupivacaine · Fentanyl

The combined epidural infusion of a local anesthetic and an opioid is widely used for postoperative pain relief, and has proven effective. However, the ideal combination of opioid and local anesthetic, and the ideal infusion rate, are not known [1]. Thomson et al. [2] reported that fentanyl, which is highly soluble in lipids, works well at low concentrations with higher infusion rates. However, the rate of spread of analgesic solutions in the epidural space is very variable. Moreover, because fentanyl may have a segmental effect when the epidural catheter tip is positioned at the level of the surgical field, a smaller volume of infused anesthetic would probably be needed to achieve the same analgesic effect as when a larger volume is infused at a distant level [3,4]. In addition, the presurgical administration of analgesics is also thought to be effective for postoperative pain relief [5], with preoperative epidural morphine being shown to be effective for postoperative pain relief after gastrectomy [6]. We therefore speculated that the preoperative epidural administration of fentanyl could reduce the need for additional postoperative pain relief after gastrectomy when patients were being given a low-rate infusion of epidural fentanyl and bupivacaine postoperatively.

The aim of this study was to evaluate the postoperative reduction in pain and the analgesic-sparing effect of preoperative epidural fentanyl, compared with a sham epidural control, when a low-rate infusion of epidural bupivacaine with fentanyl was being given postoperatively.

After institutional review board approval and written informed consent was obtained, we studied 40 patients American Society of Anesthesiologists (ASA) physical status 1 or 2 undergoing elective subtotal gastrectomy. The patients were randomly divided into two groups: One group (group P) received epidural fentanyl immediately before their skin incision, whereas the other group (group C) received epidural saline before the incision. Patients were excluded from the study if the procedure was converted to total gastrectomy, or if cholecystectomy was added.

All patients received hydroxyzine (25–50 mg) and atropine sulfate (0.5 mg) as premedication, given intramuscularly 30 min before the operation. In the operating room, an epidural catheter was inserted at the thoracic 8–9 intervertebral space, and placement was confirmed by the epidural injection of a test dose of 3 ml of 1.5% mepivacaine. The group P patients then received 100 μg fentanyl in 10 ml of saline, whereas the group C patients received 10 ml of saline alone. General anesthesia was induced with intravenous thiopental

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(3–5 mg·kg^{-1}) followed by vecuronium (0.15 mg·kg^{-1}). Anesthesia was maintained with 50%–70% nitrous oxide in oxygen, vecuronium, and 0.5%–1.0% sevoflurane. All patients were ventilated mechanically. An anesthesia gas monitor (Datex-Ohmeda, Helsinki, Finland) monitored endtidal sevoflurane and CO_2. Analgesia was maintained with 4–6 ml of 1.5% epidural mepivacaine every 50–70 min.

Just after the end of the operation, we started the continuous epidural infusion of a solution containing fentanyl 30 μg·ml^{-1} and 2 mg·ml^{-1} bupivacaine at 0.7 ml·h^{-1}.

Postoperatively, patients were transferred to the intensive care unit. Trained nurses in the intensive care unit evaluated the patients. The patients were asked to assess the severity of their wound pain, using the Prince Henry Hospital self-assessed pain scale (PHPS), at 0, 4, 12, 24, 48, and 72 h after surgery [7]. As a first extra analgesic, pentazocine (15 mg) was administered intramuscularly; as a second, 4 ml of 0.25% bupivacaine was given epidurally; as a third, 50 mg diclofenac was given rectally. Each was given on patient demand and on a PHPS score of more than 3. On one day, we used the supplementary analgesics in the order mentioned above. We then compared the total analgesics given during each 24-h period and recorded any adverse effects.

The patients' demographic data values were expressed as means ± SD, and were analyzed using Student's *t*-test. PHPS and analgesic use in groups P and C were compared using the Mann-Whitney *U*-test. The incidence of side effects was compared by the χ^2 and Fisher's exact probability tests. A P value of less than 0.05 was considered statistically significant.

All patients underwent anesthesia and surgery uneventfully. Ten patients (group P, n = 8; group C, n = 2) were excluded due to conversion to total gastrectomy or the adding of cholecystectomy. There were no significant differences in age, height, or sex between the groups. There were no differences in the incidence of nausea, vomiting, or pruritus between the groups. No patients developed respiratory depression or hypotension. The frequency of additional analgesic use was highest during the first 24 h in both groups, but did not differ between the groups (Table 1). With the exception of immediately after the surgery, the median PHPS scores were higher in group C than in group P (Fig. 1). The median score at 4 h after the surgery in group C reached 2; however, that in group P was maintained at 0.

This study examined the effect of preoperative epidural fentanyl on the postoperative analgesia requirement following subtotal gastrectomy. Our data verified that the preoperative epidural administration of fentanyl could be effective for postoperative pain relief after gastrectomy. This was shown by the higher PHPS score in group C than in group P.

Table 1. Patients' characteristics

	Group P	Group C
n	12	18
Sex (male/female)	6/6	13/5
Age (years)	63.3 ± 13.3	66.8 ± 9.4
Height (cm)	158.3 ± 11.6	156.5 ± 7.6
Weight (kg)	58.2 ± 15.5	51.0 ± 10.0
Surgery duration (min)	209.3 ± 64.3	230.8 ± 46.0
Side effects		
Nausea/Vomiting	1	3
Pruritus	0	1
Respiratory depression	0	0
Hypotension	0	0
Frequency of analgesic use		
POD 1	3 (1–8)	3 (0–6)
POD 2	2 (0–6)	2 (0–6)
POD 3	1.5 (0–5)	2 (0–5)

Data values are expressed as means ± SD or number, median (ranges). There were no significant differences between the two groups

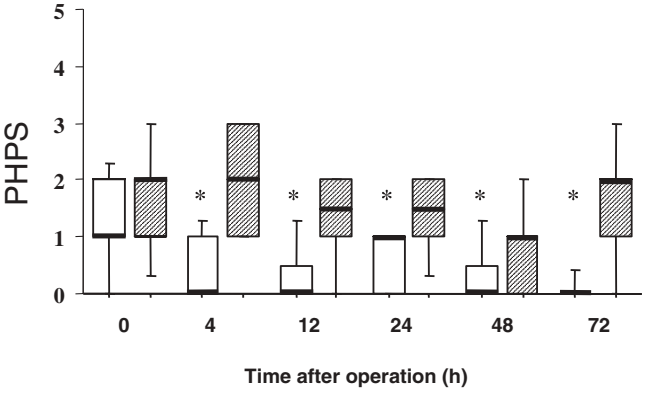

Fig. 1. Pain scores assessed by Prince Henry Hospital pain scale (*PHPS*). The *boxes* are interquartile ranges; *error bars* are 10th and 90th percentiles. The *horizontal solid lines within the boxes* refer to the median values. *(P < 0.05) Significantly different from *group C* (controls; *cross-hatched bars*). *Group P*, preoperative epidural fentanyl; *white bars*

Different groups have reported that a combination of local anesthetic and opioid gives excellent analgesia [8,9]. Moreover, many workers have shown the efficacy and safety of combined bupivacaine/fentanyl epidural infusion [8,10–12]. Because of its high lipid solubility, fentanyl produces a rapid onset of analgesia, less late respiratory depression, and a more segmental analgesic effect compared to that achieved with morphine. Thomson et al. [2] reported that lower concentrations of fentanyl could be beneficial at higher infusion rates. However, in many articles the reported postoperative infusion rates exceeded 2 ml·h^{-1} [13,14]. In contrast to these reports, we tried to show that preoperative epidural fentanyl enhanced the efficacy of a low infusion rate

given postoperatively. Although the median frequency of rescue analgesic was more than 1 in our study, this low infusion rate produced better analgesia following the preoperative administration of fentanyl than the analgesia in the control group, without an increase in the frequency of side effects.

For the reduction of postoperative pain, there have been many reports of the prophylactic use of analgesics before skin incision. Rockemann et al. [15] reported that the preoperative application of a balanced analgesia regimen reduced the postoperative consumption of analgesics. They reported that the preoperative application of a balanced analgesia regimen, including epidural morphine, showed a trend toward lower morphine requirement compared to the intraoperative application of a balanced analgesia regimen. Katz et al. [5] suggested that a standard treatment control group is important in studies of preemptive analgesia. In contrast to the findings of Rockemann et al. [15], our study did not show a reduced need for additional analgesics, but it did show a lesser amount of pain overall. Because we used epidural mepivacaine for both groups, even in the control group, intraoperative nociception and central sensitization were partially prevented. The differences in the degree of postoperative pain reduction by preoperative analgesics between the study of ours and Rockemanns' may have been due to the differing degrees of afferent blockade.

In our study, bupivacaine 0.2% and fentanyl 30 μg·ml^{-1} did not cause hypotension or respiratory depression, whereas, in contrast, an infusion rate of 4 ml·h^{-1} of these agents has been reported to produce hypotension [16]. This supports our view that a high infusion rate produces more hypotension than a low infusion rate.

In conclusion, preoperative epidural fentanyl may improve the pain relief achieved by a postoperative low-dose epidural infusion of bupivacaine with fentanyl after gastrectomy.

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