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The effect of epidural sufentanil in ropivacaine on urinary retention in patients undergoing gastrectomy

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Background. Although epidural opioids have excellent analgesic property, their side-effects limit its use in patient-controlled epidural analgesia (PCEA). This study was designed to compare side-effects of epidural sufentanil in ropivacaine with that of morphine in ropivacaine focusing on lower urinary tract function after major abdominal surgery.

Methods. In total 60 patients undergoing gastrectomy were randomly allocated to receive either sufentanil in ropivacaine (Group S, n=30) or morphine in ropivacaine (Group M, n=30) for their PCEA. Epidural catheter was inserted between the 7th and 8th thoracic spine. Visual analogue pain score and side-effects such as nausea, vomiting, pruritus, hypotension and urinary retention were evaluated during postoperative days (PODs) 1 and 2 in the postanaesthetic care unit.

Results. The incidence of serious to major micturition problem in Group S was lower than that in Group M (P<0.001). The incidence of pruritus, nausea and vomiting was also lower in Group S than in Group M on POD 1.

Conclusions. The lower incidence of major/serious micturition problem in patients receiving sufentanil in ropivacaine thoracic epidural analgesia suggests that continuation of urinary drainage may not be necessary from POD 1 onwards.

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Epidural administration of opioids mixed with a local anaesthetic has become popular in perioperative analgesia. However, the side-effects of opioids such as respiratory depression, itching, nausea, vomiting and urinary retention can be major problems. In particular, their effects on lower urinary tract function lead to routine bladder catheterization, which increases the risk of urinary tract infection.[1–3]

Recently, in healthy male volunteers, intrathecal opioids were reported to decrease bladder function by suppression of detrusor contractility, and the recovery of normal lower urinary tract function was significantly faster after intrathecal sufentanil than after morphine.[4] However, pathogenesis of postoperative urinary retention is multifactorial, and includes the use of drugs that affect urinary detrusor function, intraoperative damage to the pelvic autonomic nerve and stress-induced activation of inhibitory sympathetic reflexes.[5–7] In addition, local anaesthetic drugs are used for postoperative epidural analgesia to provide improved analgesia after major abdominal operations.

This study was designed to compare the side-effects of epidural sufentanil in ropivacaine with that of morphine in ropivacaine after a major abdominal surgery. We focused on lower urinary tract function, thereby, assessing the optimal duration of routine bladder catheterization in patients undergoing gastrectomy.

Materials and methods

After obtaining approval of the institutional Ethics Committee and written informed consent, 60 ASA I–II patients undergoing gastrectomy were recruited. Using sealed envelope system, the patients were randomly allocated to

one of the two groups to receive either sufentanil in ropivacaine (Group S, n=30) or morphine in ropivacaine (Group M, n=30) for the postoperative epidural analgesia. Before surgery, patients were instructed on the use of the patient-controlled epidural analgesia (PCEA) device and visual analogue scale (VAS) pain score. Patients and anaesthetists were blinded to the treatment group and an independent researcher prepared the study solution consisting of 275 ml mixture of ropivacaine 0.2%, and sufentanil 250 μg (0.9 μg ml^{-1}) in Group S or morphine 10 mg (36 μg ml^{-1}) in Group M.

Patients with known urological disease, spinal disease, coagulopathy and on any medication that might have influenced the sympathetic nervous system were excluded from this study. Patients who had refused neuraxial anaesthesia were also excluded. Patients who were to undergo surgery in the afternoon were excluded because the indwelling urinary catheter was to be removed in the morning of the first postoperative day (POD 1).

All the patients were premedicated with i.m. midazolam 2 mg and glycopyrrolate 0.2 mg. Before the induction of general anaesthesia, an epidural catheter was inserted between the 7th and 8th thoracic spine (T7–8) and the catheter was advanced 3 cm upwards. After a test dose of lidocaine 2%, 3 ml with epinephrine (1:200 000), lidocaine 2%, 5 ml was given via epidural route. General anaesthesia was induced with i.v. thiopental sodium (4 mg kg^{-1}), fentanyl (1.5 μg kg^{-1}), and rocuronium (0.8 mg kg^{-1}). No additional i.v. opioid agent was given after this. After induction of anaesthesia, indwelling urinary catheter was inserted. Anaesthesia was maintained with oxygen/air (50:50) and sevoflurane, and vecuronium was given for continued muscle relaxation. The end-tidal concentration of sevoflurane was adjusted to maintain arterial blood pressure within 20% of baseline values. Arterial blood pressure below 20% of baseline was treated with boluses of ephedrine. After induction of general anaesthesia, epidural analgesia was started using a silicone balloon infuser (Accufuser®, Woo Young Medical Co. Ltd, Korea) containing the study solution. The balloon pump infuser lasted for 2 days; it was set to 5 ml h^{-1} for continuous infusion and 0.5 ml for bolus dose with a 15 min lockout period. The tracheal tube was removed in the operating theatre at the end of surgery. In the postanaesthetic care unit (PACU), in addition to VAS pain score, patients were evaluated for the side-effects of epidural opioids such as nausea, vomiting, pruritus and the incidence of hypotension by an investigator blinded to group allocation of the patients. Motor block was evaluated using a previously described scale (1=no motor block, 2=knee blocked and mobility of ankle preserved, 3=mobility of ankle difficult, and 4=knee and ankle blocked) and the sensory block level was evaluated by response to a cold stimulus to the skin. Patients with VAS pain score higher than 5 were given i.m. meperidine 25 mg as rescue analgesia. In the morning of POD 1, indwelling urinary catheter was removed. A nurse who was blinded to the patient group recorded the incidence whenever a patient complained of nausea, vomiting, pruritus or micturition problem until POD 2. Motor block, sensory block and VAS pain scores at rest and during coughing were recorded in the morning of POD 1 and 2. Blood pressures were measured every 6 h until POD 2. To assess micturition problem, patients were to report the need to void, and their urine volume whether it was <200 or >700 ml. They were also to report lack of urge or feeling of incomplete micturition. If the patients were unable to void 6 h after the removal of the urinary catheter, the bladder was drained with in-and-out catheterization and urine volume was checked. Micturition problems were classified according to a previously used classification by Vercauteren and colleagues[8] (Table 1) and the bladder was drained with in-and-out or indwelling catheterization in patients with serious or major problem, respectively. Epidural catheter was removed after the silicone balloon infuser was empty.

In a previous study, Vercauteren and colleagues[8] have shown that low dose bupivacaine–sufentanil group reduced the grade of micturition problem to 1.0 (SD 1.0) compared with 1.9 (1.2) in the high dose bupivacaine–sufentanil group on POD 1. A sample size was calculated based on this effect, with α=0.05 and β=0.2. In total, 27 patients were required in each group in order to detect a statistically significant difference between the groups. A total of 30 patients were recruited in each group to compensate for loss of data during follow-up. As there was no withdrawal, the result of 30 patients were included in this study. Retrospective power calculation showed the power of this study to be 91%.

Statistical analyses were performed using the statistical package for social sciences statistical software (SPSS 10.0, SPSS Inc., Chicago, IL). Chi-square test, t-test, Mann–Whitney U-test and Fisher's exact test were used to compare variables between the groups where appropriate. Results are expressed as mean (SD) or number of patients. P-value <0.05 was considered statistically significant.

Table 1 Classification of micturition problems

Minor problems
(1) Urge to void with urine volume ⩾700 ml
(2) Report or observation (once) of either
(a) Feeling of incomplete micturition
(b) Difficult micturition but volumes >200 ml
(c) Too low volume of urine (<2 ml kg^{-1})
Serious problems
(3) No urge to void but producing volumes ⩾700 ml
(4) Repeated or combined observation of feeling of incomplete voiding, difficult urination (>200 ml), and/or too low volume
Major problems, requiring bladder catheterization
(5) Incontinence
(6) Globus and inability to urinate
(7) Impossibility to void 18 h after surgery or >6 h after previous micturition
(8) Unpleasant/painful feeling in the groin with inability to void
(9) Repeated and combined observation of feeling of incomplete voiding, difficult urination (>200 ml), and too low volume

Results

Patient characteristics and data from the perioperative periods are listed in Table 2. The duration of surgery, blood loss, urine output and amount of fluids infused between the two groups were comparable (Table 2). The level of the sensory block to cold stimulus ranged from T3–T6 to T10–L2. The ranges of the level of sensory block (upper and lower segments) were similar between the two groups. None of the patients had motor block (all were scale 1). The extension of sensory blockade was not checked because patients were unable to distinguish the level of cold sense during continuous infusion of study mixture. There were no significant differences in VAS pain scores at rest and during coughing between two groups throughout the study period (Table 3). The dose of study mixture infused was the same for all patients because the balloon infuser was removed when the container became empty, with an average time of 44.4 (5.4) h in Group M and 43.3 (6.6) h in Group S.

Side-effects of epidural opioids except micturition problems are listed in Table 3. Two patients in Group M and one in Group S were hypotensive in PACU. They were treated with ephedrine and discharged from PACU when the blood pressure was maintained near normal for over an hour. The blood pressure was stable in all patients in the ward. The incidence of pruritus was significantly higher in Group M than that in Group S on POD 1 ($P<0.05$). The incidence of nausea and vomiting was also significantly higher in Group M than in Group S on POD 1 ($P<0.05$). None of the patients had respiratory depression.

The number of patients with micturition problems is listed in Table 4. The number of patients with serious to major micturition problem in Group S was significantly less than that in Group M on POD 1 and POD 2 (all $P<0.001$). Throughout the study period, no patient in Group S had any serious or major micturition problem. On the other hand, 12 (40%) patients in Group M complained of serious micturition problem and one patient needed indwelling bladder catheterization because the patient produced <200 ml urine twice, complained of incomplete voiding sense and could not void for more than 6 h after previous micturition. No patient had urinary problems at 30 days follow-up.

Table 2 Patient characteristics and data from the perioperative period. Data are mean (range), mean (SD) or number of patients

	Group M (n=30)	Group S (n=30)
Sex (M/F)	17/13	15/15
Age (yr)	61 (52–78)	63 (58–75)
Ht (cm)	161.7 (10.0)	164.2 (9.0)
Wt (kg)	57.9 (11.1)	59.6 (11.2)
Amount of fluids during surgery		
Crystalloid (ml)	1780 (620)	1670 (970)
Colloids (ml)	530 (93)	493 (82)
Packed red blood cells (ml)	110 (50)	103 (90)
Blood loss during surgery (ml)	259 (83)	238 (92)
Urine output during surgery (ml)	277 (69)	318 (124)
Intraoperative ephedrine use (mg)	5.7 (5.1)	5.8 (5.8)
Duration of surgery (min)	146.0 (17.3)	151.7 (27.4)
Duration of anaesthesia (min)	173.0 (19.5)	176.7 (27.3)

Table 3 Postoperative visual analogue scale (VAS) pain score and side-effects in the postanaesthetic care unit (PACU), and on postoperative days (PODs) 1 and 2. Values are mean (SD) or the number of patients. The incidence of pruritus was significantly higher in Group M than in Group S on POD 1 (P=0.012). The incidence of nausea and vomiting (PONV) was also significantly higher in Group M group than in Group S on POD 1 (P=0.021)

	Group M (n=30)	Group S (n=30)
VAS-resting		
PACU	23.3 (10.9)	22.7 (9.8)
POD 1	16.7 (7.6)	17.3 (7.8)
POD 2	14.0 (5.0)	14.7 (6.8)
VAS-coughing		
POD 1	19.0 (7.6)	20.3 (8.1)
POD 2	15.3 (5.1)	16.0 (7.2)
Pruritus		
PACU	1	0
POD 1	8	1
POD 2	2	2
PONV		
PACU	0	0
POD 1	9	1
POD 2	2	0
Hypotension		
PACU	2	1
POD 1	0	0
POD 2	0	0

Discussion

The results of this prospective, randomized, double-blind study indicate that, during postoperative epidural analgesia, compared with epidural morphine, epidural sufentanil has a lower incidence of opioid-induced side-effects including micturition problems that may necessitate the bladder catheterization.

Studies on the effect of neuraxial morphine on lower urinary tract function have shown that intrathecal morphine suppresses bladder contraction.[4 9 10] However, the exact mechanism has not been elucidated. In 1983, Rawal and colleagues[10] reported that 2, 4 and 10 mg of epidural morphine decreased detrusor contractility with increased maximal bladder capacity, and that these effects were reversed with naloxone. Intravenous or intramuscular morphine had little effect on detrusor muscle. The authors

Table 4 Number of patients with micturition problems. The number of patients with serious to major micturition problems in Group S group was significantly less than that in Group M group on POD 1 and POD 2

	Group M (n=30)	Group S (n=30)	P-value
POD 1 none/minor/serious/major	6/11/12/1	26/4/0/0	<0.001
POD 2 none/minor/serious/major	10/19/0/1	27/3/0/0	<0.001

suggested the spinal action of morphine was because of the rapid onset of detrusor relaxation after epidural morphine administration. Regardless of the mechanism, urinary retention is one of the side-effects of epidural opioids.

The pharmacokinetics of an epidurally administered drug has been a subject of much discussion. The site of action of epidurally administered lipophilic opioids is under debate. Some studies report that epidurally administered lipophilic opioids such as alfentanil, sufentanil and fentanyl produce their effects mostly via systemic mechanism and little via spinal mechanism.[11–15] Bernards and colleagues[11] measured drug concentration in each compartment after epidural administration of different opioids and reported that in the epidural space, lipophilic drugs had negligible access to the spinal cord; thus had less bioavailability because of possible sequestration, and/or rapid vascular uptake from the epidural space. However, this does not indicate that the action of lipophilic opioids on the spinal cord is not the predominant one. Other studies on epidural fentanyl or sufentanil after thoracotomy report that thoracic epidural administration of lipophilic opioids show superior analgesic effect when compared with that in lumbar epidural space.[16–18] Hansdottir and colleagues[16 17 19] published a series of studies on epidural sufentanil infusion after thoracotomy. They demonstrated that concentrations of epidural sufentanil were higher in CSF than in plasma and that sufentanil was highly localized in CSF to the level of administration both after single bolus and infusion.[16 19] They also proved in a clinical study that after thoracotomy, epidural sufentanil analgesia was optimal when tailored to the site of nociceptive input and combined with bupivacaine.[17] These data support dermatomal restriction of lipophilic opioids, which allows reduction in the drug amount to be administered. In this study, epidural catheters were inserted at the T7–8 interspace, which corresponds to the surgical incision site but not associated with detrusor activity. Therefore, probably both systemic absorption and dermatomal restriction of epidural sufentanil caused the reduction in micturition problem during epidurally administered sufentanil.

The concentration of sufentanil used in this study (0.9 $\mu g\ ml^{-1}$) was based on other studies, in which the dose ranged from 0.5 to 1 $\mu g\ ml^{-1}$ for major abdominal surgical pain.[20–22] The equianalgesic concentration of epidural opioids used in this study was based on the recommended 50 $\mu g\ ml^{-1}$ for epidural morphine and 1–2 $\mu g\ ml^{-1}$ for epidural sufentanil to be continuously infused at a rate of 4–8 ml h^{-1}.[23]

In this study, the opioid was mixed with a local anaesthetic, ropivacaine, to reduce the incidence of opioid-related side-effects and to improve analgesia.[24–26] The effects of neuraxial local anaesthetics on bladder function are different from those of opioids. A complete absence of urge and detrusor contractility with spinal anaesthesia was reported up to recovery of sensation of pinprick in the S2–S3 dermatome, which contains most of the fibres concerned with the control of the bladder and urethral sphincters.[27] As the epidural block was administered at the thoracic level using segmental technique and the concentration of the ropivacaine was the same (0.2%) for both groups, this would not have influenced the result of this study.

Unlike epidural morphine, none of the patients who received epidural sufentanil had serious and/or major micturition problems on POD 1 in this study. This result suggests that urinary catheter inserted in the operating theatre could be removed in the morning of POD 1. This may have important clinical implications because routine catheterization beyond 24 h may increase the risk of subsequent urinary infection and voiding problems.[1 2 18] Furthermore, if recently introduced portable ultrasound scan is available, indwelling urinary catheter may be removed at the end of the surgery because the ultrasound is reported to measure bladder volume accurately.[28–30]

In conclusion, the low incidence of micturition problems in patients receiving sufentanil in continuous thoracic epidural analgesia suggests that routine bladder catheterization from POD 1 onwards may not be necessary.

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