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Comparison of bupivacaine and fentanyl as an adjuvant of epidural morphine for postoperative analgesia

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Abstract: We conducted a retrospective study to determine whether bupivacaine or fentanyl is a better adjuvant to epidural morphine for postoperative analgesia using 108 patients. Following epidural lidocaine anesthesia with or without light general anesthesia for major gynecological surgeries, 59 patients received epidural morphine (EPM) 2 mg (group M), 21 patients received morphine 2 mg plus 0.25% plain bupivacaine 6–10 ml epidurally (group B), and 28 patients received morphine 2 mg plus fentanyl 100 μg epidurally (group F). The analgesic interval, defined as the duration from EPM injection to the first request of analgesics for incisional pain, was significantly longer in group F than in group M (29 ± 11 *vs* 19 ± 17 h, $P < 0.05$), but similar to group B (22 ± 14 h). Group F patients required the least amount of analgesics for incisional pain of the three groups during the first 24 h postoperatively ($P < 0.01$). The incidence of adverse effects was similar among all three groups. In conclusion, fentanyl appears to be a better adjuvant to epidural morphine than bupivacaine.

Key words: epidural, morphine, bupivacaine fentanyl, postoperative analgesia

Introduction

Epidural morphine (EPM) is used increasingly for postoperative pain relief. However, one of the disadvantages of EPM is its slow onset of analgesia [1]. The latency of onset is reported to be 20–60 min, and the peak analgesic effect is 1–3 h after administration [1–3]. Recently we reported that, within the first 4 h postoperatively, 20% of patients who were given EPM 4 mg during major gynecological surgeries under epidural lidocaine requested analgesics for incisional pain. In contrast, epidural fentanyl 100 μg added to EPM immediately produced analgesia to all the patients in the postoperative period lasting for 17 h [4]. We speculated that fentanyl would provide analgesia during morphine's latency period. Therefore, the results would have been different if a longer-acting local anesthetic had been used.

The purpose of the present retrospective study was to determine whether bupivacaine or fentanyl is a better adjuvant to EPM with respect to postoperative analgesic use and with fewer incidence of undesirable adverse effects.

Materials and methods

The medical records of patients who received EPM during abdominal hysterectomy, oophorectomy, or both at the University of Tsukuba Hospital between January, 1990 and February, 1992 were reviewed. Those who were diabetic or had neurological disorders, those who received i.v. analgesic or droperidol intraoperatively, and those whose sensory analgesia to pin-prick was not recorded at the end of surgery were excluded from the study.

All the patients were premedicated with diazepam 5–10 mg and roxatidine acetate 75 mg p.o. 90 min before induction of anesthesia. After insertion of an epidural catheter at the L2–3 or L3–4 interspace, surgical anesthesia was obtained with epidural injection of 1.5% or 2% lidocaine with a 1:200 000 epinephrine solution. Sensory analgesia to pin-prick was ascertained at or above T4 bilaterally before skin incisions. For those who had light general anesthesia in addition to epidural lidocaine, thiamylal 5–6 mg/kg for induction, and vecuronium 0.1–0.2 mg/kg for endotracheal intubation were administered via i.v. They were then connected to a mechanical ventilator, and anesthesia was maintained with nitrous oxide, oxygen ($FiO_2 = 0.33–0.5$) and isoflurane (0.4%–1.0%). Some patients without general

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anesthesia received diazepam 5–10 mg or midazolam 2–10 mg i.v. Incremental doses of epidural lidocaine were given at the discretion of attending anesthesiologists.

Patients were retrospectively divided into three groups depending on the drug(s) given epidurally in addition to lidocaine. Patients who received preservative-free morphine hydrochloride 2 mg diluted in 10 ml normal saline through the epidural catheter approximately 1 h before estimated completion of the surgery comprised group M. Patients who received, in addition to EPM 2 mg as described above, 0.25% plain bupivacaine 6–10 ml within 15 min before completion of the surgery comprised group B. Patients who received, in addition to EPM 2 mg, fentanyl 100 μg diluted in 10 ml normal saline [5] within 30 min before completion of the surgery comprised group F. Residual muscle relaxation was reversed with atropine 0.02 mg/kg and neostigmine 0.05 mg/kg i.v. All the patients returned to their rooms without endotracheal tubes in place. Analgesics were given i.m. on patients' requests by nurses within 10 min of their requests. When satisfactory pain relief was not obtained within the next 30 min, the same regimen was repeated. Equipotent dose conversions were made as follows: morphine 5 mg = buprenorphine 0.2 mg = pentazocine 15 mg [6].

During the first 48 h postoperatively, respiratory rate (RR) was monitored every 15 min for the first 2 h, and then every 3 h during the next 46 h. Those who had RR less than 10 were defined as having respiratory depression. Those unresponsive to noxious stimulus were defined as being sedated.

The following variables were compared: demographic data, ASA physical status, duration of surgery, estimated blood loss, interval from EPM injection to the end of surgery, intraoperative lidocaine dose, analgesic interval defined as the time interval from EPM injection to the first request of analgesic for incisional pain, quantity of analgesics within the first 24 h postoperatively, incidence of adverse effects (nausea and/or vomiting, pruritus, and respiratory depression requiring therapy) within the first 48 h postoperatively.

For statistical analyses, analysis of variance (ANOVA) was used to compare patients' demographic data, intraoperative lidocaine dose, duration of surgery, estimated blood loss, analgesic interval, and number of analgesics within the first 24 h. Chi-square test and Fisher's exact probability test were used to compare ASA physical status, types of surgery, proportion of patients who required analgesics at a given time after the surgery, and the incidence of adverse effects. All values were expressed as mean ± SD. A P value less than 0.05 was considered statistically significant.

Results

The three study groups were demographically comparable (Table 1). Patterns of postoperative analgesic use in the three groups are shown in Fig. 1. The analgesic interval was significantly longer in group F than in group M (Table 2, $P < 0.05$), but similar to group B. Analgesic use in the first 24 h in group F was significantly less than in groups M and B (Table 2, $P < 0.01$). Types and durations of surgery, estimated blood loss, intervals from EPM injection to the end of surgery, and intraoperative lidocaine doses were not significantly different.

There were no significant differences between groups with respect to the incidence of adverse effects (nausea or vomiting/pruritus that required therapy in groups M, B, and F; 20.3%/8.5%, 14.3%/9.5%, and 14.3%/21.4%. None developed sedation). A 42-year-old, ASA class I patient in group F developed respiratory depression 70 min after epidural fentanyl injection. Her RR was 6, and $Paco_2$ was 53 mmHg with concomitant end-tidal isoflurane concentration being 0.1%. Incremental naloxone i.v. up to 200 μg improved respiration and the level of consciousness. Urinary retention was not assessed because all the patients had indwelling urinary catheters.

We also divided the patients into two groups based on the anesthetic technique (with *s* without general anes-

Table 1. Demographic data and intraoperative lidocaine dose

	Group M	Group B	Group F
Number of patients	59	21	28
Age (years)	43 ± 11	43 ± 9	46 ± 11
Body weight (kg)	53 ± 8	55 ± 8	51 ± 7
Height (cm)	154 ± 6	154 ± 6	155 ± 5
ASA I/II (%)	60/40	63/37	59/41
Intraoperative lidocaine (mg/kg)	12.2 ± 2.3	13.0 ± 1.9	12.1 ± 2.5

Mean ± SD.
No significant differences were found among the 3 groups.

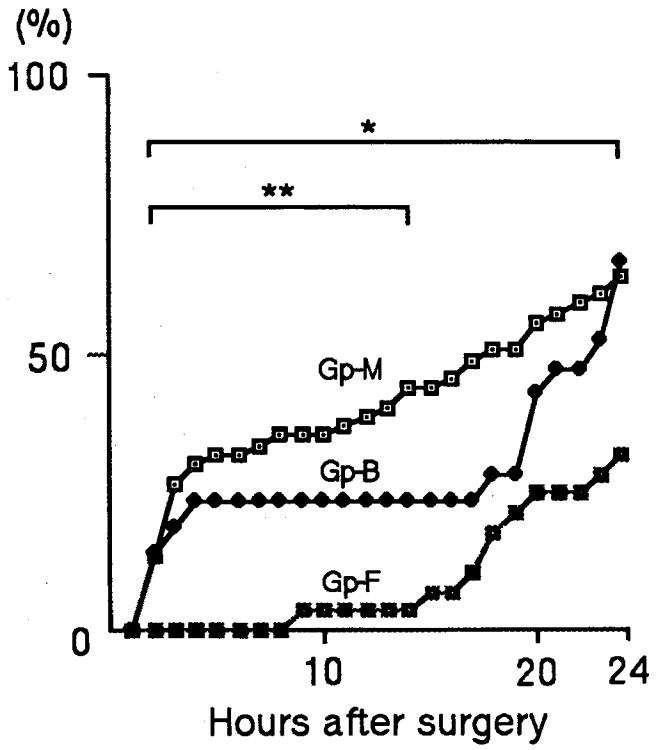

Fig. 1. Cumulative percentage of patients requiring supplemental analgesics as a function of time after surgery. A significantly smaller percentage of group F patients required analgesics than group M between 2 and 24 h, and group B between 2 and 13 h. *$P < 0.05$, group F *vs* group M; **$P < 0.05$, group F *vs* group B

thesia) and the following variables were compared: patients' demographic data, ASA physical status, analgesic interval, quantity of analgesics within the first 24 h postoperatively, and incidence of adverse effects. We found no significant differences between groups B and F with respect to the above variables.

Discussion

Smaller analgesic requirement in the early postoperative period as well as throughout the study period in group F suggests clinical usefulness of narcotic combination regimen. The synergistic interaction of morphine and fentanyl was first studied in rats, and a remarkable prolongation of antinociceptive action was observed [7]. This potentiation was not observed with epidural morphine and a local anesthetic combination. The present observation is also in agreement with a previous clinical study by Naulty et al. who found that the addition of sufentanil, similarly highly lipophilic as fentanyl, to EPM produced a prolonged duration and more profound analgesia than EPM alone [8].

Addition of an opioid of high lipid solubility to EPM reportedly provides analgesia during the delayed onset of EPM, decreases subsequent analgesic use, provides profound analgesia in the early postoperative period, and thus prevents postoperative pulmonary complications [4,8–11]. Our previous report demonstrated the potential desirability of such a combination where morphine 4 mg and fentanyl 100 μg were combined [4]. The present study, using morphine 2 mg combined with the same dose of fentanyl favorably resulted in a similar pattern of postoperative analgesic use without increasing the incidence of adverse effects compared with EPM alone.

It is not clear from our results what the predisposing factors of respiratory depression following epidural combination of morphine and fentanyl may be. Development of respiratory depression was reported following epidural fentanyl alone [12], epidural fentanyl-morphine combination [4], and intrathecal fentanyl-morphine combination [13]. Of note, respiratory depression occurred in each case within 100 min of neuraxial administration of fentanyl. Ahuja and Strunin studied the effect of prior administration of parenteral morphine in addition to epidural fentanyl, and found a consistently lower respiratory rate and significantly higher end-tidal CO_2 than epidural fentanyl alone [14]. We cannot exclude the possibility that circulating morphine, and rostrally migrating fentanyl as a passive flow of CSF, may synergistically result in respiratory depression of early onset. It is our view, therefore, that respiration should be closely monitored within the first 2 h of administration whenever epidural combination of morphine and fentanyl is used.

In conclusion, the combined use of EPM and fentanyl provided better analgesia than the combination of EPM

Table 2. Postoperative analgesic use

	Group M	Group B	Group F
Analgesic interval[a] (h)	19 ± 17*	22 ± 14	29 ± 11
Number of supplemental analgesics within 24 h	1.1 ± 1.0**	0.9 ± 0.9**	0.3 ± 0.5

Mean ± SD.
* $P < 0.05$ *vs* group F, ** $P < 0.01$ *vs* group F.
[a] For those who did not require any analgesics within the first 48 h postoperatively, the analgesic interval was defined to be 48 h.

and bupivacaine. The optimal dose combination of EPM and fentanyl remains to be determined.

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